Simultaneous Multiple Congenital Anomalies in a Young Male

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Congenital malformations associated with disorders of neuronal migration leading to seizure disorder in a young population are rarely seen. Here, we report, six congenital malformations simultaneously present in brain imaging in a young patient. A 35-year-old male presented with a history of seizure disorder since childhood presented in the clinic with on and off episodes of seizures. The seizures were right focal with secondary generalized tonic-clonic or generalized tonic-clonic type but he was not taking medications regularly. His peri-natal history was asymptomatic. There was no developmental delay in milestones. Furthermore, there was no significant family history. General, systemic, and neurological examinations were within normal limits. On investigations, his magnetic resonance imaging brain showed open lip schizencephaly, polymicrogyria, hetero-trophic grey matter in the left frontoparietal region, focal cortical dysplasia, and corpus callosum agenesis (Fig. 1a-e). He also had evidence of cerebrospinal fluid signal intensity cystic spaces in the posterior fossa directly communicating with the fourth ventricle, compressing the cerebellar hemispheres, and absence of vermis suggestive of Dandy-walker malformation (Figure 1f). Genetic analysis was not done in this patient. The patient earlier tried various antiepileptics, but his seizures finally got well controlled on tablet zonisamide 150 mg twice daily and tablet clonazepam 0.25 mg thrice daily. At present, the patient is working in the education department and doing well despite all these malformations. (Figure 1)

Various congenital malformations associated with seizure disorders are described [1-3]. Most of them are due to a direct result of faulty neuroblast migration [4]. During early gestation (8–15 weeks), most severe migratory defects occur, affecting events in the gross formation of the neural tube and cerebral vesicles. Later defects of neuronal migration can present as disorders of cortical lamination or gyration such as lissencephaly, pachygyria, and cerebellar dysplasias [5]. In our patient, six different congenital malformations were present with the main presentation of generalized tonic-clonic seizures, and seizures were adequately controlled with anti-epileptic drugs. Therefore, congenital malformations, especially disorders of neuronal migration need to be identified as an important cause of seizure disorder. Medical management is effective despite multiple malformations.

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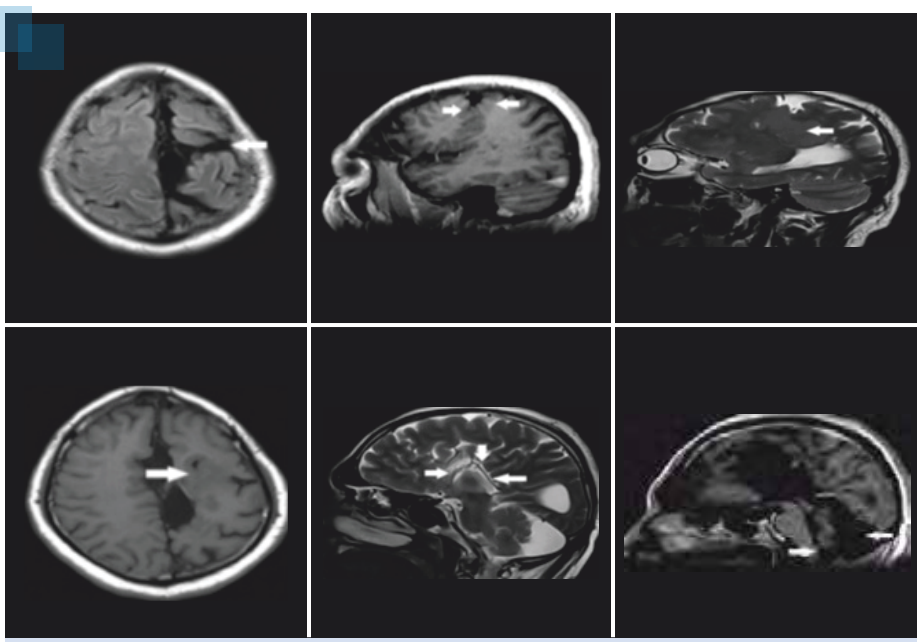

Figure 1: Multiple congenital abnormalities seen in MRI marked with white arrows. (a) Open lip schizencephaly, (b) polymicrogyria, (c) hetero-trophic grey matter in left fronto-parietal region, (d) focal cortical dysplasia, (e) corpus callosum agenesis, and (f) Dandy-walker malformation

Acute Stroke with Incidentally Detected Active Neurocysticercosis - Lessons Learned

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A 65 years old female, diagnosed case of diabetes mellitus, hypertension with history of paroxysmal episodes of loss of consciousness with sudden falls, up rolling of eyeballs with posturing of limbs, lasting for few minutes had presented with sudden onset weakness of right upper and lower limbs with inability to speak and comprehend commands for one day. On examination, she had global aphasia, right hemianopia, right facial palsy, right upper and lower limb power of 1/5. NIHSS was 20/42.

MRI was done which showed diffusion hyperintensity involving the right MCA cortical territory M2, M3, M4, M5, insula and internal capsule with MR ASPECTS OF 4/10. The MR angiogram had shown M3 occlusion on the left. In addition to the moderate sized infarct, there was evidence of multiple cystic lesions with central hyperintense scolex without any contrast enhancement consistent with the radiological diagnosis of neurocysticercosis (NCC) in the vesicular stage. CT head showed multiple calcified lesions which suggested calcified NCC. NCC serology was positive. (Figure 1)

As she had presented with stroke, she was started on antiplatelets and statins. NCC as a cause of stroke was considered. Points against NCC as a cause of stroke were

1. Infarct in a single vascular distribution- Inferior division of middle cerebral artery. Infarcts due to neurocysticercosis do not respect vascular territories and can be bilateral.
2. Presence of vascular risk factors- She was hypertensive, diabetic and during evaluation for etiology of stroke, she was found to have rheumatic heart disease and the Holter had shown evidence of paroxysmal atrial fibrillation.

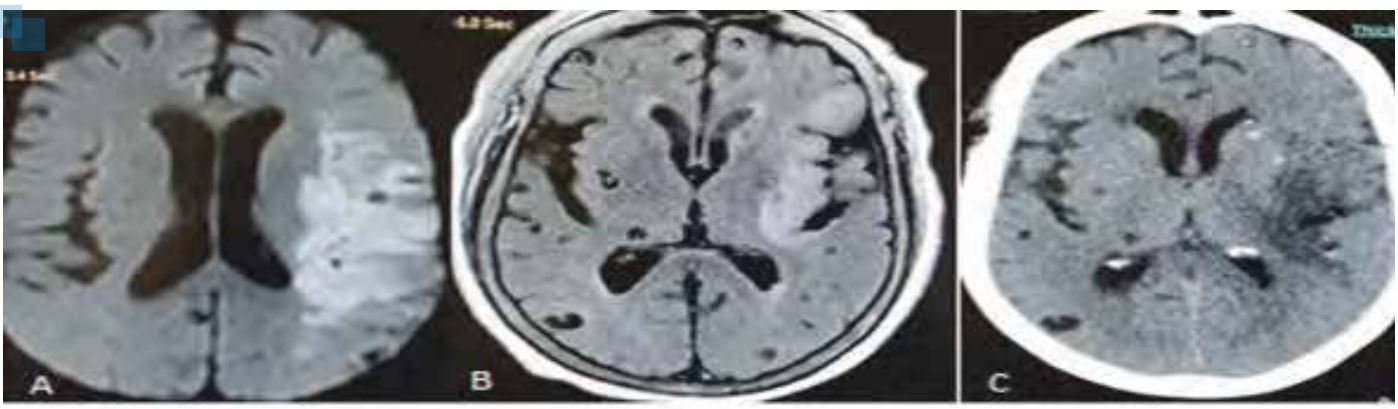
She was put on anticoagulation, anti-epileptics and was kept under observation for any worsening. As she had no edema around the cysts or features of raised intracranial pressure and no worsening of infarcts, treatment specific for NCC was withheld.

After 10 days of onset of stroke, she was started on steroids (0.1mg/kg of dexamethasone) and was started on albendazole (15mg/kg) and praziquantel (50mg/kg) after ruling out ocular and spinal involvement which was continued for 10 days. The treatment was completed successfully without any worsening of edema or sensorium.

She has been planned for repeat MRI after 6 months for confirmation of eradication.

Learning points

1. There are case reports of neurocysticercosis as a cause of stroke but there is paucity of data on treatment of incidentally detected neurocysticercosis in patients in whom imaging was done for stroke.
2. Patients can be started on treatment for NCC if there are infarcts in multiple territories but if infarct involves a single vascular territory and there are conventional vascular risk factors, it is better to treat stroke and wait for 7-10 days for infarct stabilization and then treatment for NCC can be given.



A.DWI MR sequence showing infarct involving Left MCA territory
B.FLAIR sequence showing multiple NCC cysts.
C. CT Head showing evolved infarct with multiple cysts in vesicular and calcified stages.

Figure 1

Fourth Ventricular Neurocysticercosis – An Interesting Case Report

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Introduction

Neurocysticercosis is one of the common helminthic infections of the central nervous system. Cysticercosis occurs when eggs from taenia soleum are ingested by humans to become dead end intermediate host. In intraventricular neurocysticercosis the larva reach the cerebral ventricles via the choroid plexus and causes symptoms by either obstructing the CSF flow-, ependymitis or both.

We report a case of intraventricular neurocysticercosis that illustrates the natural history, diagnosis and management.

Case Report

A 26-year-old female with no other comorbidities presented with holocranial headache of severe intensity associated with vomiting. Patient was evaluated with CT brain which showed no significant abnormality. Patient deteriorated in the following days and became drowsy. MRI brain was done which showed mild dilatation of the 4th ventricle and minimal leptomeningeal enhancement for which ATT was started.

CSF analysis was done which was normal. Repeat MRI done showed dilatation of the 4th ventricle with a possibility of cystic lesion and upstream dilatation of the lateral and third ventricles. The Patient underwent suboccipital craniotomy and excision of the 4th ventricular lesion. The histopathology of the lesion was consistent with neurocysticercosis. Post operatively patient was given antihelmintic medications and corticosteroids. he improved symptomatically. (Figure 1) (Figure 2)

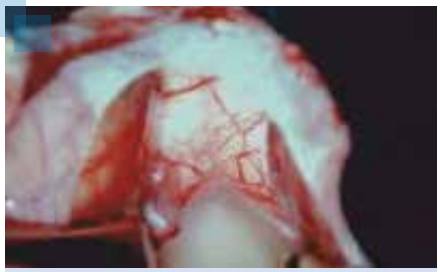

Figure 2

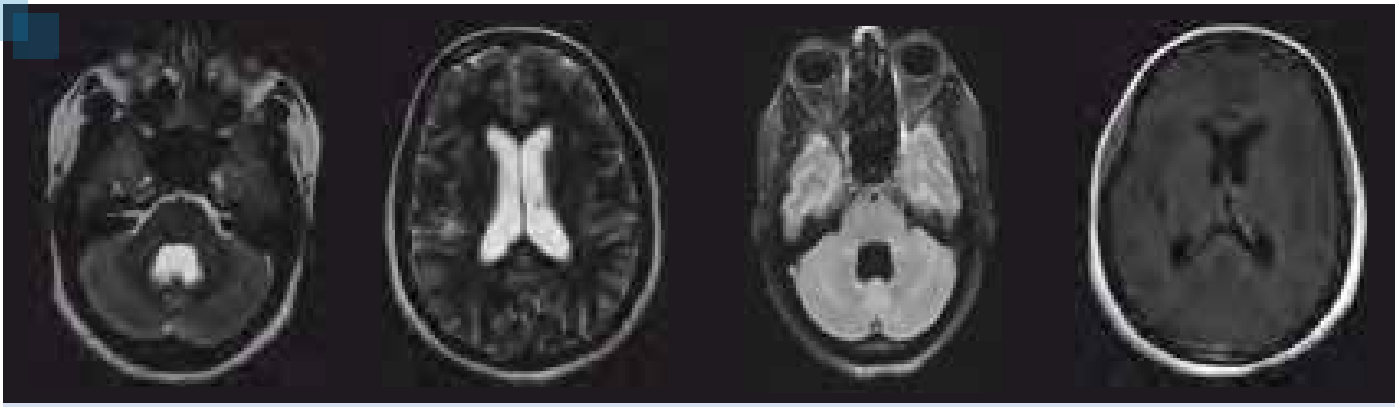

Figure 1

A Rare Case of Guillain Barre Syndrome Presenting with Stroke Like Onset with Predominant Facio-Brachial Paresis with Relatively Sparing Lower Limbs

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Guillain barre syndrome (GBS) is an acute immune mediated inflammatory demyelinating motor polyradiculoneuropathy characterised by ascending symmetrical limb weakness with areflexia with bilateralfacial weakness and may involve the respiratory muscles.

Cranial nerve palsies are frequent in GBS and among these patient's facial nerve palsy is the most common cranial nerve involved and is usually bilateral.

We present a case of GBS presenting like stroke1-3 and progressed bilaterally but predominantly had facio brachial paresis and relatively sparing the lower limbs.

Case Presentation

A 62-year-old diabetic and hypertensive female, presented with a six-hour history of sudden onset numbness of left half of the body with left sided facial weakness. On examination she had lower motor neurone type of left facial palsy, the left-hand grip showed mild weakness (around 90%), minimal gait ataxia, with preserved deep tendon reflexes and the plantares were down-going. A provisional diagnosis of stroke was made and MRI brain was done which did not show any acute infarct or haemorrhage. Post the MRI Brain a provisional diagnosis of left LMN facial with TIA was made After 36 hours of symptoms onset, facial weakness became bilateral, the hand grip was bilaterally weak (75%) but the power in the lower limbs was 5 /5. All the deep tendon reflexes were absent with plantars flexor. Urgent NCV of all the four limbs was done which was suggestive of severe motor demyelinating polyradiculo-neuropathy (prolonged distal latency, reduced CMAPS, decreased conduction velocity, f- waves were absent in bilateral upper limbs, bilateral h reflex was absent) s/oAIDP/GBS. IV immunoglobulin (IVIG) was given; (a total dose of 140 gm) over five days. The Patient did not deteriorate and gradually improved after the third day of IVIG. The CSF routine study was done, s/o albumino-cytological dissociation (total cell count-5/cm, proteins- 58.1 mg, glucose-72mg/dl with a, corresponding RBS of -120mg/dl). At the time of discharge, the- bilateral facial weakness was much better and bilateral hand grip was >90%. On follow up visit after 2 weeks, she had significantly improved with only mild bilateral facial paresis persisting.

Conclusion

The Present case is a very rare case on account of sudden onset of unilateral symptoms which progressed but predominantly involved bilateral facial, bilateral distal upper limbs while relatively sparing the lower limbs.

GBS presenting like stroke is very rare (1-3), with only few cases being reported till now. Further there is no case report that we could find where GBS presented with stroke like symptoms, predominantly affecting the facial and distal upper limbs and relatively sparing the lower limbs.

The clinician must have a high index of suspicion and be aware of the atypical presentations of Guillain Barre Syndrome so that treatment may be started without delay.

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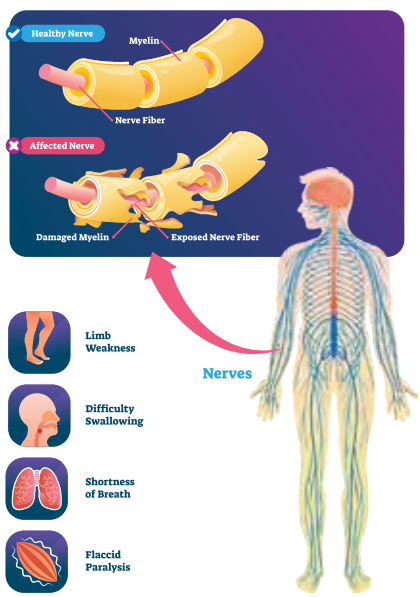

Unusual Case of Clivus & Pituitary Tuberculoma

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Presenting an unusual case of clivus & pituitary tuberculoma, which is not only a rare location for tuberculosis but the patient also experienced multiple problems after intervention which were managed. The patient is recovering well &has no neurological deficit.

Intracranial tuberculomas account for 0.15 to 4% of space occupying lesions, commonly located in the cerebral cortex and the cerebellum but have also been reported in the brainstem, thalamus, basal ganglia, CP angle and the ventricles. Tuberculosis of clivus & pituitary is uncommon and only very few cases are reported in literature.

Skull base & clivus as a primary site is unusual; only five cases have been reported in literature; with only two cases of tubercular involvement of the clivus and the pituitary gland having been reported.

A 21 years old female presented with 3 months history of headache, decreased vision in both eyes, amenorrhea and occasional difficulty in walking. Patient had GTCS a day prior to admission. On examination patient was conscious, oriented with no focal motor deficit. VN was 6/9 inn both eyes with no evidence of papilledema. MRI brain revealed T1 hypo and T2 hyperintense 22x18x16mm size lesion in the sellar & suprasellar region with ring enhancement and erosion of the sellar floor. There was T1 iso &T2 hypointense lesion involving the clivus dorsum sella and the post clinoid showing homogenous enhancement. Endoscopic endonasal decompression of the pituitary and the clivus mass was done on 31/5/2021. Post operatively the patient remained stable. Biopsy taken separately from the pituitary &; clivus mass was s/o necrotising granulomatous lesion s/o tuberculosis aetiology. Patient was put on ATT. on the third POD the patient became disoriented, drowsy, aphasic & had neck rigidity. Contrast MRI revealed generalized exudates with no evidence of HC or Infarcts. The patient continued to have altered sensorium. A lumbar puncture with CSF examination was done which was suggestive of Tubercular meningitis. The Patient developed sudden onset right UL weakness (Power 0/5)., Repeat CT on the seventh POD revealed a left thalamic infarct. The Patient continued to be febrile & had hypotension and hypernatremia, which were managed. Gradually the patient started improving and became fully conscious, with improving power in right UL. The Patient continued to improve and was discharged on the 16th POD. In follow up, OPD patient had deranged LFT for which antitubercular medications were modified. Patient gradually improved and after one year of follow up, the lesions have resolved and the patient has no neurological deficit.

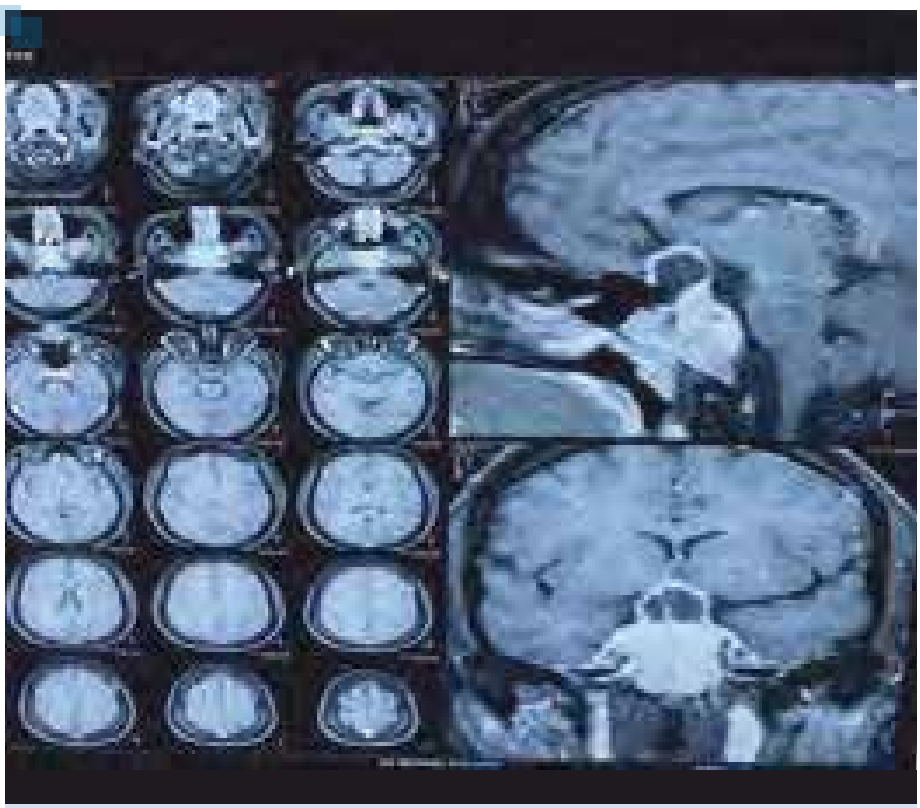

Figure 1: T1 hypo and T2 hyperintense 22x18x16mm size lesion in the sellar & suprasellar region with ring enhancement and erosion of the sellar floor. There was T1 iso &T2 hypointense lesion involving the clivus dorsum sella and the post clinoid showing homogenous enhancement

'The Clue is in the Origin, Watson!' The Tale of a DBS Surgery for Misdiagnosed Parkinson's Disease

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A 78-year-old male earlier diagnosed with Parkinson's Disease, reported for the Re-programming of bilateral STN-DBS implant after having poor relief of his PD symptoms. Re-programming of the DBS IPG offered no significant change in the UPDRS-III, however with worsening Dysarthria. The implanted electrodes were on target as visualised using Lead-DBS-V2 pipeline [Figure1]. The patient had a history of a pseudo-RBD (REM sleep Behavioural Disorders) for 9-years, U/L rest + action tremor in left-upper- limb and bradykinesia for 7-years and a dysarthria for 3-years. According to the patient, tablet Levodopa + Carbidopa offered 10-15% of relief of PD symptoms and DBS offered no benefit. Patient denied any Micro/Macro-graphia, instead his handwriting had simply worsened. History revealed an early Erectile-Dysfunction and Restless Leg Syndrome. Considering the ethnic origin of the patient (Hindu-Aggarwal) and atypical presentation, gene testing was requested due to a suspicion of Spinocerebellar Ataxia-12 (SCA-12), which is common in Hindu-Aggarwal population. SCA-12 is due to CAG repeats in the PPP2R2B gene on chromosome 5q32. The genetic test revealed 42 CAG repeats in PPP2R2B region which fell into the grey zone (32-51 CAG repeats). Thus, it was concluded that the patient was a case of SCA-12 consistent with his Hindu-Aggarwal origin, therefore DBS surgery offered no relief. Due to the initial presentation with extrapyramidal symptoms, Pseudo-RBD and subtle response to Levodopa, SCA 12 is often confused as PD. The table summarizes the clinical differences between PD and SCA-12 [Table]. Management: Levodopa-Carbidopa were tapered off. Previously DBS Contacts C2 and C8 were used to stimulate STN. As SCA-12 responds to cZi (Caudal Zona Incerta) stimulation, we used the Dorsal- most contacts [Figure2] to stimulate the cZi leading to a significant reduction in the tremor, reduction of bradykinesia, and improvement of gait. Low frequency stimulation (90Hz) was used in order to minimise the dysarthria.

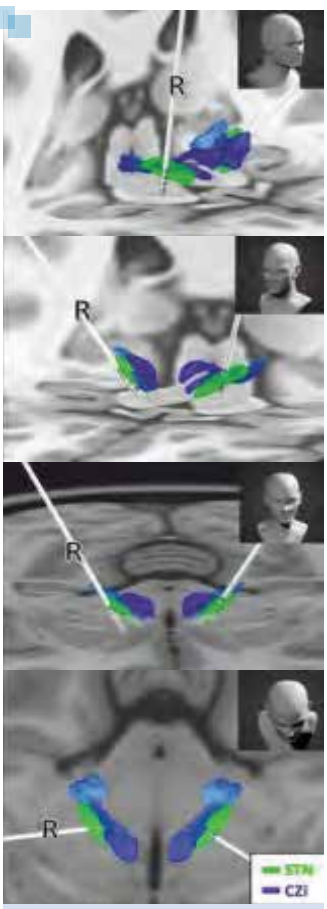

Figure 1: Placement of electrodes of STN DBS

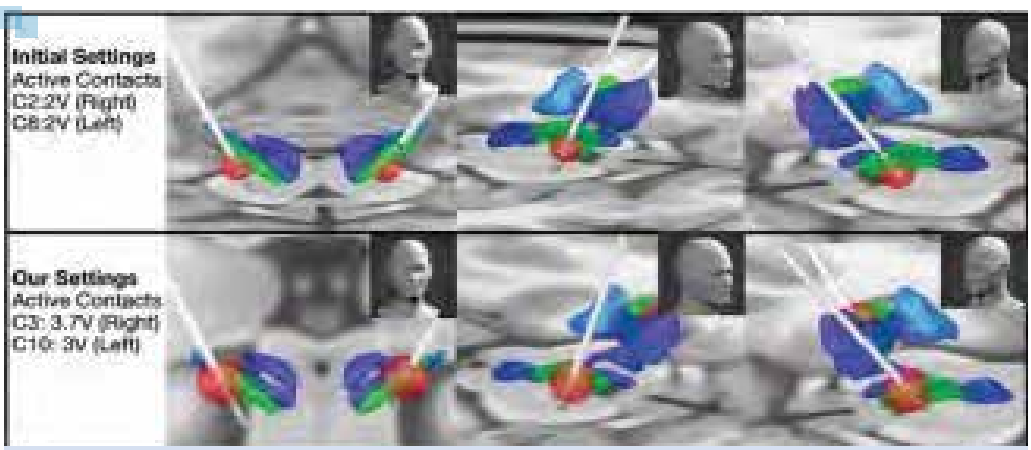

Figure 2: Initial programming for STN stimulation vs Re-Programming for cZi stimulation

Differences between Parkinson's Disease and Spinocerebellar Ataxia (SCA-12)

	Parkinson's Disease	SCA-12
Non-Motor Symptoms	Anosmia and RBD* Present	Anosmia and RBD* Absent
Tremor	Higher Frequency, Lower Amplitude	Lower Frequency, Higher Amplitude
Handwriting	Micrographia	Macrographia
Family History	Present	Present
Erectile Dysfunction	Late	Early
Restless Leg Syndrome	Uncommon	Common
Cerebellar signs	Not seen	Seen later in the course
Ethnic groups in India	No particular	Commonly seen in Hindu-Aggarwals

*Rem Sleep Behavioral Disorders

Figure 3

Unilateral Vertical Pendular Nystagmus in Multiple Sclerosis: A Distinctive Neuro-Ophthalmological Sign

Source:- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6327690/

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Keywords

Brain-stem. multiple sclerosis, nystagmus, optic nerve

Lesions in multiple sclerosis can involve brain, optic nerve and spinal cord. We here report a patient of multiple sclerosis, who had unilateral vertical pendular nystagmus, because of simultaneous involvement of optic nerve and asymmetric brain stem lesions. This specific combination is rarely seen in other disorders, therefore can be considered as a distinctive neuro-ophthalmological sign of multiple sclerosis.

Eye movement's abnormalities are very common in multiple sclerosis (MS). MS has few characteristic neuro-ophthalmological signs like "internuclear ophthalmoplegia" and "one-and-a-half syndrome." These specific signs are due to characteristic and discrete brainstem structures involved and propensity to have multiple lesions at a single time in MS. We have encountered a case of left eye vertical pendular nystagmus in MS, where the possible cause of this rare presentation was simultaneous involvement of left optic nerve and asymmetric brainstem lesions

A 31-year-old male, with history of numbness in both upper limbs with complete recovery over 4–5 days 2 years back, presented now with unsteadiness of gait for 3 months and painless mild diminution of vision in the left eye for 15 days. Clinical examination revealed left eye diminished vision (6/12 by Snellen's chart) with relative afferent pupillary defect with partial optic disc atrophy. The right eye was normal. He had dysarthria with gait ataxia, with swaying toward the left side. Eye examination also showed isolated, unilateral pendular vertical nystagmus (UVPN) in primary gaze in the left eye [Video 1]. All deep tendon reflexes were brisk with bilateral planter response extensor. Visual evoked potential showed mildly reduced amplitudes in the left eye. Contrast-enhanced magnetic resonance imaging of brain and spine showed multiple ovoid T-2 and FLAIR hyperintense lesions in bilateral periventricular and juxta cortical white matter, thalamus, centrum semiovale, gangliocapsular region, and brainstem. Many of these lesions showed postcontrast peripheral open-ring enhancement. Cervical spine showed similar intramedullary lesions from C-3 to C-5 levels. (Figure 1)

These findings were suggestive of relapsing-remitting MS. Workup for other demyelinating disorders and infective disorders were negative. The patient was started on intravenous methylprednisolone 1 g daily for 5 days. The vision of the patient improved to 6/9 and nystagmus disappeared gradually. Speech and gait also got better. The patient was started on interferon beta-1a 30 g once weekly and asked to follow-up regularly.

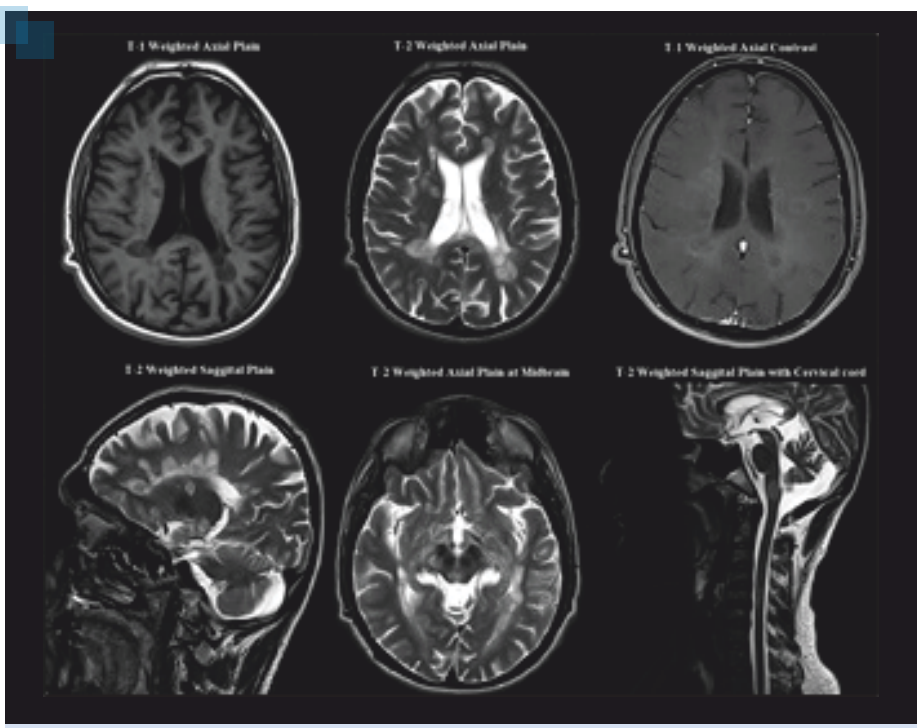

Figure 1: Magnetic resonance imaging of brain and cervical spine showing multiple ovoid lesions in bilateral periventricular and juxta cortical white matter, brainstem, and spinal cord, with few of these lesions showing postcontrast peripheral open-ring enhancement. These imaging findings are suggestive of multiple sclerosis

Discussion

Nystagmus is to-and-fro biphasic ocular oscillations. It can be jerk nystagmus where there is a slow drift of eyes and a quick corrective component, or pendular nystagmus, where eyes move with the same speed in both directions. Nystagmus is mostly a symmetric binocular disorder, but monocular eye oscillations and asymmetric binocular eye oscillations are also rarely seen. UVPN is a rare type of acquired monocular eye oscillations where only one eye moves to-and-fro with same speed in vertical direction.

UVPN has been earlier described in profound visual loss (Heimann-Bielschowsky [HB] phenomenon), MS, syphilis, optic chaisamal tumors, and brainstem infarction (midbrain or thalamic). [1-3] Patients with profound visual loss may have monocular vertical nystagmus characterized by slow, coarse, pendular, and variable amplitude movements known as HB phenomenon. Disruption of the fusional vergence mechanism or the monocular visual stabilization system is probable cause in this condition. [3] As this patient did not have profound visual loss, HB phenomenon can be ruled out. UVPN may also be caused by asymmetric brainstem disease as described by few studies. [4] However, it may be related to optic nerve dysfunction since it is found that larger oscillations correlate with greater optic neuropathy. Studies suggested that asymmetric signs of optic neuropathy were more common in patients with dissociated pendular nystagmus than in those with symmetric nystagmus. Role of asymmetric brainstem lesions, especially midbrain and thalamus, has been also evident in different case studies. [5] Although the cause of UVPN is still debatable, it has been postulated that UVPN is most likely caused by abnormal brainstem feedback circuits for eye position, which is calibrated by visual factors. This implies that any condition where both abnormal brainstem lesions and unilateral optic nerve lesions are temporally associated can result in UVPN. In our patient, unilateral lesions of midbrain affecting the rostral interstitial nucleus of the MLF in midbrain (which integrates the neural input into a final command for vertical gaze), along with unilateral optic neuropathy, may have culminated in vertical rather than horizontal or torsional nystagmus.

Therefore, in our patient, UVPN was seen as both optic neuropathy and asymmetric brainstem lesions were present. This combination of unilateral optic neuropathy and asymmetric brainstem lesions occurring simultaneously at a time is rare, that is why UVPN is a rare entity but is possible in MS. Other diseases where optic nerve and brainstem lesions can be seen are syphilis, Wernicke's encephalopathy, few vasculitis syndromes, and neuromylitis optica, but cooccurrence of both the lesions at a time together is very uncommon.

Hence, UVPN can be considered as distinguishing ophthalmological sign of MS as "internuclear ophthalmoplegia" or "one-and-a-half syndrome." However, still, other more specific and targeted studies are required to support the above-mentioned proposition.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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Gum Hyperplasia in an Elderly Male

Source:- file:///C:/Users/HP/Downloads/3335-Main%20Article%20Text%20(Blinded%20Article%20File)_-7773-2-10-20220515.pdf

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A 50-year-old male presented in the clinic with a complaint of swelling in the gums. According to him, the patient noticed swelling in the maxillary and mandibular regions of gums both from outside and inside 15 days back. There was no history of any bleeding, infection, or discharge from gums. The patient was a known case of ischemic stroke and hypertension and was on aspirin 150 mg, atorvastatin 20 mg, and telmisartan 40 mg once daily along with baclofen 10 mg twice daily for around 3 years. One and a half months back, due to uncontrolled blood pressure, amlodipine was added. On examination, the oral hygiene of the patient was adequate. The swelling was irregular, lobulated, with a granular surface spreading over the inner aspect of teeth in the oral cavity and the outer aspect of the gingival surfaces of the teeth, almost covering the teeth completely.

The gingival hyperplasia was present throughout the gum enclosing teeth. Normally, the gingival thickness is 2–3 mm, but in this case due to hyperplasia, the thickness has increased to 7–10 mm. Furthermore, it was progressively increasing leading to some difficulty in eating and speaking. On investigating, the haematological and metabolic parameters of the patient were normal. The patient was diagnosed as a case of drug-induced gingival hyperplasia.

Gum/gingiva is the protective mucosal surface surrounding the teeth in a collar form. It is comprised of gingival epithelium and gingival connective tissue (lamina propria). Gingival connective tissue is comprised of collagen fibres, cells, and ground tissue. Adjacent teeth gingival surface is separated with gingival sulcus. In this patient, there was hypertrophy of gingival connective tissue, leading to overgrowth around the tooth both on the inner and outer surface, leading to obliteration of gingival sulcus and overall disfigurement. In view of the recent addition of amlodipine leading to the development of a sequence of events temporally, gingival hyperplasia was corroborated to amlodipine. Furthermore, all other possible causes of gum hyperplasia such as infection, poor dental hygiene, blood malignancies, and other drugs causing gum hyperplasia were ruled out by history and appropriate investigations. The patient refused any surgical intervention for gum hyperplasia; therefore, meticulous oral hygiene was advised along with the replacement of amlodipine with Losartan 50 mg twice daily with stringent blood pressure monitoring. Following this, his gum swelling slowly started regressing but did not get completely resolved until his last follow-up.

Drugs that can cause gum hyperplasia are anti-epileptic drugs, immunosuppressants, and calcium channel blockers (CCB) [1,2]. Amlodipine, a CCB may rarely cause gum/ gingival hyperplasia as in this patient, but the exact mechanism is unknown [3-5]. Upregulation of keratinocyte growth factor due to blockage of aldosterone

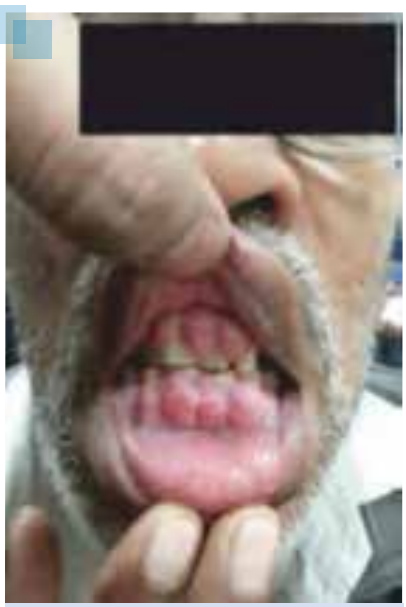

Figure 1: A 50-year-old male with gingival hyperplasia in both upper and lower gums

Figure 2: A 50-year-old male with gingival hyperplasia seen in both upper and lower gums

synthesis in the adrenal cortex is the most accepted mechanism of gum hyperplasia by CCBs [6,7]. Stopping the offending drugs along with surgical correction is the treatment of choice and shows good results in most cases. Among CCBs, nifedipine is the most common culprit for gum hyperplasia, but in this case, amlodipine caused gum hyperplasia, and also, this occurred quite rapidly (within 15 days) and massively. As amlodipine is the most commonly used anti-hypertensive in clinical practice, therefore, it is important for clinicians to know about this adverse drug reaction and take timely action.

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Two Very Complex Neurosurgical Pathologies Managed Successfully in a Single Patient

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Case Report

A 40 years old female, our follow up patient presented to us with spastic quadriparesis. She was a known case of rheumatoid arthritis for last 10 years and taking medications as advised by Rheumatologist.

Dynamic CT Cranio-vertebral (CV) junction and MRI CV junction was suggestive of Atlanto Axial Dislocation (Atlanto dental interval of 68 mm) with narrowing of foramen magnum and compression of cervical-medullary junction.

This patient in the past in February 2016 had presented with subarachnoid haemorrhage.

CT angiography was suggestive of three aneurysms in right supra-clinoid ICA at different sites. Patient underwent Rt peritoneal craniotomy and clipping of all three aneurysms and was discharged with no neurological deficit.

Patient since then had been in regular follow up and in March 2019 had complained of neck pain and MRI CV junction done at that time was suggestive of increased Atlanto dental interval. Patient was advised cervical collar and prognosticated about MRI findings.

In present admission after adequate work up and counselling, patient was posted for surgery.

Patient underwent foramen magnum decompression with removal of posterior arch of C1. C1-C2 joint spaces were approached and spacers put thereby somewhat reducing the dislocation. C1 lateral mass & C2 pedicle screw fixation was done. Further reduction was achieved using sublaminar wire placed from occiput to C2 lamina and this was confirmed intraoperatively using C-arm, before final locking of screws.

The patient was discharged with improved neurological outcomes.

Post-operative CT CV junction was suggestive of complete reduction of the Atlanto axial dislocation.

This case is being shared to highlight two very complex neurosurgical pathologies with high morbidity and mortality, which were managed successfully in the same patient without any complications.

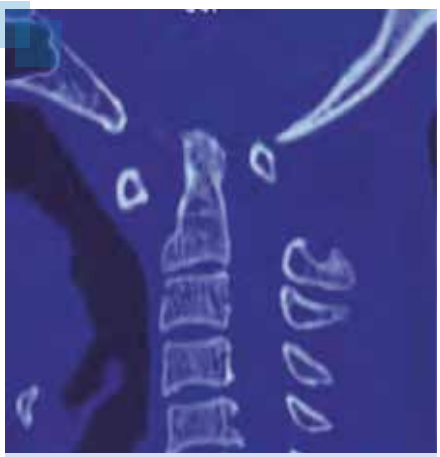

Figure 1: Pre-operative CT CVJ showing Atlanto Axial Dislocation

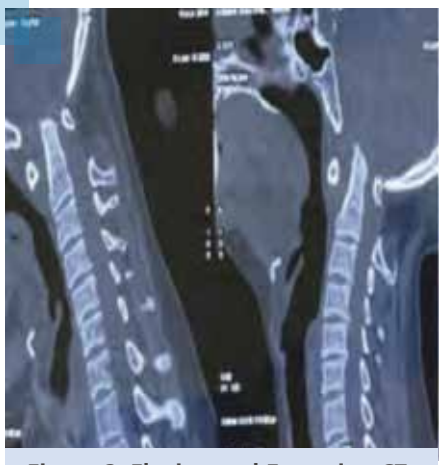

Figure 2: Flexion and Extention CT CVJ images showing non-reducing of AAD

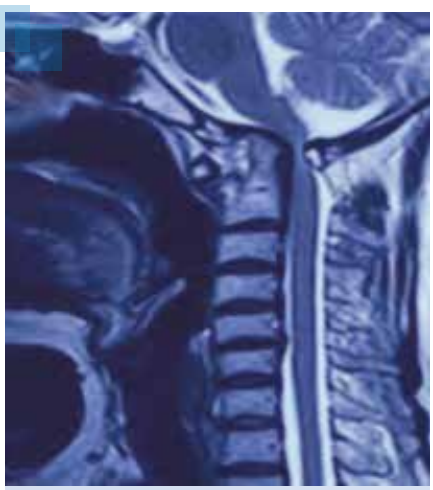

Figure 3: Pre-operative MRI CVJ showing significant compression of Cervico Medullary Junction by odontoid

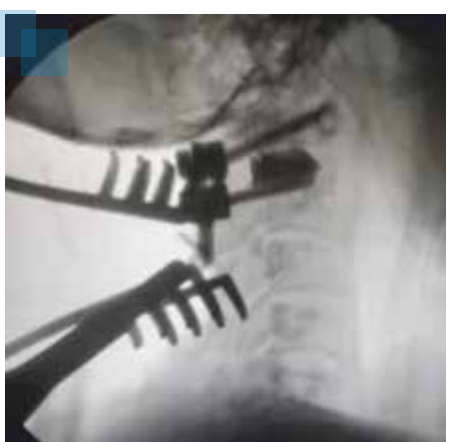

Figure 4: Intra operative C arm image with C1 lateral mass and C2 pedicle screws with C1-C2 joint spacer and Occiput to C2 sub laminar wire

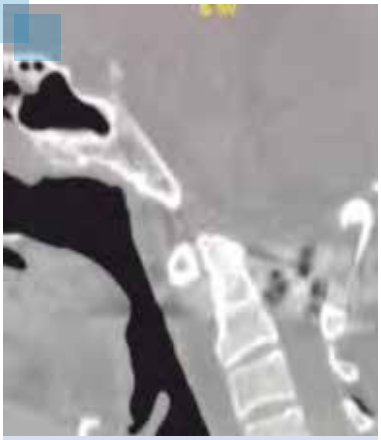

Figure 5: Post-operative CT CVJ showing reduced AAD

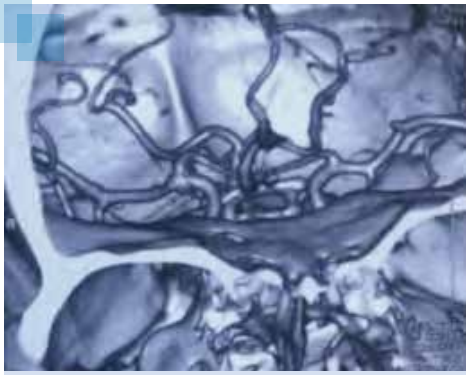

Figure 6a: Pre-operative (before first surgery in 2016) CT Angiogram suggestive of three right supra clinoid intracranial aneurysms

Figure 6b: Pre-operative (before first surgery in 2016) CT Angiogram suggestive of three right supra clinoid intracranial aneurysms

Figure 7: Intra operative microscope image showing multiple aneurysm clips applied

Figure 8: X-ray CVJ showing three intra cranial aneurysm clips applied in first surgery and craniotomy bone flap plate and screws

Planum Sphenoidale Meningioma

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Case Report

A 70-year-old lady noticed gradual decrease in vision, first in the right eye followed by the left for 5-6 months. Initially she consulted an ophthalmologist for refractive error. Detailed visual assessment was done. Her Visual Acuity in the Right eye was 6/24 and 6/9 in the left eye. Visual perimetry revealed restriction in all quadrants in both eyes. She was advised for an MRI brain and came to us for further management. MRI Brain revealed Planum sphenoidale meningioma. She underwent right frontotemporal orbit zygomatic craniotomy and excision of lesion. Post operatively she had transient memory disturbances but no further worsening of vision. Histopathology reported WHO Grade 2 Meningioma.

Review of Literature

Planum sphenoidale meningiomas are extra-axial slow-growing tumors arising from the roof of the sphenoid sinus and the area between the optic nerves and the anterior clinoid processes. Enlargement of this meningiomas usually pushes the optic nerves dorsally and caudally causing vision loss as a primary manifestation. Planum sphenoidale meningiomas represent 5% to 10% of intracranial meningiomas with female predominance.

MRI remains the confirmatory diagnostic procedure where the lesion appears hypo to isointense on T1-weighted imaging and possesses variable signal intensity on T2-weighted images. Gadolinium MR imaging demonstrates intense homogeneous enhancement with well-circumscribed margins and dural tail. Although meningioma is known to enhance homogenously on contrast uptake, atypical ones may have heterogeneous enhancement. The enhancement may be heterogeneous secondary to the presence of intrinsic calcification, cysts, and necrosis. Such a differential enhancement in this MRI image has an uncanny resemblance to a "flower". This appearance with central island and multiple projecting spokes closely replicate an "Evening Primrose flower". Early accurate diagnosis of these tumors is possible through the use of neuroimaging which is recommended for all patients with gradual and progressive impairment of vision.

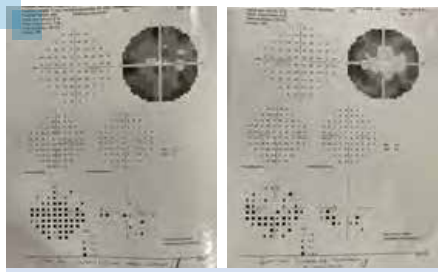

Figure 1:
Pre-op visual field charting - Gross constriction of vision

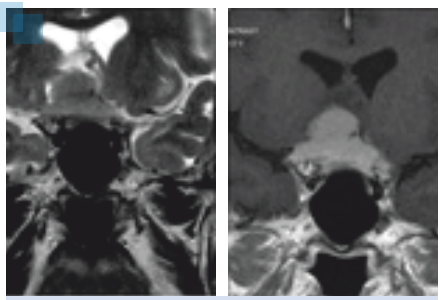

Figure 2: MRI Brain – Planum sphenoidale meningioma

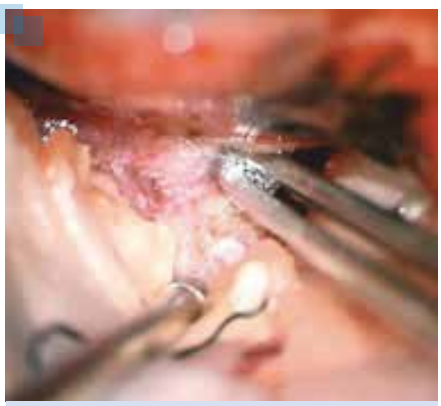

Figure 3:
Intraop image showing internal decompression of the tumour

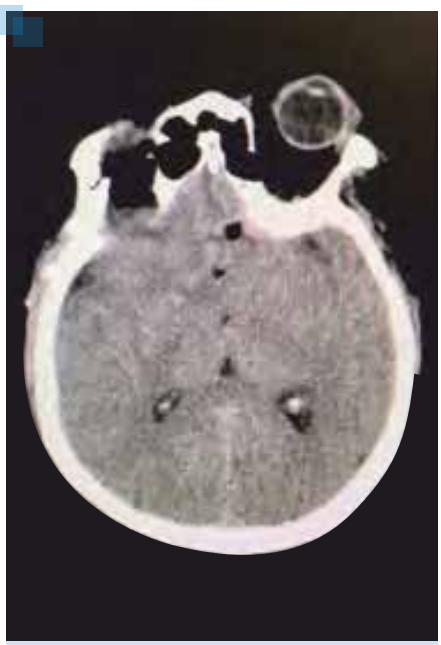

Figure 4:
Post-op CT Brain - Relevant Post-op changes. No tumour bed hematoma

Approach to a Case of Optic Nerve Cavernoma

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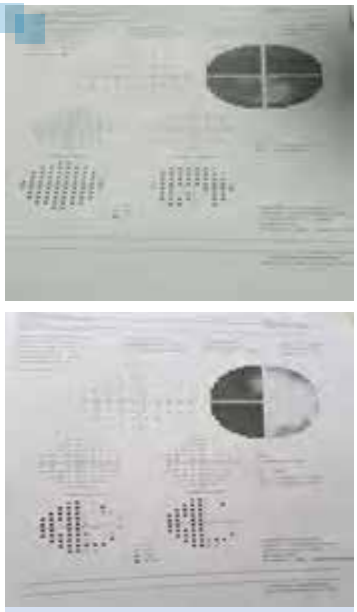


Figure 1: Visual field charting showing total constriction in Right Eye

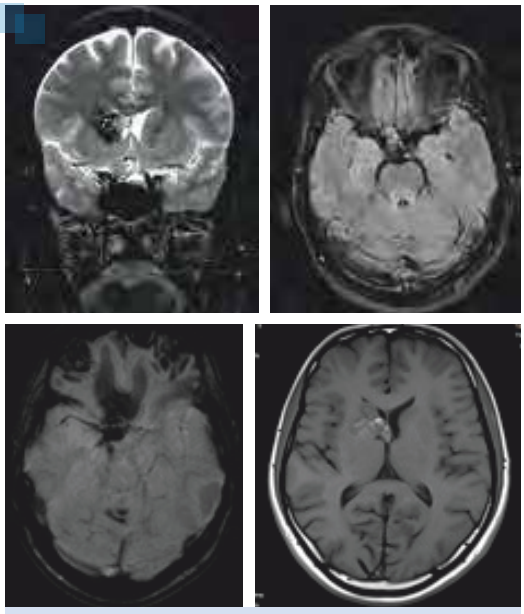


Figure 2:
MRI Brain sequences showing right optic nerve cavernoma

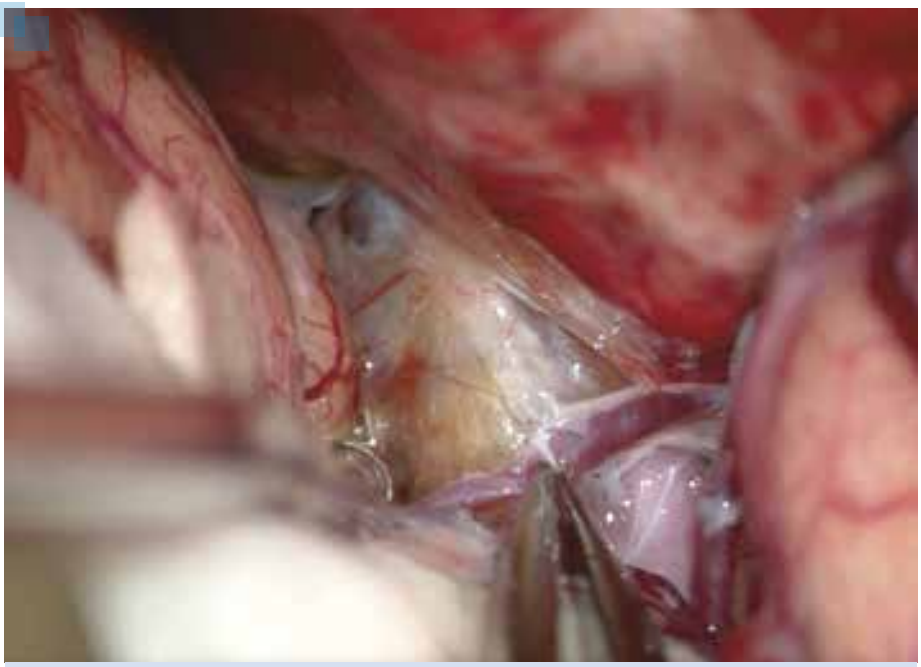


Figure 3: Intra-op image of right optic nerve cavernoma

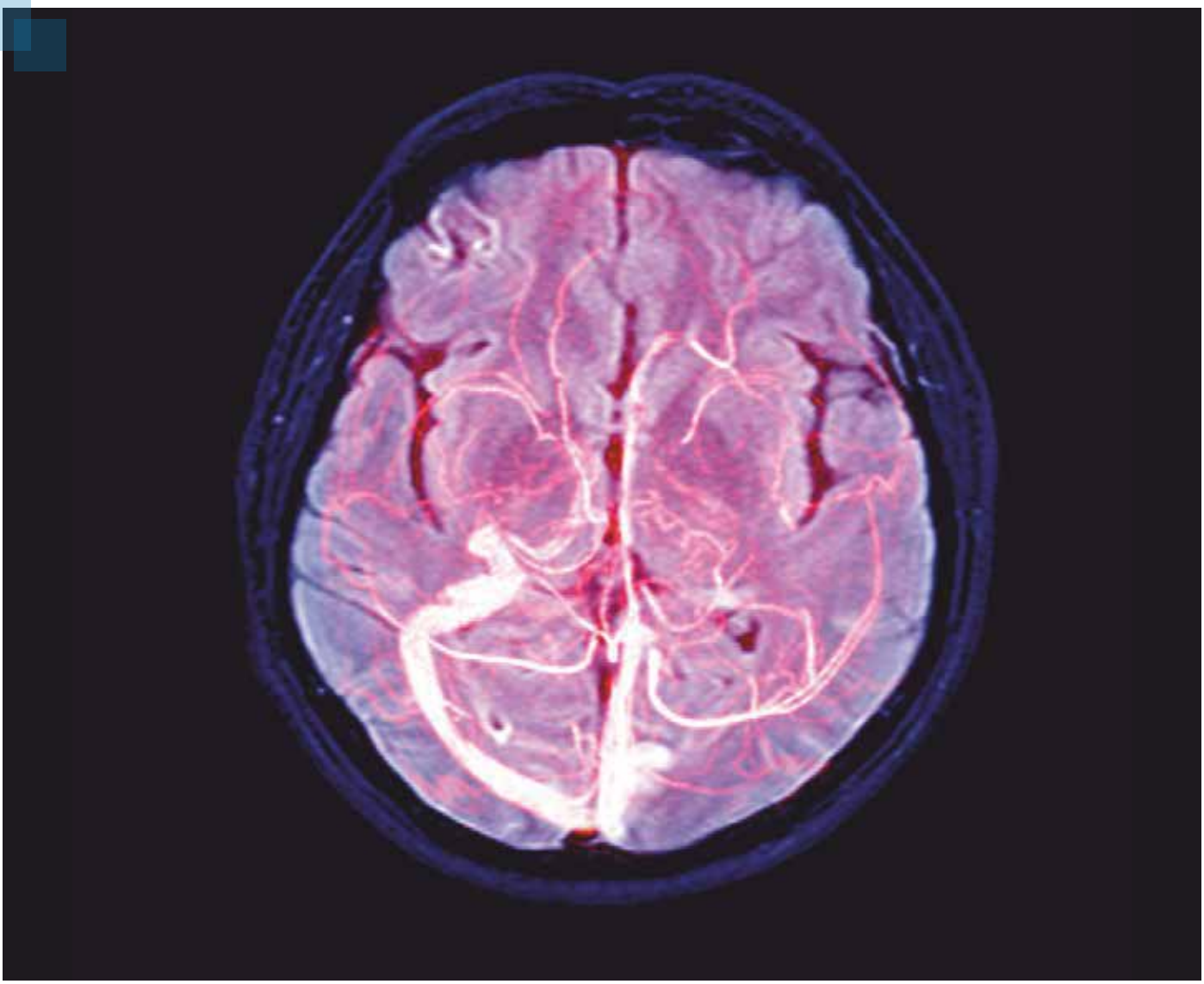
Case Report

A 39-year-old gentleman with history of decreased vision in the right eye which was first noticed in 2005 was evaluated. He was found to have an intracranial lesion and was advised surgery, but he refused. Over the next 2 years, his vision improved. In 2017, vision in his right eye started decreasing, he was unable to see far objects on the left side while driving. He underwent repeat imaging and came to us for further management. Detailed visual assessment with visual field charting revealed total constriction in the right eye with temporal hemianopia in the left eye. Repeat imaging showed multiple cavernous malformations in the brain. There was one lesion in the caudate nucleus bulging into the ventricle. This lesion showed intralesional and perilesional haemorrhage, but no evidence intraventricular bleed. As the patient's present problem was visual deterioration, we decided to explore the lesion around the right optic nerve. We chose a right frontotemporal craniotomy and decided to explore the suprasellar area. Gross total excision achieved. Post operatively his vision remained the same. HPE report confirmed an Optic nerve cavernoma.

Review of Literature

Intracranial cavernous angiomas (cavernomas) account for 5%-13% of all vascular malformations. CMs of the optic nerves (Ons), chiasm, and optic tract are very rare, occurring in fewer than 1% of patients with brain CM. A "venous angioma" of the optic chiasm, later called a cavernous haemangioma of the ON, was successfully resected in 1978. They consist of endothelial cell-lined, dilated vessels (caverns) packed together without intervention to the neural parenchyma Through 2005, only 28 case reports or short series (two to four patients) involving 42 patients had been published. An analysis in

2010 described 65 patients with CM of the hypothalamus and optical pathways, with an update in 2014 including 70 patients. The latter remains the largest review to date of patients with CM of the ONs and chiasm. Three patterns of clinical onset have been described: acute (chiasmal apoplexy), subacute, and progressing. Acute CM of the ONs and Chiasm is characterized by sudden blurred vision, headache, nausea, and retroorbital pain. The other two patterns include the gradual loss of vision, similar to that observed in patients with suprasellar tumours and ON gliomas. On computed tomography (CT) scanning they appear as well-demarcated inhomogeneous hyperdense lesions. MRI findings are which show a high signal intensity on the Tl-weighted images with surrounding irregular dark rim, more evident on the T2-weighted images. Although cavernomas are vascular malformations with a convolution of thrombosed and non-thrombosed atypical vessels their specific hemodynamic features usually prevent direct angiographic visualization. Blood coming from feeding micro arteries circulate slowly in dilated vessels, and thrombosis of these is thought to be one cause of haemorrhage. Total microsurgical resection is the optimal treatment strategy for patients with CMs of the chiasm and optic nerve because it usually results in improved vision and long-term benefits. Surgical strategies used for CM of visual pathways include gross total resection, subtotal resection, and resection following optic canal unroofing biopsy with decompressive evacuation of the haemorrhage, pure biopsy, and biopsy with radiation. Clinically and radiologically, ON cavernomas may mimic other focal lesions of the ONs, including inflammations, gliomas, and demyelination. Thus, despite their rarity, optic CM should be considered in the differential diagnosis of patients with these pathologies, especially ON gliomas.



Intracanalicular Vestibular Schwannomas – Case Report with Review of Literature

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Case Report

29-year-old male patient presented with history of progressive loss of hearing on the left side for 1 year. Pure tone audiogram revealed left moderate sensorineural hearing loss (SNHL). He was evaluated further with an MRI Brain with CISS sequence and was diagnosed with a left internal auditory canalicular lesion. As the patient was already symptomatic with progressive deterioration of hearing, he was given the option of either undergoing surgery and or radiotherapy. He opted for surgery and underwent left intracanalicular lesion excision. HPE report confirmed Vestibular Schwannoma.

Pure Tone Audiometry

Pure tone audiogram done showed left moderate SNHL.

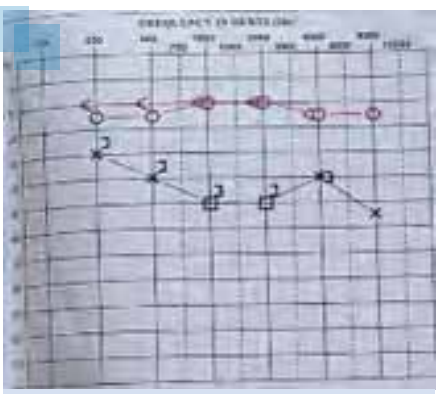

Figure 1: PTA of left ear

Pre-op MRI Brain with Contrast with CISS Sequence

Expansion of the left internal auditory canal that is occupied by a well-defined small rounded intracanalicular mass along the course of the vestibulo cochlear nerve. Small CSF cap is separating the intracanalicular mass from the cochlea. No evidence of extra canalicular extension (CPA component). Normal right internal auditory canal.

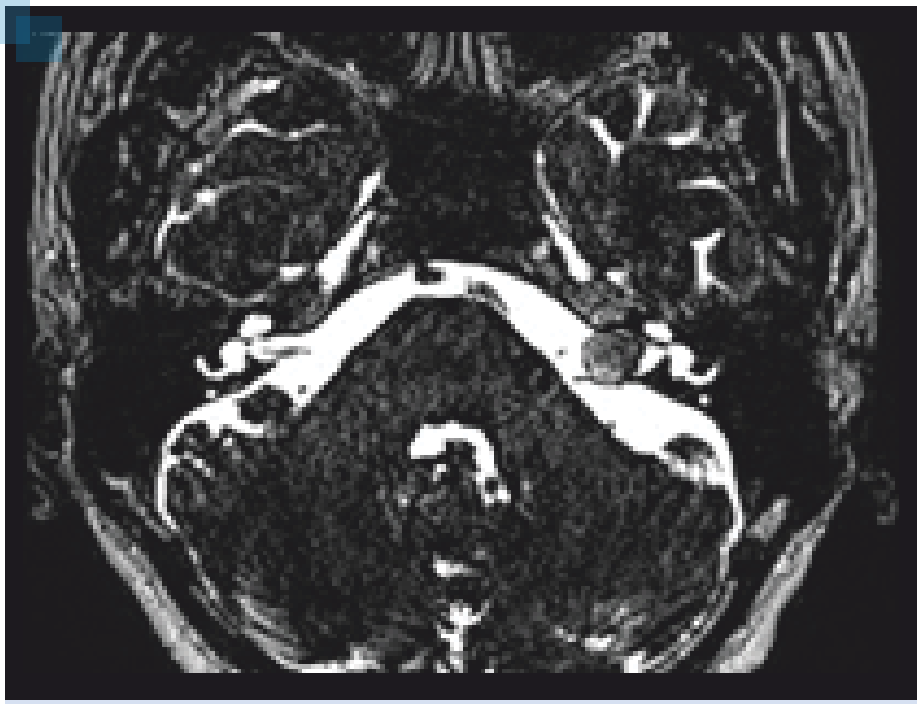

Figure 2: Left internal auditory meatal lesion

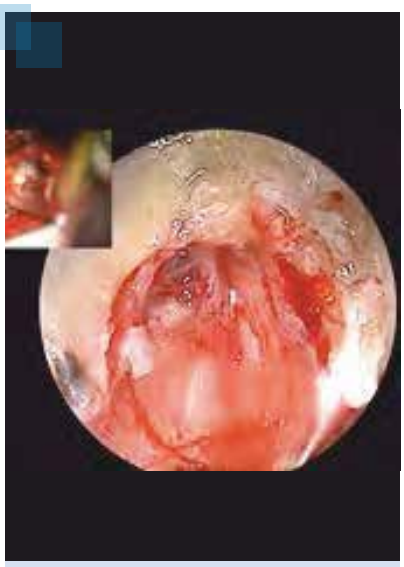

Figure 3:
Endoscopic view of left IAC

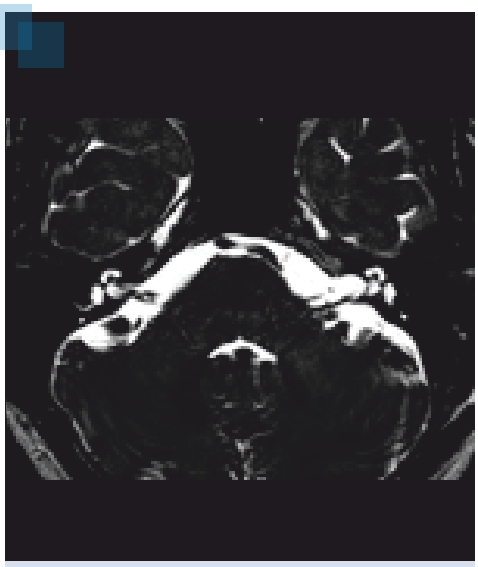

Figure 4:
Complete excision of lesion

Review of Literature

Vestibular schwannoma (VS) is defined as intracanalicular when it is limited to the internal auditory canal the mean diameter of the tumor at diagnosis has decreased from 30 mm in 1979 to 10 mm in 2008, most likely from an increase in magnetic resonance imaging (MRI) availability. Before the advent of the Gd-enhanced MR imaging, such tumors could be demonstrated only by invasive tests and even the symptomatic patient might not be evaluated until deafness or other neurological symptoms occurred. About 50% of patients with serviceable hearing at the time of diagnosis of an intracanalicular acoustic tumor will show progressive hearing loss over the next 2 years. Coupled with the fact that the majority of patients in whom such a diagnosis is made are evaluated because asymmetrical hearing loss has been noted, this strongly suggests that intracanalicular acoustic neuroma causes progressive hearing loss in the majority of affected patients. As the best predictor of the quality of postoperative hearing is the quality of the patient's preoperative hearing function, hearing will be best preserved when intracanalicular acoustic neuromas are removed shortly after diagnosis.

How Do We Manage These Patients?

Multiple factors, including status of hearing, presence of vestibular symptoms, patient age, medical comorbidities, institutional outcomes, and patient preferences, help determine the management strategy for patients with an intracanalicular vestibular schwannoma. Watchful waiting is an important management option for patients with minimal symptoms. The literature on the natural history of small vestibular schwannomas continues to expand, with particular emphasis on the expected hearing outcomes. Microsurgical techniques also focus on hearing preservation. Presence of fundal fluid and good or normal hearing preoperatively are positive predictors of hearing preservation after surgery. Long-term follow-up after radiation therapy for vestibular schwannomas continues to demonstrate excellent tumor control rates, although hearing preservation rates are modest.

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2 Neves Cavada, Marina*,†; Fook-Ho Lee, Michael‡; Jufas, Nicholas Emmanuel*,||,¶,#; Harvey, Richard John*,§; Patel, Nirmal P.*,||,¶,# Intracanalicular Vestibular Schwannoma: A Systematic Review and Meta-analysis of Therapeutics Outcomes, Otology & Neurotology: March 2021 - Volume 42 - Issue 3 - p 351-36

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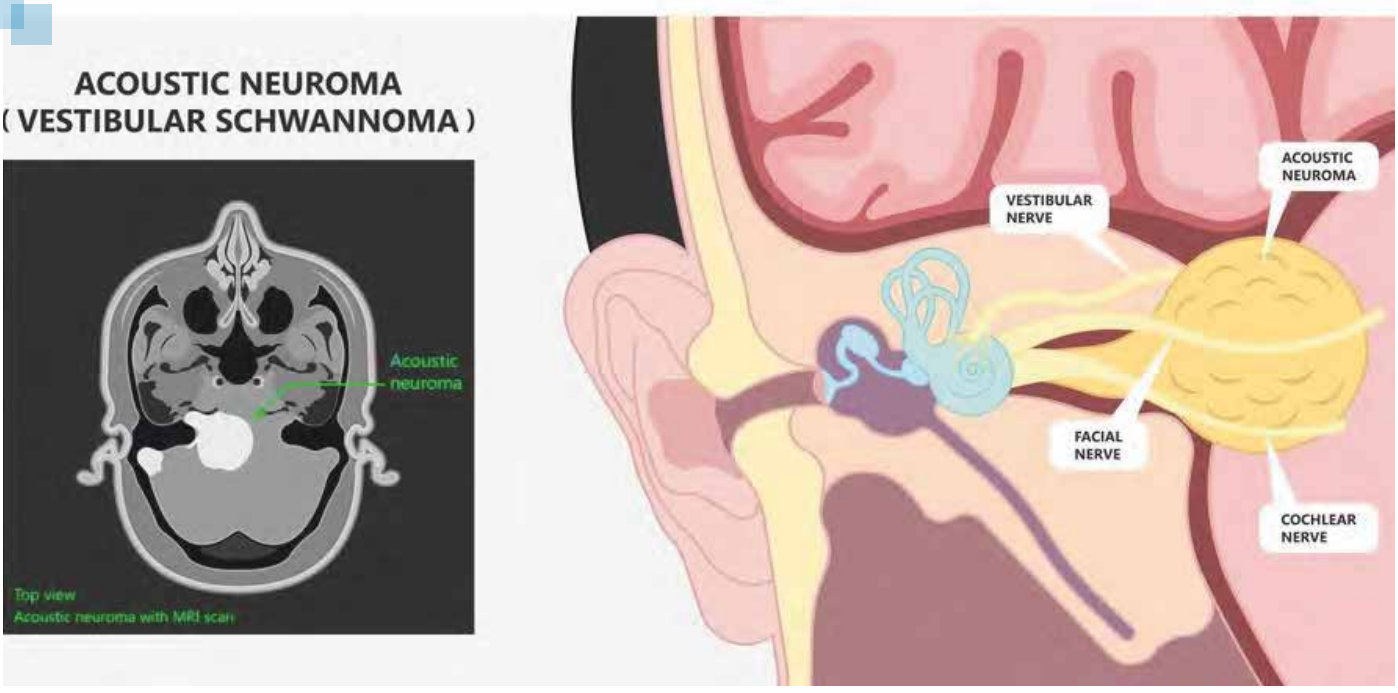

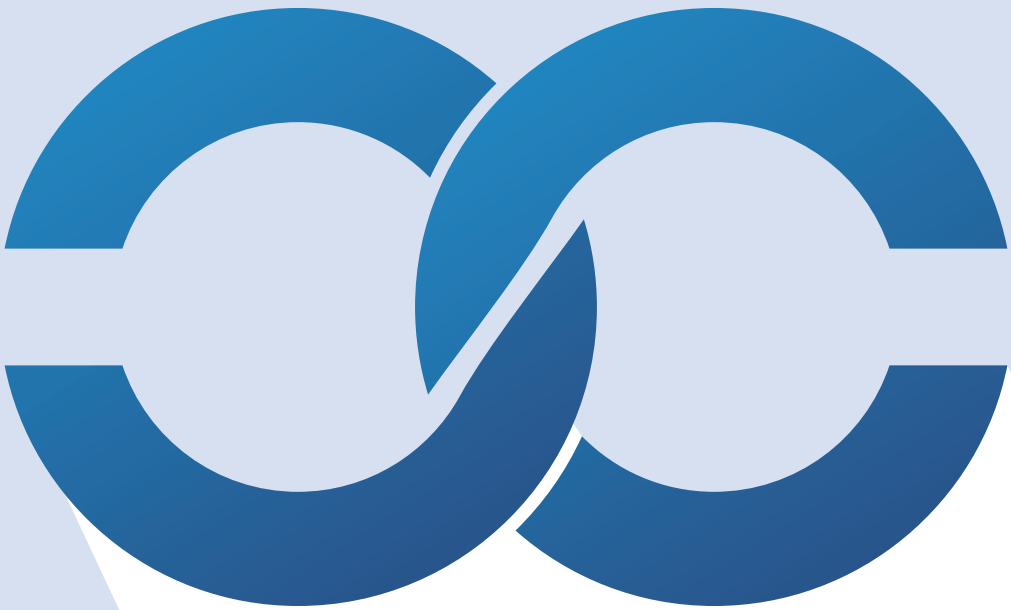

LETTER TO THE EDITOR

Isolated Lingual Epilepsia Partialis Continua in a Case of Hyponatremia

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Introduction

Epilepsia partialis continua (EPC) is a rare variety of focal status epilepticus which may present with repetitive and sometimes persistent movements of different body parts with retention of awareness. These involuntary jerky movements could last from a few hours to days and remain localized to the part of the body in which they originate. Varied etiologies have been linked with EPC like vascular, inflammatory, neoplastic lesions, and metabolic disorders. Isolated lingual EPC involves the only tongue and is rarely described in the literature.

Case

A 64 year old lady presented in emergency with abrupt onset abnormal tonic clonic movements of all limbs followed by altered sensorium. The patient's consciousness improved over one hour but she had slurred speech on regaining consciousness. Before this event, the patient was cognitively sound without any behavioral abnormalities. On examination, the patient was conscious, oriented to time and place, and was following simple commands. Tongue examination showed continuous jerky movements suggestive of lingual EPC. Tongue weakness was noticed ictally and postictally, but the rest of the cranial nerves were normal. Motor, sensory, cerebellar, and extra pyramidal systems examination were normal. Investigations showed low serum sodium levels (112 meq/L) suggestive of severe hyponatremia, which was probably due to the recent addition of hydro chlorothiazide as anti hypertensive. The patient had no history of any psychiatric illness in the past and was not on any other medicine except anti hypertensive drugs (amlodipine, telmisartan, and hydro chlorothiazide). Her other routine blood investigations were normal. Anti nuclear antibodies and antithyroid peroxidase antibody were negative. Cerebrospinal fluid (CSF) examination was normal. Autoimmune encephalitis panel in serum and CSF was negative. Paraneoplastic profile was negative. MRI brain was normal. Electroencephalogram was suggestive of intermittent epileptiform discharges in bilateral fronto temporo pareital leads.

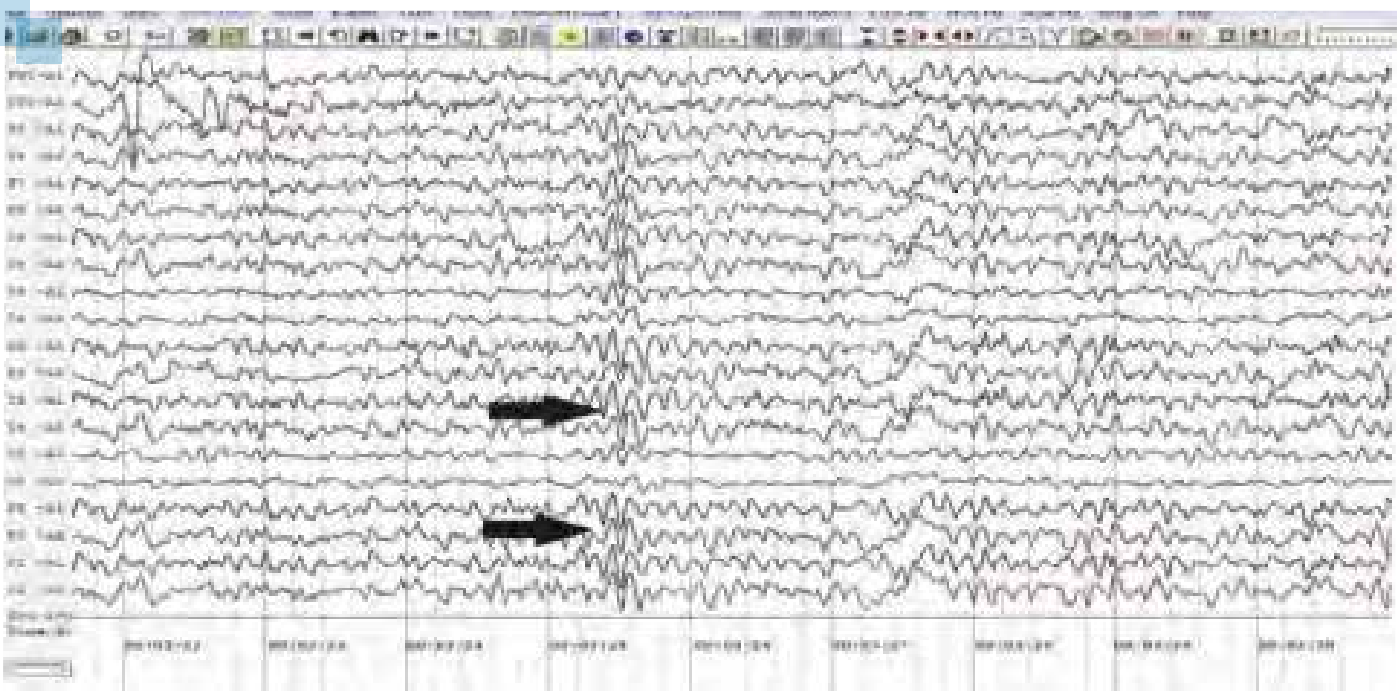

Figure 1: Electroencephalography showing bilateral Fronto-temporo-parietal epileptiform discharges

This patient was diagnosed and treated as isolated lingual EPC, probably caused by hyponatremia, as other causes were ruled out by relevant investigations. Possibility of tongue dyskinesia or tremors were less likely, as jerky movements of the tongue, in this case, were involuntary and due to visible tongue muscle contractions, and were continuously present in rest, as well as during protrusion or retraction. Also, no specific offending drug for causing dyskinesia/tremors or lesion in extrapyramidal circuitry of the brain was identified in brain imaging. The patient's hyponatremia was slowly corrected with hypertonic saline and antiepileptic drugs (Levetiracetam 500 mg twice daily, Clobazam 10 mg twice daily and Phenobarbitone 30 mg once daily) started because of lingual EPC. The patient started responding to the treatments and her abnormal tongue movements subsided over 3 days but post ictal tongue weakness persisted, which also improved in 3 4 days.

Discussion

EPC is defined as the continuous motor activity of specific body parts and mostly is cortical in origin. The prevalence of EPC is much lower than the generalized status epilepticus. But isolated Lingual EPC is very rare, only described in few case studies. The first case of isolated lingual EPC was described by Peter Kinirons et al. in 2006 in a case of paraneoplastic limbic encephalitis associated with anti Hu antibodies. [1] Thereafter, lingual EPC has been described in neurocysticercosis, Rasmussen's encephalitis, and herpes simplex encephalitis [2 4] [Table 1]. A possible mechanism for lingual EPC is the excitation of the opercular motor cortex, but how different aetiologies cause this excitation is still unknown. This is a unique case, as here lingual EPC was associated with hyponatremia and the patient improved completely following correction of hyponatremia. Possible differentials such as encephalitis (autoimmune and infectious), inflammatory, vascular, or demyelinating central nervous system diseases have been ruled out in this case by appropriate blood investigations and imaging studies. Therefore, a metabolic cause like hyponatremia can also lead to lingual EPC and can be effectively treated by correction of the metabolic conditions along with appropriate anti epileptic drugs.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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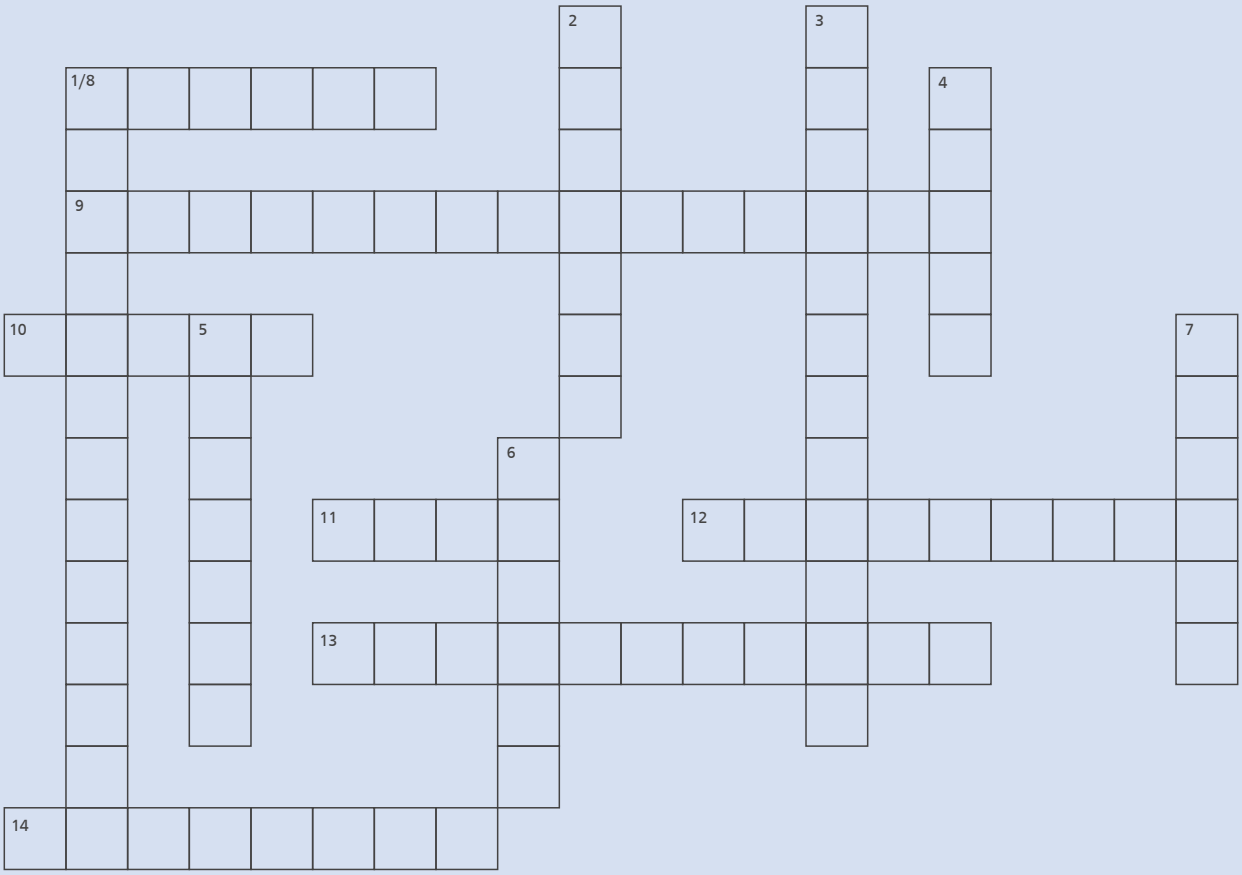
Table 1: Review of all cases of Lingual Epilepsia Partialis continua

Year	Author	Age/sex of patient	Cause	Treatment	Outcome
2006	Peter Kinirons *et al.*	48/Female	Paraneoplastic limbic encephalitis (Small cell carcinoma lun associated anti-Hu anti-bodies)	High dose steroids with chemotherapy and radiotherapy	Death after 6 months
2006	Nayak D *et al.*	25/Male	Rasmussen's encephalitis	Right frontal opercular focal cortical resection	Complete resolution
2007	Zoran Vukadinovic *et al.*	11/Female	Rasmussen's encephalitis	Topiramate and carbamazepine	Resolution of seizures
2014	Rajesh Shankar Iyer *et al.*	5/Male	Herpes simplex virus	Lorazepam, phenytoin, Levetiracetam and Acyclovir	Complete Resolution
2016	Sachin Sureshbabu *et al.*	60/Female	Neurocysticercosis	Levetiracetam and oxcarbazepine	Complete Resolution

Table 1: Review of all cases of Lingual Epilepsia Partialis continua

TRIVIA

Crossword

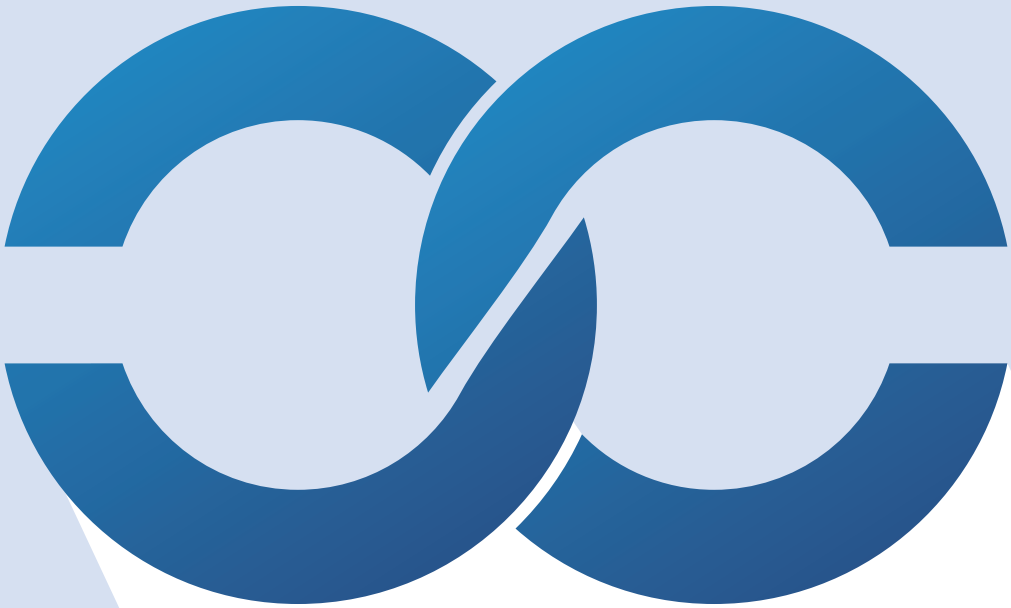


DOWN

1. _____ of London was the first surgeon to specialize in neurosurgery. (6,7)
2. Fibers of the striamedullares in the floor of fourth ventricle are derived from the ____ Nucleus.(7)
3. A toxin that blocks Na+ permeation through voltage-gated sodium channels, thereby blocking action potentials. (12)
4. The _____ ganglia is the most common location for spontaneous intracerebral hemorrhage secondary to hypertension. (5)
5. The _____ Equation is a mathematical relationship used to predict membrane potential from the concentrations and membrane permeabilities of ions. (7)
6. The gland that helps control the circadian cycle of sleep and wakefulness by secreting melatonin. (6)
7. The _____ area is located in the inferior frontal gyrus. (6)

ACROSS

8. The midline region of the cerebellum.(6)
9. The myxopapillaryependymomas usually arise from the floor of the 4th_____. (15)
10. The _____Stain is the method of staining brain tissue that shows neurons and all of their neuritis; named for its discoverer. (5)
11. A functional neuroimaging procedure using MRI technology that measures brain activity by detecting associated changes in blood flow. (4)
12. The history of trepanation dates back to the _____period. (9)
13. A dopaminergic agonist: _____. (11)
14. The intracranial tumor most likely to be encountered in a middle-aged man with AIDS is_____. (8)



ONCO CONNECT

Tumour Board Cases

Duodenal GIST -Dilemma in Starting Adjuvant Treatment

Dr Sandeep Nayak
Director, Surgical Oncology
Fortis Hospitals, Bangalore

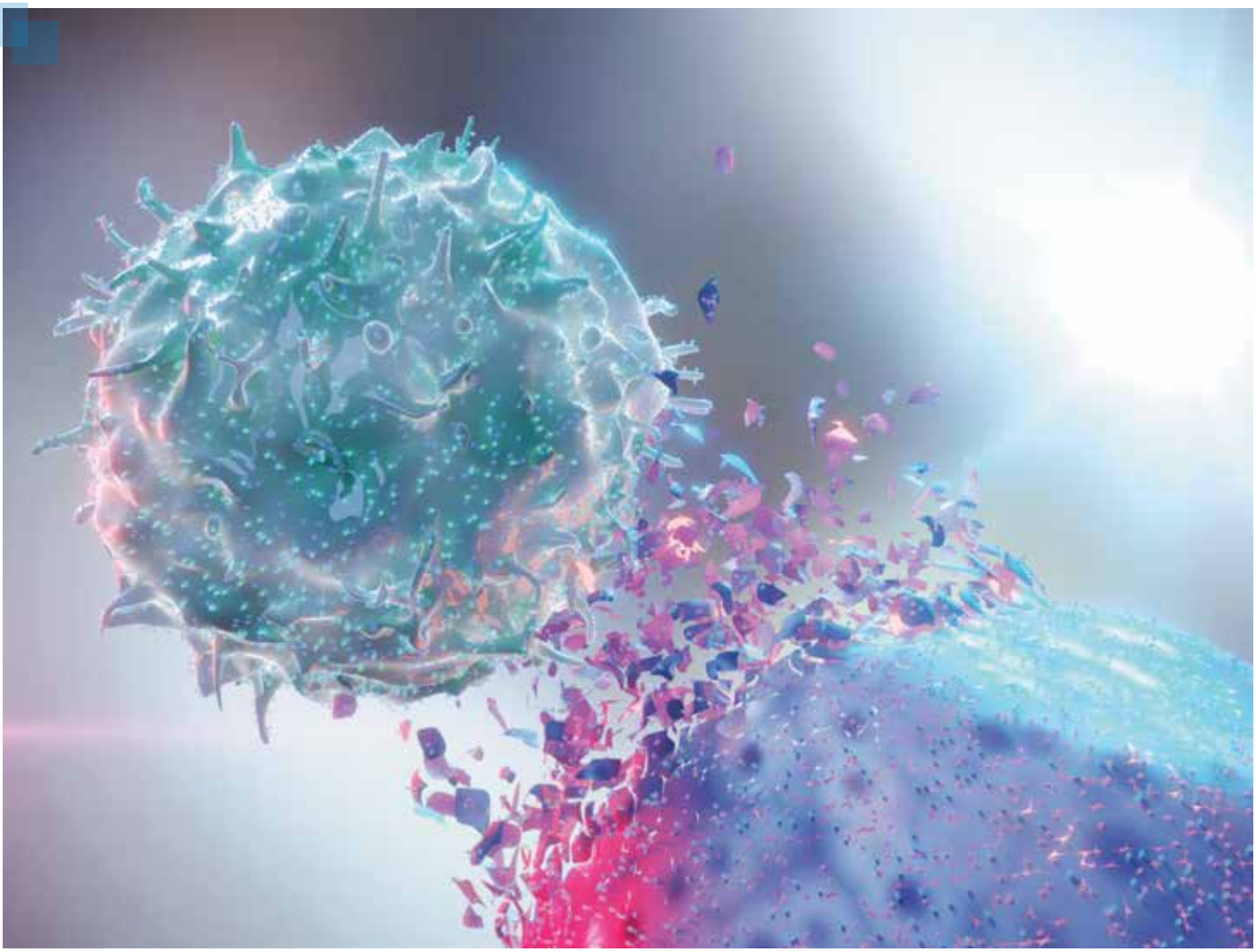
A 60 years old male presented with anaemia and was evaluated for the same. Upper GI Endoscopy revealed an ulcerative lesion and was biopsied. During evaluation a differential diagnosis of Neuroendocrine Tumor and duodenal GIST. Chromogranin levels were 486.CT scan was done which showed the lesion at junction of 2nd and third part of Duodenum with also an enhancing lesion in Adrenal gland. As the patient was bleeding and the surgical plan docent change in case of NET or GIST patient was considered for Surgery and Laparoscopic duodenectomy was performed with duodenojejunostomy. Postoperatively histopathology was reported as GIST.

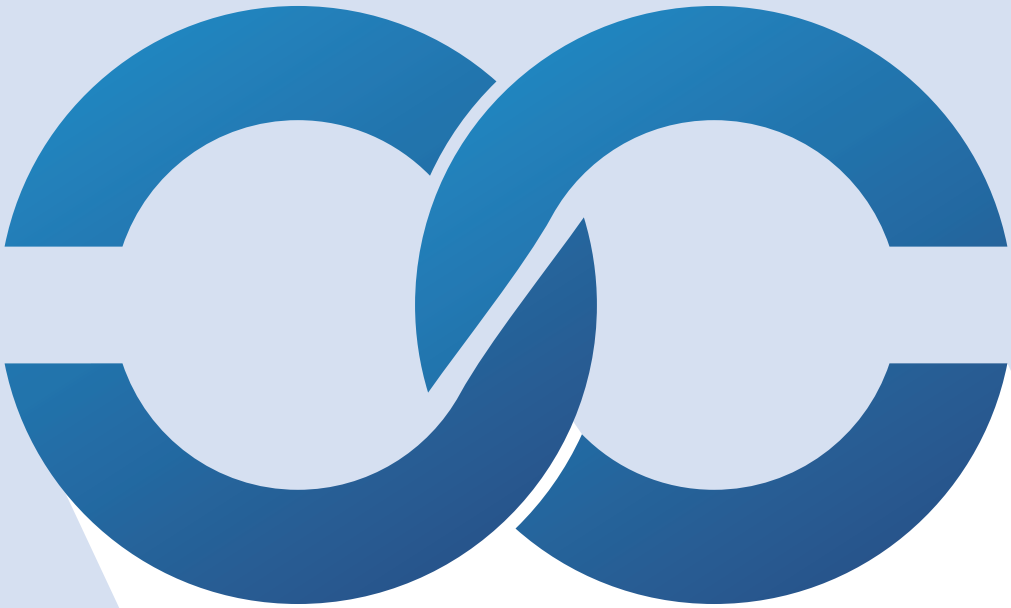
In view of raised Chromogranin levels DOTA PET CT SCAN is done which dint show any uptake elsewhere in the body.

Question to the Board; -As the GIST lesion was Solitary and less than 4cms in size, is there a role for Adjuvant therapy in the form of Imatinib?

Board Opinion

Though the size if the lesion is small the location of the GIST in Duodenum is a high risk feature and in view of this patient is considered for adjuvant treatment in the form of Imatinib for a duration of 6 months and asses the tolerability and Plan further.





FORTIS COVID WORK

Robots and Artificial Intelligence be Helpful in Future COVID Research

Source:- https://www.japi.org/x2b4a454/robots-and-artificial-intelligence-be-helpful-in-future-covid-research

Dr Debashis Chakraborty
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Fortis Hospital, Anandapur, Kolkata

The world for over almost one and half year now has faced the pandemic of Corona, a disease by the Flu virus, diagnosed both by certain clinical and lab imaging tests.

The most important issue which is a hindrance of treatment types and vaccine discovery is mutation. During replication, a virus often undergoes genetic mutations that may create what are called variants. To understand the concept of the article one has to first understand basics of Mutation. Artificial intelligence has helped robots to identify the types of mutations and hence in demographic and geographical distinctions. We have observed, being inspired by the notable discovery of the famous mathematician, Alan Turing, that only a machine can decipher the encoded signals used during German bombings, an invention of the modern computer, which cut short the second world war by at least three years saving millions of lives. Hence it is a feeling that a Robot instilled with AI can identify mutations in the Corona virus before it occurs. References in this article are related to AI but not the topic directly as if everything was found in literature no scientific discovery would have taken place.

Mutation

Mutation causes the DNA in the virus to send altered signals to its RNA and finally the RNA produces such proteins which after binding to the specific (ACE-2 receptor in humans) receptor enter the body and can create new kinds of damage to various organ systems. Some mutations however may weaken the virus too fortunately. Others may yield some advantage that enables the variant to proliferate. (8) Variants with distinctly different physical characteristics may be co-termed a strain. (7) The variant that emerged in England in September, B.1.1.7, contributed to a surge in cases that sent the U.K. back into lockdown in January. In southern Africa, hospitals faced pressure from a resurgence driven by another variant, 501Y.V2. (South African strain). The Brazilian strain, so-called P.1 variant spotted in Manaus, Amazonas state, in December may have driven a surge in cases that strained the health system and led to oxygen shortages.

At present in India that what is being thought to be a 2nd Covid-19 wave is actually mixed with a new mutant strain –B.1.167 which is affecting young people, not responding to standard regimens, responding with great difficulty to monoclonal antibodies(costly), killing, in days normal apparently absolutely healthy individuals in 18-45 years age group, the bread earners and the country's future.

How quickly have the strains spread?

Rapidly, aided by year-end holidays traditionally associated with increased family and social mixing.

Broadly, they pose different concerns of varying degrees. These relate to their:

State	B.1.1.7 (VOC)			B.1.351 (VOC)			P1 (VOC)			B.1.617 (VUI)			Total VOC/VUI
	Tr&Co	Community	Total	Tr&Co	Community	Total	Tr&Co	Community	Total	Tr&Co	Community	Total	
ANDHRA PRADESH	28	32	60	3	3	6					143	143	209
BIHAR	4	5	9			0					5	5	14
CHANDIGARH		51	51			0						0	51
CHATTISGARH	1	19	20			0					75	75	95
DELHI	91	391	482	4	19	23				1	106	107	612
GOA	4	2	6			0					1	1	7
GUJARAT	18	42	60	2		2					102	102	164
HARYANA	6	14	20			0					1	1	21
HIMACHAL PRADESH		34	34			0					2	2	36
JAMMU & KASHMIR		25	25			0				1	13	14	39
JHARKHAND		14	14								61	61	75
KARNATAKA	40	42	82	0	0	0				15	131	146	234
KERALA	15	3	18			0						0	18
LADAKH	1	5	6			0					1	1	7
MADHYA PRADESH	4	51	55			0					53	53	108
MAHARASHTRA	35	53	88	5	1	6	1		1		870	870	965
ODISHA	3	28	31			0					39	39	70
PUDUCHERRY	23		23	1		1					23	23	47
PUNJAB	8	508	516	1	1	2					1	1	519
RAJASTHAN	5	18	23			0						0	23
SIKKIM		0	0			0					0	0	0
TAMIL NADU	14	1	15	2		2						0	17
TELANGANA	148	53	201	62	7	69	0			1	76	77	347
TRIPURA		0	0		0	0					0	0	0
UTTAR PRADESH	17		17	1		1						0	18
UTTARAKHAND	1	25	26			0					5	5	31
WEST BENGAL	14	26	40	6	3	9					124	124	173
Total	480	1442	1922	93	34	127	1	0	1	18	1832	1850	3900

Figure 1

- Transmissibility, or propensity to spread
- The severity of illness they cause
- Neutralization capacity, or the likelihood they will infect people who have recovered from a previous bout of Covid-19
- Potential impact on vaccination through their ability to evade the protection that immunizations are designed to generate
- They increase in the basic reproduction number, or R0 (the average number of new infections estimated to stem from a single case) in the range of 0.39 to 0.93 – a "substantial increase." The international spread of these variants has also helped drive a rebound in Covid-19, with the number of new cases reported worldwide increasing each week since mid-February.
- U.S. health officials said in late March that a variant-induced resurgence of cases in some regions could augur a long-feared possibility:
- That another surge could occur even as states are flinging open vaccine eligibility criteria, trying to get shots in arms as quickly as possible.

How many mutations are there?

- Many thousands of mutations and distinct lineages have arisen in the SARS-CoV-2 genome since the virus emerged in late 2019. A variant with a so-called D614G mutation emerged in early 2020. By June, it had replaced the initial strain identified in China to become the dominant form of the virus circulating globally.
- Months later, a novel variant linked to farmed mink was identified in a dozen patients in North Jutland, Denmark, but doesn't appear to have spread widely.
- As SARS-CoV-2 continues to circulate, more mutations will arise, potentially leading to more variants. (9)

State-wise Variants of Interest and Variants of Concern in India as of 05.05.2021

Data from INSACOG, May 2021

Algorithm of Artificial Intelligence

Concept of Artificial Intelligence (AI)

AI-powered early warning systems can help detect epidemiological patterns by mining mainstream news, online content and other information channels in multiple languages to provide early warnings, which can complement syndromic surveillance and other healthcare networks and data flows.

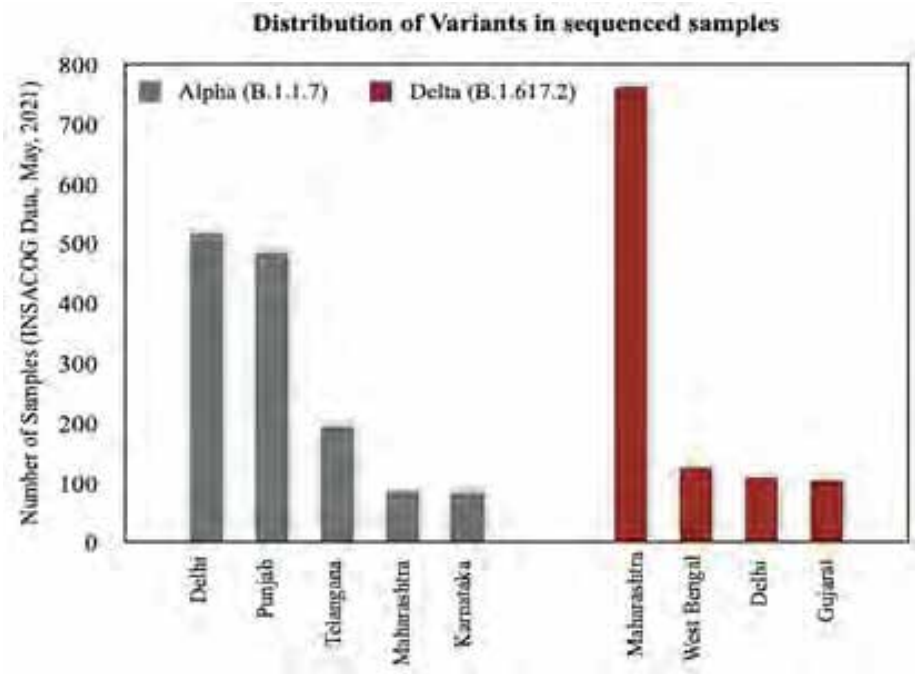

Figure 2: Distribution of variants in sequenced samples

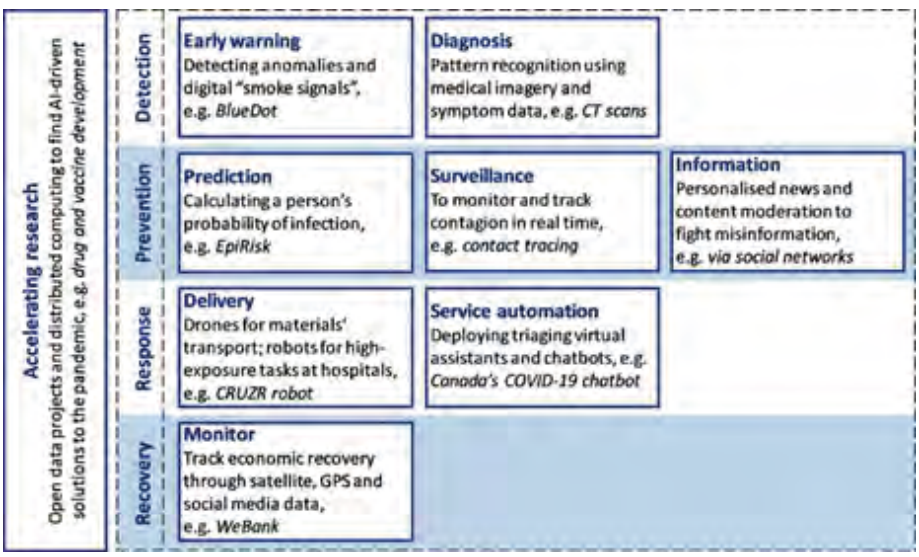

Figure 3: Algorithm of Artificial Intelligence

AI tools can help identify virus transmission chains and monitor broader economic impacts. In several cases, AI technologies have demonstrated their potential to infer epidemiological data more rapidly than traditional reporting of health data. Institutions such as Johns Hopkins University and the OECD (oecd.ai) have also made available interactive dashboards that track the virus' spread through live news and real-time data on confirmed coronavirus cases, recoveries, and deaths. (2)

Rapid diagnosis is the key to limit contagion and understand the disease spread. Applied to images and symptom data, AI could help to rapidly diagnose COVID-19 cases. Attention must be given to collecting data representative of the whole population to ensure scalability and accuracy. Limiting contagion is a priority in all countries and AI applications are helping prevent the virus' spread.

Role of Robots or Drones

Semi-autonomous robots and drones are being deployed to respond to immediate needs in hospitals such as delivering food and medications, cleaning and sterilisation, aiding doctors and nurses, and performing deliveries of equipment.

AI can assist the response to the crisis, and the recovery to follow

Conversational and interactive AI systems help respond to the health crisis through personalised information, advice and treatment, and learning.

To fight misinformation – the COVID-19 "infodemic" – social networks and search engines are using personalised AI information and tools and relying on algorithms to find and remove problematic material on their platforms.

Identifying, finding and contacting vulnerable, high-risk, individuals. For example, Medical Home Network, a Chicago-based non-profit, has implemented an AI platform to identify Medicaid patients most at risk from COVID-19 based on risk of respiratory complications and social isolation.

AI may eventually play a role in accelerating training and education of healthcare personnel.

Finally, AI tools can help monitor the economic crisis and the recovery – for example, via satellite, social networking and other data (e.g. Google's Community Mobility Reports) – and can learn from the crisis and build early warning for future outbreaks. (4)

AI in Detection of COVID-19 Variants

Artificial Intelligence (AI) has been applied in the field of medical applications extensively in order to improve the effectiveness, productivity and consistency of health care. It has also tasted success in basic research. Protein sequences and genetic codes can be modelled using Natural Language Processing (NLP) techniques and to detect mutations. A study by Berger et al. highlights the idea of a viral immune escape through mutation and how NLP can be instrumental in detecting this. Viral samples from patients may take weeks to get sequenced in a lab and then the mutations need to be re-created and studied to understand variations. AI based models can speed this up and predict potential mutations immediately. (6)

Grammar and semantics have been used to identify a virus - a successful virus is grammatically correct while an unsuccessful one is not. For viruses, the embedding of the genetic sequences grouped viruses according to how similar their mutations were. The system looks for similar grammatical structures but very different meanings, and it flags mutations for review if their meanings have changed the most. The top mutations detected by the NLP algorithm were checked against real viruses in a lab to see how many were escape mutations. The accuracy scores ranged from 0.69 for HIV to 0.85 for coronavirus.

The ability for viruses to mutate and evade the human immune system, a term called viral escape, is an obstacle vaccine development, hence understanding the complex rules of this escape, using machine models, could design therapeutic design.

Such designs preserve viral infectivity but cause the virus to look different to the immune system.

This approach language models of Influenza hemagglutinin, HIV-Envelope protein and presently, SAARS CoV2 spike proteins can accurately predict structural escape patterns which be a promising conceptual bridge between natural language and viral evolution.

Using these tools accelerates the process of detecting virus behaviour - and time is of essence in this ongoing battle against COVID19. (10)

Will this concept be able to change the idea of investing on development of vaccines of combining them?

This might be true if this concept of AI can be used in robots to detect mutations, by using AI in them vaccination picture will also change in future.

Data are emerging, and no clinical studies have directly compared different vaccine types and their ability to protect against the new strains. Overall, 10 vaccines have proved effective in clinical trials at preventing severe disease and death from Covid-19. The studies suggest, however, that some may not be as good at stopping less severe illness in countries where particular variants predominate.

The impact, (Vaccine combination) though, isn't likely to be significant, according to the WHO but still is an interesting area of research. That further intensifies the idea that development of one after other vaccine or combining them may actually change once Robots instilled wit AI can detect the exact anticipated mutation.

Summary

Thus, if AI can be of help in such rapid detection of Covid in demography, there can be a scope to research on further. (5)

Likely this means that instilling in Robots can in future help them to identify the DNA coding change in virus, before it occurs, the main idea behind anticipating a new mutant of Corona virus before its outbreak. (10)

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WHO label	Pango lineage	GISAID clade/lineage	Nextstrain clade	Earliest documented samples	Date of designation
Alpha	B.1.1.7	GRY (formerly GR/501Y.V1)	20I (V1)	United Kingdom, Sep-2020	18-Dec-2020
Beta	B.1.351	GH/501Y.V2	20H (V2)	South Africa, May-2020	18-Dec-2020
Gamma	P.1	GR/501Y.V3	20J (V3)	Brazil, Nov-2020	11-Jan-2021
Delta	B.1.617.2	G/478K.V1	21A	India, Oct-2020	

Figure 4

An Approach to a Wrist Wearable based COVID-19 Prediction System to Protect Healthcare Professionals

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Fortis Hospital, Anandapur, Kolkata

Abstract— With healthcare professionals being the frontline warriors in battling the Covid pandemic, their risk of exposure to the virus is extremely high. We present our experience in building a system, aimed at monitoring the physiology of these professionals 24/7, with the hope of providing timely detection of infection and thereby better care. We discuss a machine learning approach and model using signals from a wrist wearable device to predict infection at a very early stage. In a double-blind test on a small group of patients, our model could successfully identify the infected versus non- infected cases with near 100% accuracy. We also discuss some of the challenges we faced, both technical and non-technical, to get this system off the ground as well as offer some suggestions that could help tackle these hurdles.

Synopsis

Currently there is one doctor for every 1,445 Indians as per the country's current population estimate of 1.35 billion, which is lower than the WHO's prescribed norm of one doctor for 1,000 people [1]. This shortage of doctors (and nurses) coupled with the fact that frontline health care workers are most likely to be exposed to the virus than anybody else, makes protecting them critical.

Most of the prior art revolve around detection of Covid- 19 from radiology images such as X-rays of lungs via image processing techniques and deep learning models [2]– [4]. But such methods can prove successful, only when subjects opt for such test post a doctor consultation. Recently a study using two years of Fitbit data from nearly 50,000 users found that wearable data could more accurately predict local flu outbreaks than the standard system used by the Centers for Disease Control and Prevention [5]. Other works such as [6], [7], show how self-reporting and wearable data can act complementary to virus testing. Since coronavirus and the seasonal flu share some symptoms, it could be possible to develop an algorithm that utilizes physiological data in building an artificial intelligence (AI) based early warning system. Such a system could help predict the onset of symptoms and identify whether a health care worker might have been infected with the virus (and thus assist in timely action). Also, it would give confidence to frontline health care professionals (HCP) that they are healthy and continuously being monitored for risk.

Our approach was to develop an AI based system that will provide an early warning to the health care professionals who are actively involved in the Covid-19 wards and ICUs. The system will monitor the vital parameters such as Heart Rate, Respiratory Rate, Activity, Skin Temperature on a continuous basis with the facility to visualize the trends at individual level. We also propose to collect continuous photo plethysmography (PPG) signals and develop an AI model which can be used to predict early signs of infection.

We teamed up with Fortis Healthcare Limited, a leading integrated healthcare services provider in India that had an active Covid-19 ward to conduct a study involving HCP involved in management of Covid-19. The study was registered as a cross sectional type observational trial at the Clinical Trials Registry-India (CTRI)1, approved by the ethical committee at Fortis and conducted on volunteers in the age group of 19 to 60. All the volunteers signed an informed consent before participation.

The pilot study, that started in the mid-week of June, 2020, involves 10 healthcare professionals (7 doctors, 2 nurses, 1 Technician) from Fortis hospital in India treating coronavirus patients. The device would be worn for 24 hours (including during their 8-12-hour shifts) a day, except when there is some discomfort or during use of wash room/shower, with data synchronization and device charging/sanitization occurring prior to the start of their shift. At the time of onboarding, data such as blood pressure, body temperature (Axila), oxygen saturation (SpO2) and heart rate are captured using medical grade device to serve as a baseline measure. To maintain data privacy, the hospital staff handle mapping of device to participant and only a user ID stored in the database.

Given the restriction of carrying a mobile device during their shift, and in particular within the covid ward, the E4 device operates in 'record'

mode where data is stored locally on the device and later synchronized offline to the Empatica cloud. The Empatica portal allows us to download this synchronized data post which we upload (and process) on our EzyDoc analytics server. The EzyDoc portal also has an interface through which the hospital can view the different measures of their staff.

Conclusion

This paper proposes a pipeline to detect abnormalities from a normal behaviour, based on trained classifier and smoothened version of longitudinal prediction over a period of time. In this paper we demonstrate the same with a use case of current COVID-19 pandemic, where data from several front-line workers from a reputed hospital in India is collected, analysed to build a machine learning model which is then used further to obtain prediction on a longitudinal basis to assert whether a subject is at risk. This pipeline is not limited to COVID 19 pandemic but can be re-used to obtain a generic framework for such other use cases. Proposed systems is primarily for HCP as they are at the highest risk due to continuous exposure. The idea is to boost their confidence by providing a system for early warning. Patients have already turned positive and hence such monitoring is not useful. Further the system is not limited to only frontline workers but can easily reused for general consumers for longitudinal monitoring.

We would further like to make it clear, as per above use case, our objective is not to replace RT-PCR tests, by longitudinal monitoring via a wearable device, instead we want develop a system that can act as an assistive aid for the subject to monitor the vitals as well as raise alerts for the subject when the pipeline foresees a risk. Our key contribution is a system that can predict the onset of the infection trend a few days in advance of the actual clinical deterioration/classical symptoms appear. As we know, in asymptomatic patients, RT-PCR becomes positive in 5 to 7 days of contracting the virus. The alerts can be used to initiate a standard physical examination and RT-PCR test to confirm the findings leading to early interventions and thereby avoiding clinical complications of the disease such as cytokine storm.

In our study, we have proposed a Boolean model and architecture for implementation in an automated fashion, along with how we have overcome the technical and non-technical challenges. Although our results are very good, the number of subjects available for training and testing are very limited. Hence the results have to be further validated on larger datasets. Currently the final verdict of a subject being Covid positive is given based on manual observation of the positive ratio plots which needs to be automated for future needs.

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COVID-19 Neurological Manifestations: A Collaborative Work

Dr Rajesh Benny
Senior Consultant - Neurology
Fortis Hospital, Mulund

The COVID-19 pandemic caught the nation and most of us unawares about the magnitude of the medical problem that was going to unravel over the next 2 years. COVID-19 was recognized initially as a primary respiratory infection, but complications due to its ability to cause thrombosis and multisystem involvement were being increasingly reported. Involvement of the nervous system was first published in March 2020, not surprisingly, from the medical centres at ground zero (Wuhan). The authors found neurological manifestations to be rare in COVID- 19 and observed it only in those with very severe infections or in the later stages of the disease, usually in the second week of illness after the onset of respiratory symptoms.

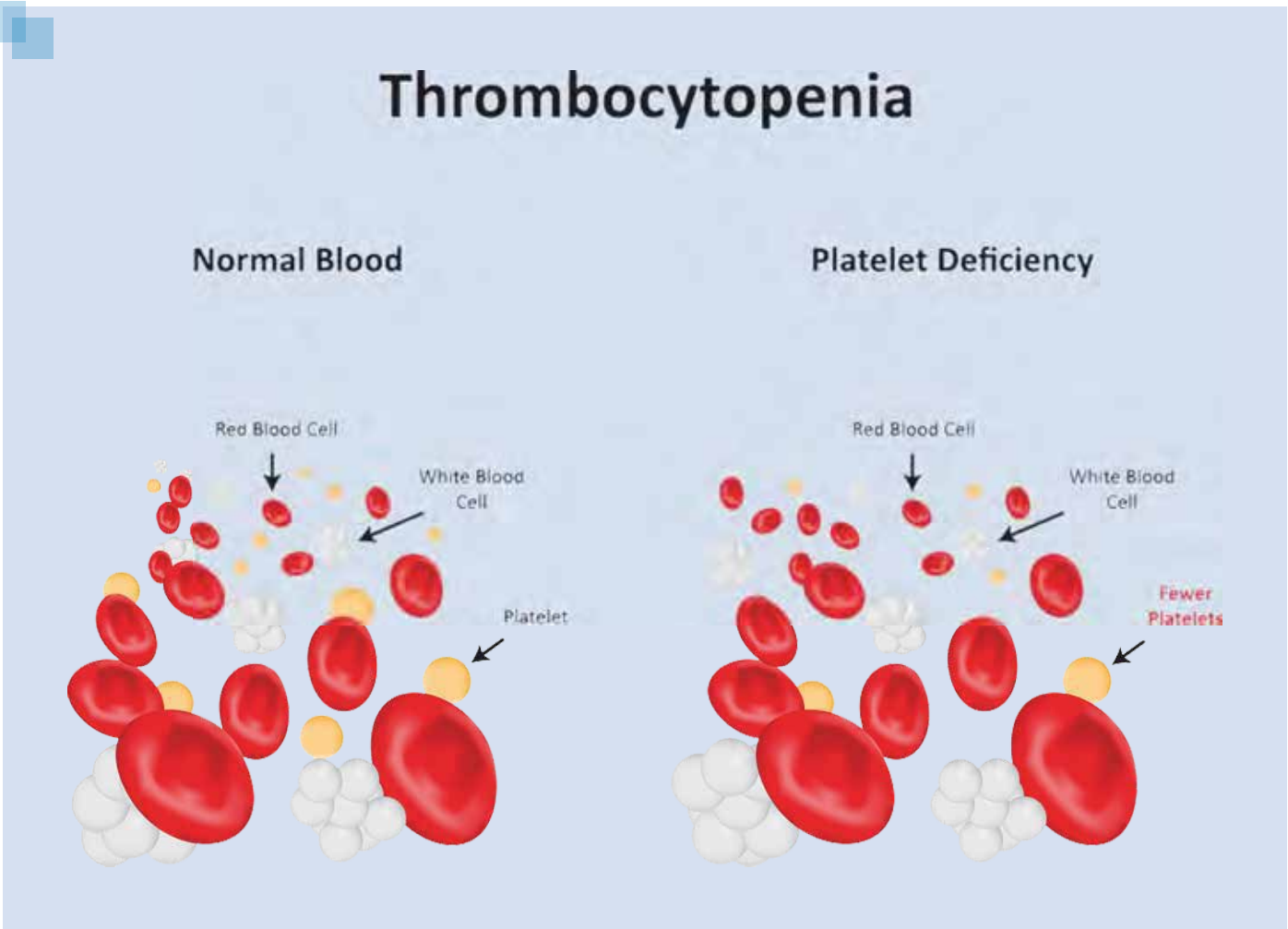
We were already witnessing a deluge of COVID- 19 cases at our institute (Fortis Hospital, Mulund). Day after day we were observing a greater number of patients presenting to the emergency room with neurological manifestations, in much higher numbers and varied presentations that were not yet reported in the literature. To study them further, we devised a Google form in March 2020 comprising 106 questions, to prospectively collect data to characterize all the neurological features of those with COVID- 19. We also shared this google form with neurologists managing COVID- 19 cases in local nursing homes around the periphery of our institute. This was our first attempt at a collaborative work between the neurology department of our institute and neurologists practicing in smaller nursing homes. The data which was collected was standardized and anonymized.

ChAdOx1 nCoV-19 Vaccine Induced Thrombotic Thrombocytopenia: A Case Report

Dr Shivani Juneja
Head - Pharmacology
Fortis Hospital, Mohali

Dr (Lt Col) Harmandeep Singh Brar
Consultant – Neurosurgery
Fortis Hospital, Mohali

The case report is of an 18-year-old patient who suffered from multiple site thrombosis with thrombocytopenia. The patient was apparently well before vaccination and had no comorbidity. After five days of the first dose of COVID vaccination, he started having fever, headache, chills, with worsening of symptoms such as left side limb weakness. All relevant tests were performed in view of the symptoms at the time of presentation in a tertiary care hospital. Subsequently, various life-saving surgeries were performed in the hospital, including decompressive craniotomy, IVC filter insertion and laparotomy and resection and anastomosis. The possible cause for this event was attributed to vaccination with Covid-19 vaccine (Covishield). VITT was reported as a rare adverse effect following immunization for otherwise healthy young adults. The findings of our case report suggest that VITT needs thorough analysis and can be more frequent than has been reported in previous studies in which the safety of the ChAdOx1 nCoV-19 vaccine has been investigated.



Characteristics and Outcomes of 100 Consecutive Patients with Acute Stroke and COVID-19

Dr Rajesh Benny
Senior Consultant - Neurology
Fortis Hospital, Mulund

This article was the largest series about acute strokes in COVID- 19 in world literature when it was published in 2021. We analyzed data from 100 consecutive patients presenting with acute stroke (ischemic, hemorrhage, or venous infarcts) and COVID- 19 over a 5-month period in 2020. Prior to this study, stroke was reported to be an unusual complication (1.44%- 1.74%) of COVID- 19, which occurred late in the disease course (usually in the second week) and especially in those with severe infections.

In our study, we observed stroke as a presentation of COVID- 19 in 67% of patients. During that period, most centers across the country and the world were doing an HRCT chest to dichotomize patients as COVID- 19 or noninfected. 22% of our study patients with stroke who underwent an HRCT of the chest to look for subclinical COVID- 19, had a normal scan. These patients would have been misdiagnosed as non-COVID-19 strokes if the hospital policies did not dictate the need for RT PCR testing for SARS-CoV-2 virus for all those needing hospitalization. We emphasized that stroke as a distinctive presenting feature of COVID-19 needed to be recognized as these patients can be responsible for the nosocomial spread of infection.

51.3% of patients in our study with acute ischemic stroke (AIS) had non-severe COVID-19 implying that even those with mild COVID-19 disease were at a risk to develop stroke. In our study, we observed raised CRP (87.5%) and D dimer (75%) levels even in those with non-severe COVID-19 and AIS. This perhaps explained the propensity to AIS even in those with mild to moderate COVID-19 as both CRP and D dimer is considered to be thrombogenic.

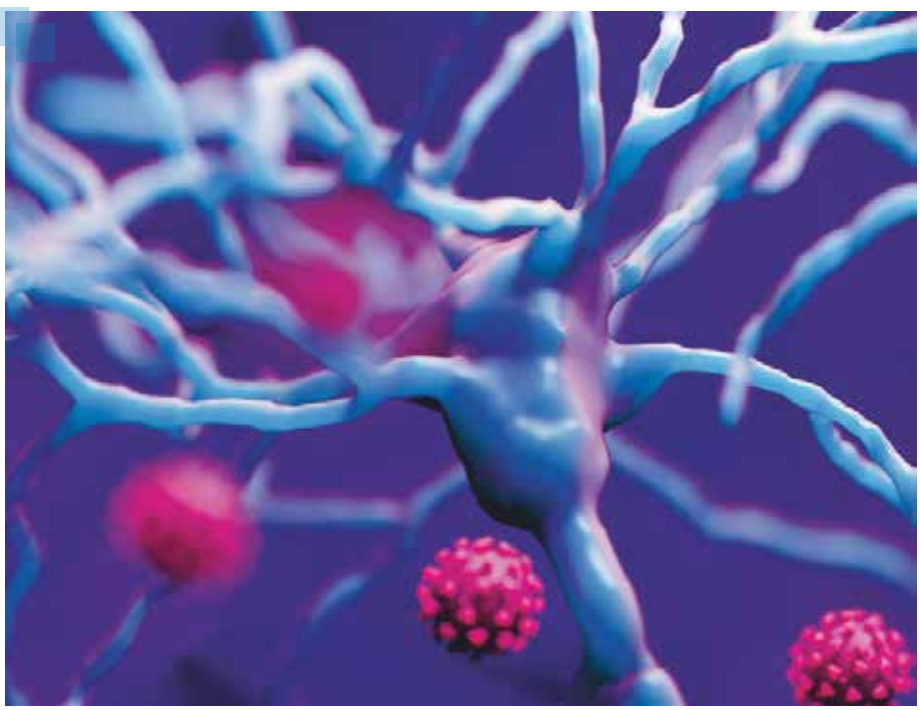
We observed certain neurological markers which could predict the progression from mild COVID- 19 at admission to severe disease eventually during their stay in the hospital: These patients were more likely to present with altered sensorium and a low GCS on admission, had a propensity for multiple territory strokes and large vessel occlusion.

The prevalent understanding during that period was that COVID- 19 strokes had higher mortality when compared to non-COVID- 19 strokes. We compared the data of 78 of our COVID-19 patients with AIS to 100 patients with non-COVID-19 AIS (admitted during the same period). Though deaths were higher in those with COVID-19 strokes (28.2% versus 17%), they did not differ statistically between the two groups in our study.

We also included those with intracerebral hemorrhage (ICH) and cerebral venous thrombosis (CVT) in this study. Though their numbers were small, we observed some interesting findings. We reported 9 patients with ICH who were young (mean age 55 years), most did not have the traditional risk factors associated with ICH and had ICH as a presentation of COVID- 19 (most earlier studies had reported ICH due to the use of heparin in those with severe COVID- 19).

All our 13 patients with CVT and COVID- 19 had raised D dimer levels, were young, 76.9% had non-severe COVID- 19, and had low mortality (most studies were reporting CVT associated with COVID- 19 only in those with severe disease, old age and with higher mortality). This contrasting data encouraged us to study this subset of stroke patients in much more detail. This formed the basis of our second study.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7887446/



Cerebral Venous Thrombosis in COVID-19

Dr Anil Venkitachalam
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Fortis Hospital, Mulund

Dr Rakesh Lalla
Consultant - Neurology
Fortis Hospital, Kalyan

Dr Rajesh Benny
Senior Consultant - Neurology
Fortis Hospital, Mulund

This was a multicentric, retrospective study conducted between April 4 and October 15, 2020, that included adult patients with CVT who were positive for the SARS-CoV-2 virus and compared them with CVT patients who were negative for the SARS-CoV-2 virus hospitalized during the same period.

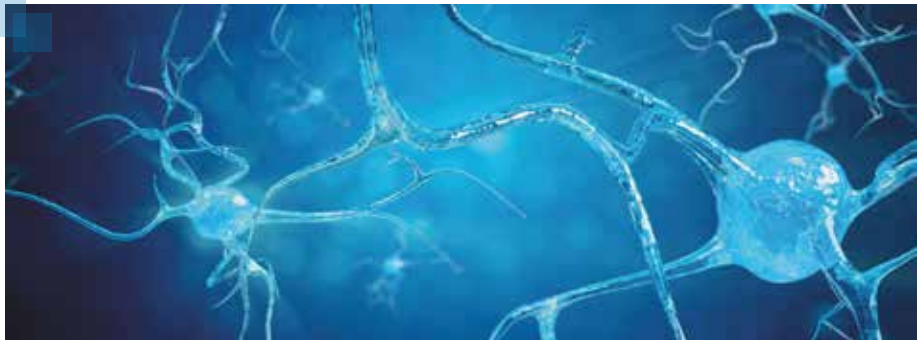
We included 18 COVID-19 patients (the largest series in world literature during that period) and compared them with 43 non-COVID-19 CVT patients. The majority of our subjects (73.7%) with COVID- 19 and CVT presented with clinical manifestations of CVT (headaches, seizures, focal neurological dysfunction, or drowsiness) without the other typical features of COVID-19.

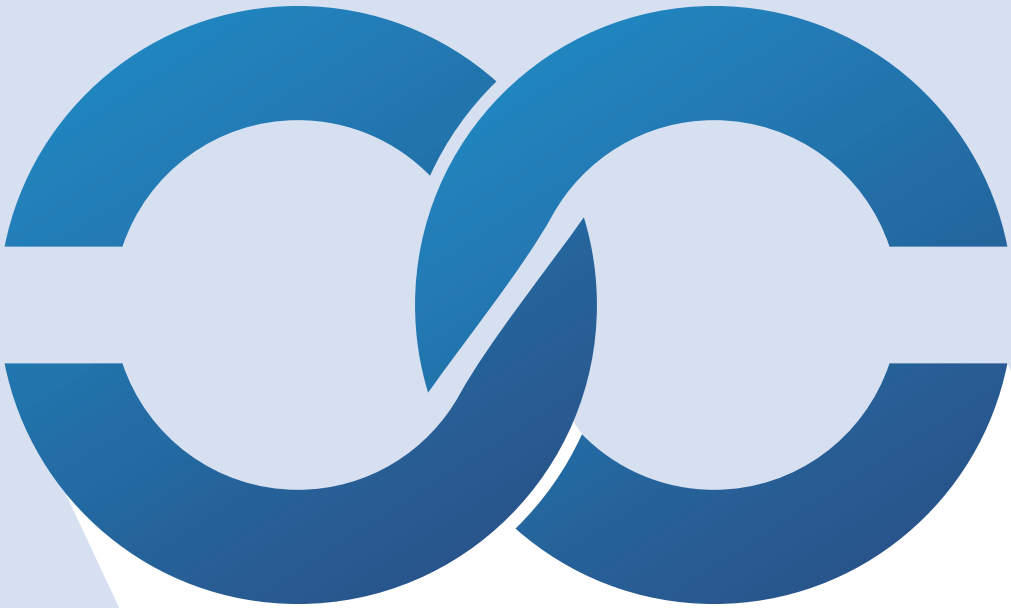
Most of our patients (72.2%) had non-severe COVID-19 and had a good outcome (mRS ≤2) (66.7%). Mortality and disability outcomes were not significantly different between the two groups.

Our non-COVID-19 CVT patients were more likely to have at least one risk factor for thrombosis as compared to those with COVID-19-infected CVT (76.4% vs. 44.44%); suggesting that COVID-19 infection possibly leads to CVT. Our study was among the pioneering work that suggested a possible association between COVID-19 and CVT. We also observed CVT as a presenting manifestation of an underlying COVID-19, which could occur early in the course of COVID-19 and even in those with mild disease. Only those patients with a worse GCS on admission, abnormal HRCT chest, severe COVID-19, and need for invasive ventilation had a poor outcome in our study.

We were also invited to write a review for the Annals of Indian Academy of Neurology (the official journal of the Indian Academy of Neurology) on the neuromuscular manifestations of COVID- 19 in March 2020.

These were the early days of COVID-19 pandemic and neuromuscular complications were rarely reported. Myositis was observed in 10.7% of patients with severe COVID- 19 by the Wuhan group. When this review was written in April 2020, we found only a single case of Guillain- Barre` syndrome (GBS) reported from Wuhan associated with COVID- 19. This encouraged us to design another study as we had already observed two cases of GBS associated with COVID- 19.





CLINICAL RESEARCH

A Phase-III, randomized, double-blind efficacy and study comparing SAR442168 to teriflunomide (Aubagio®) in participants with relapsing forms of multiple sclerosis (GEMINI 2)

Dr Praveen Gupta
Principal Director & Head - Neurology
Fortis Memorial Research Institute,
Gurugram

- A chronic, typically progressive disease involving damage to the sheaths of nerve cells in the brain and spinal cord, whose symptoms may include numbness, impairment of speech and of muscular coordination, blurred vision, and severe fatigue.
- Total no. of sites in India - 06
- Total sample size from India: 50

Dr Praveen Gupta from FMRI has successfully enrolled 06 patients

Primary Objective

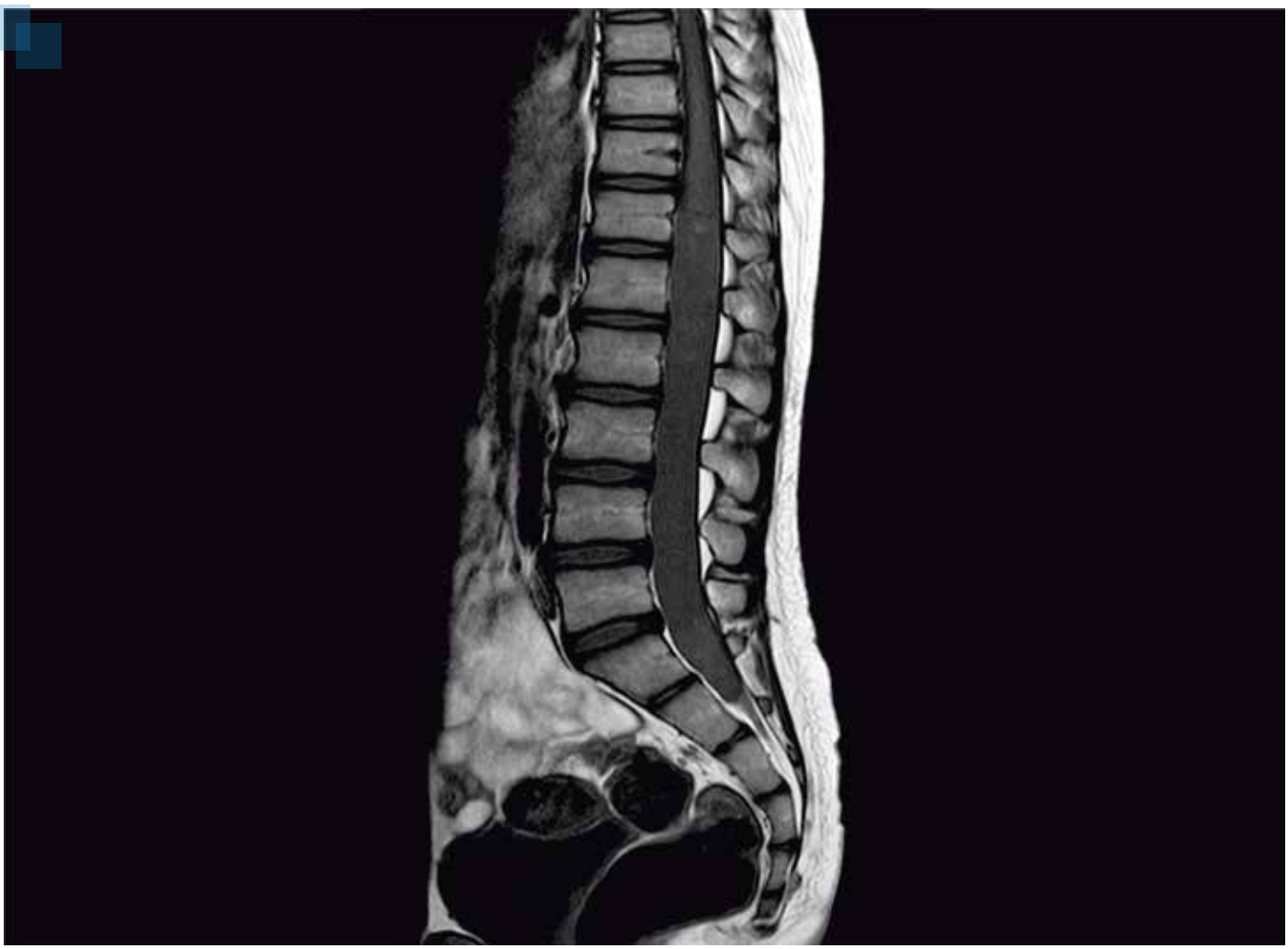
To assess efficacy of Study medication compared to 14mg Teriflunomide (Aubagio) in participants with relapsing forms of Multiple Sclerosis.

Potential Benefits

- Study Medication is expected to reduce MS relapse rate, disability progression, and underlying CNS damage through its dual action on adaptive immunity in the periphery and innate immunity and the inflammation process in the CNS.
- Trend toward normalization of brain volume loss.
- Reduction in neuro inflammation.

PI Opinion

Multiple sclerosis is chronic remitting relapsing and progressive illnesses that damages the nervous system of young adults. Though there are many available disease modifying treatments there are still number of patients not responding to current treatments. In this context BTK1 inhibitors offer a new avenue for treatment to patients with all forms of multiple sclerosis. At this point of time, patients are doing well with low incidence of side effects.



Title 1: A Phase-III Multicentre, Randomized, Parallel Group, Double Blind, Double Dummy, Active Controlled Study of Evobrutinib Compared with Teriflunomide, in Participants with Relapsing Multiple Sclerosis to Evaluate Efficacy & Safety (RMS1_MS)

Title 2: A Single Arm Phase IV Clinical Trial to Describe the Safety & efficacy of Teriflunomide in Patients with Relapsing Forms of Multiple Sclerosis (SAFE study)

Dr Madhuri Behari
Director and Head - Neurology
Fortis Flt Lt Rajan Dhall Hospital,
Vasant Kunj, New Delhi

Dr Madhuri Behari is doing two studies on Multiple Sclerosis. One is a Phase III study in which site has enrolled three patients and other Phase IV study in which site has enrolled nine patients.

Title 1: Phase-III Study

Total No. of Sites in India – 4

Total Sample size from India - 14

Title 2: Phase IV SAFE Study

Total No. of Sites in India – 15

Total Sample size from India - 193

Primary Objective

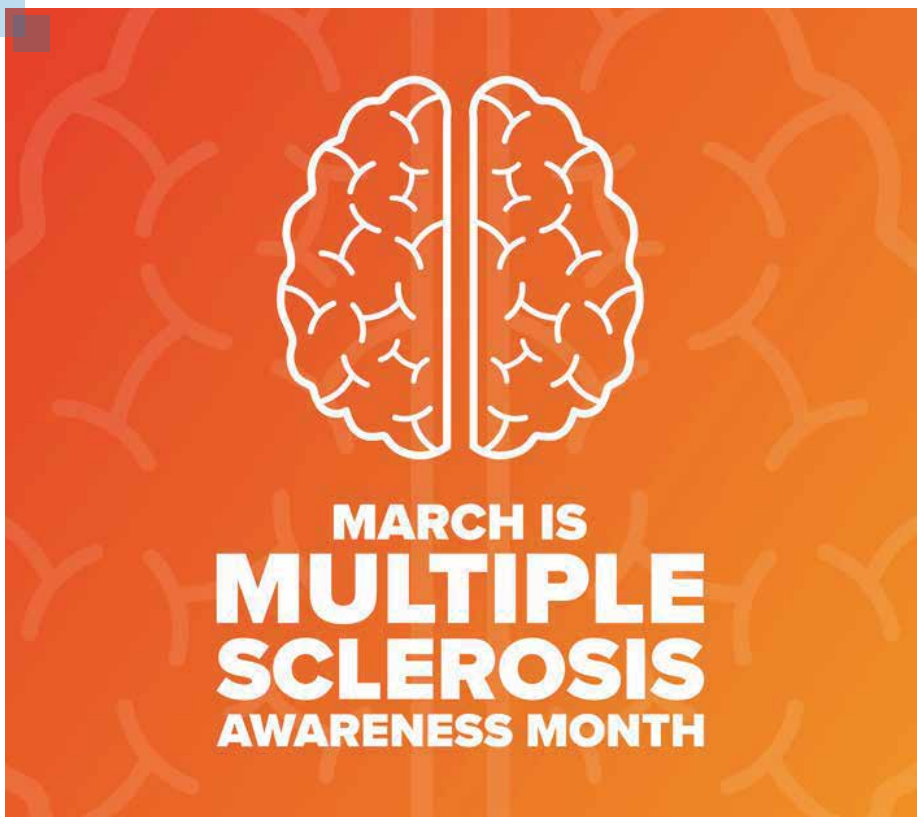
To demonstrate superior efficacy with Evobrutinib Compared with Teriflunomide in terms of Annualized Relapse Rate (ARR) and to describe the safety & efficacy of teriflunomide in patients with relapsing forms of multiple sclerosis.

PI Opinion for RMS1_MS Study

Relapsing Remitting Multiple Sclerosis is an autoimmune disorder of central nervous system, characterized by visual loss in one or both eyes, ataxia, double vision, hemiparesis, quadriparesis, bladder bowel disturbance and sensory disturbance in various combinations. Affecting young people, it can lead to dependence and even dementia. Several therapeutic agents are available which can modify the course of the disease (DMT), but none is free from side effects or with reasonable control of disease. In a quest for better DMT Evobrutinib is tested in this study against a well tried and tested DMT i.e. teriflunamide.

PI Opinion for SAFE Study

There is a need to find the best DMT for Relapsing remitting form of MS. MS is a devastating disease affecting young adults which can lead the severe disability in the bread earner of the family. Teriflunomide has been found to significantly reduce relapse rates in patients with RMS. This study was done to establish its safety in a post marketing trial.



A Phase-II, Randomized, Double-Blind, Placebo-Controlled Study of K0706 in Subjects with Early Parkinson's disease (SPARC Study)

Dr Madhuri Behari
Director and Head - Neurology
Fortis Flt Lt Rajan Dhall Hospital,
Vasant Kunj, New Delhi

Total no. of sites in India- 7

Sample Size in India- 50

Dr Madhuri Behari from Fortis Vasant Kunj has successfully enrolled 6 patients.

Primary Objective:

To determine if K0706 (Burton's Tyrosine Kinase Inhibitor) reduces the rate of progression of early-stage Parkinson's disease (PD) versus placebo over 40 weeks, as defined by the sum of MDS-UPDRS Part 2 &3 scores.

Potential Benefits

There is no cure for PD, this drug may fill the unmet need of persons with PD, if successful

PI Opinion

Parkinson's disease (PD) is a chronic progressive Neurodegenerative disease with loss of neurons of substantia nigra, resulting in decrease in dopamine levels and symptoms which are characterised by resting tremor, bradykinesia, rigidity and postural disturbance. Currently there is no cure of this malady. Tyrosine kinase is an enzyme in the pathway of synthesis of dopamine. This drug when given to patients with PD will increase the level of dopamine and prevent progression of PD.

Sprint India Study

Dr Neetu Ramrakhiani
Director - Neurology
Fortis Escorts Hospital, Jaipur

Total No. of sites in India – 25

Total Sample Size from India – 5830

Dr Neetu Ramrakhiani from Fortis Escorts Hospital, Jaipur has successfully enrolled 16 patients.

Recurrent stroke, cardiovascular morbidity, and mortality are important causes of poor outcome in patients with index stroke. Despite the availability of best medical management recurrent stroke occur in up to 15–20% of patients with stroke in India. Education for stroke prevention could be a strategy to prevent recurrent strokes.

Primary Objective

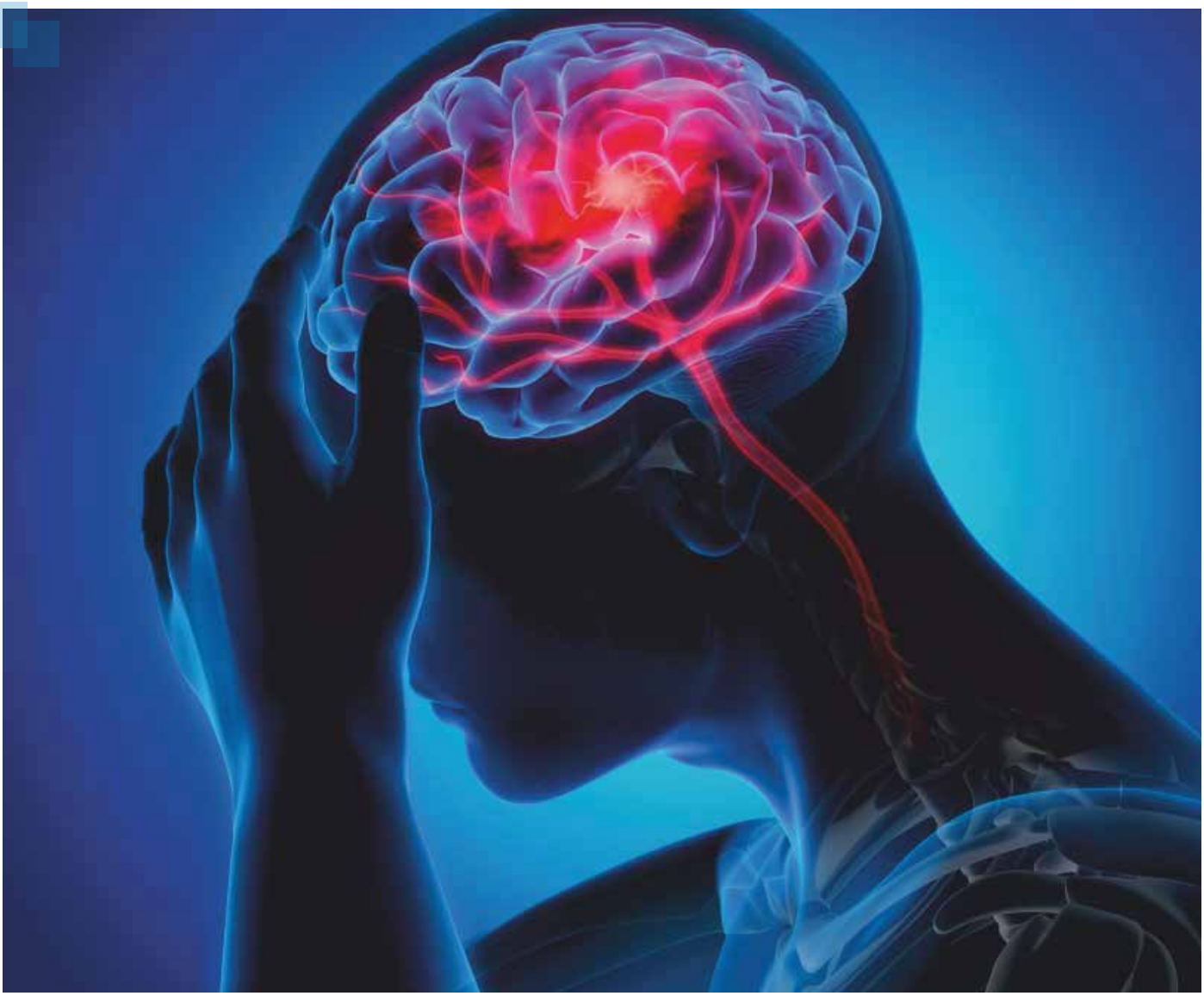
To reduce the risk of recurrent strokes, acute coronary artery syndrome, and death in patients with sub-acute stroke at the end of one year with the help of a structured semi-interactive stroke prevention package.

Potential Benefits

A structured semi-interactive stroke prevention package can reduce the risk of recurrent strokes, acute coronary artery syndrome, and death in patients with sub-acute stroke at the end of one year

PI Opinion

This study will encourage the development of appropriate tools for both pharmacological and non-pharmacological measures for reduction in recurrence of stroke and other end points of cardiovascular mortality.



Medication Safety Update: An Initiative of Fortis Central Pharmacy & Therapeutics Committee (CPTC)

MEDICATION SAFETY UPDATE
JULY 2022

TRAMADOL

IS A UNIQUE SHORT ACTING OPIOID THAT IS CONSIDERED BY MANY PHYSICIANS TO BE SAFER THAN OTHER SHORT ACTING OPIOIDS.

SCHEDULE / CONTROL

SCHEDULE H1 PRESCRIPTION DRUG- CAUTION

High Alert Medication

RECOMMENDED DOSING

- Adults (not approved in patients less than 17 years of age):
  Tolerability is improved by a slow titration regimen: Start with 25mg q day (at bedtime). Titrate in 25mg increments as separate doses every 3 days to 25mg q.i.d. Thereafter, increase the daily dose by 50mg every 3 days to 50mg q.i.d. After titration, 50mg to 100mg may be given q 4 to 6 hours prn, not to exceed 400mg/day.
- Impaired renal function: In patients with CrCl < 30ml/min, adjust dosing interval to q 12 hours; max dose should not exceed 200mg/day. Dialysis patients can receive their dose on dialysis days.
- Impaired liver function: In patients, with cirrhosis, dose should be adjusted to 50mg q 12hours.
- The Elderly: In patients over 65, titrate more cautiously. In patients over 75, max dose is 300mg.
- Discontinuation: Withdrawal symptoms may occur if tramadol is discontinued abruptly. Symptoms may include anxiety, sweating, insomnia, rigors, pain, nausea, tremors, diarrhoea, upper respiratory symptoms, piloerection, and rarely hallucination. Clinical experience suggests that withdrawal symptoms may be relieved by tapering the dose.
- **Use for severe acute pain only for period, not exceeding 5 days**

PRECAUTIONS

- Concomitant use of Tramadol increases risk of seizures in patients taking SSRIs, anorectics, neuroleptics, tricyclics, cyclobenzaprine, promethazine, opioids, MAOIs or any other drugs that lower the seizure threshold.
- Seizures have been reported in patients receiving Tramadol within the recommended dosage range, and even following the first dose.
- Serotonin syndrome – characterized by atypical chest pain, sinus tachycardia, confusion, psychosis, sundowning, agitation, diaphoresis, and tremor – has been reported when tramadol was administered with an Selective Serotonin Reuptake Inhibitors (SSRI).
- Prolongation of the INR and PT and extensive ecchymoses have been reported in patients receiving Tramadol with warfarin.
- Tramadol should be used with caution in patients with increased intracranial pressure or head injury. Pupillary changes (miosis) from Tramadol may obscure the existence, extent, or course of intracranial pathology.

IMPORTANT NOTES CONCERNING POTENTIAL DEPENDENCE & ABUSE

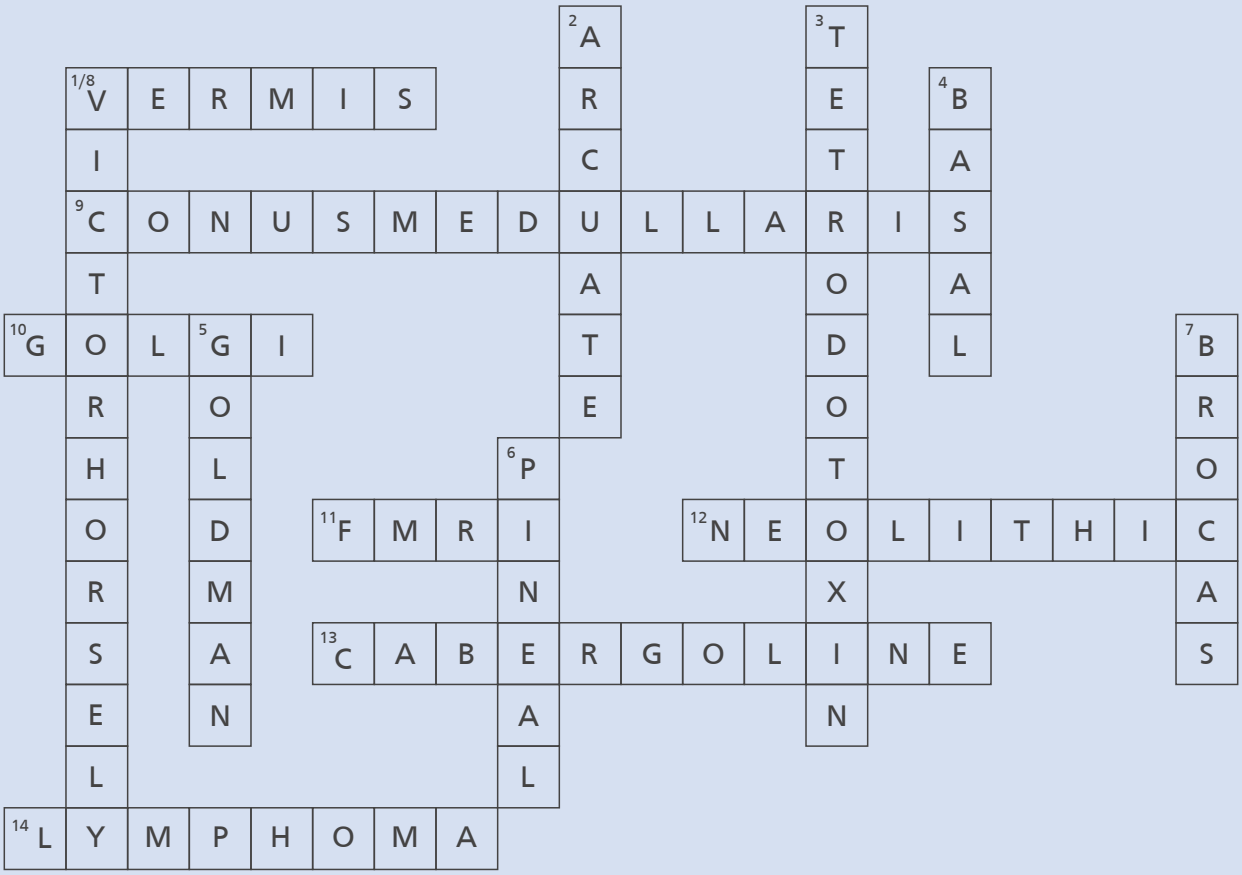
- Tramadol may induce psychic and physical dependence of the morphine (μ-opioid) type, thus should not be used in patients that are currently opioid-dependent. Methadone is a reasonable alternative.
- Tramadol has been associated with craving, drug-seeking behaviour, and development of tolerance. Tramadol has been shown to reinitiate physical dependence in some patients that have been previously dependent on other opioids.

CONTRAINDICATIONS

- Tramadol should not be administered to patients who have previously demonstrated hypersensitivity to Tramadol, any other component of this product or opioids.
- Tramadol is contraindicated in any situation where opioids are contraindicated, including acute intoxication with any of the following: alcohol, hypnotics, narcotics, centrally acting analgesics, opioids or psychotropic drugs. Tramadol may worsen central nervous system and respiratory depression in these patients.

ADVERSE EFFECTS OF TRAMADOL

Answers To The Crossword



DOWN

1. **Victor Horsely** of London was the first surgeon to specialize in neurosurgery. (6,7)
2. Fibers of the striamedullares in the floor of fourth ventricle are derived from the **Arcuate** Nucleus.(7)
3. A toxin that blocks Na+ permeation through voltage-gated sodium channels, thereby blocking action potentials. **Tetrodotoxin** (12)
4. The **Basal** ganglia is the most common location for spontaneous intracerebral hemorrhage secondary to hypertension. (5)
5. The **Goldman** Equation is a mathematical relationship used to predict membrane potential from the concentrations and membrane permeabilities of ions. (7)
6. The gland that helps control the circadian cycle of sleep and wakefulness by secreting melatonin. **Pineal** (6)
7. The **Broca's** area is located in the inferior frontal gyrus. (6)

ACROSS

8. The midline region of the cerebellum. **Vermis** (6)
9. The myxopapillaryependymomas usually arise from the floor of the 4th **Conusmedullaris**. (15)
10. The **Golgi** Stain is the method of staining brain tissue that shows neurons and all of their neuritis; named for its discoverer. (5)
11. A functional neuroimaging procedure using MRI technology that measures brain activity by detecting associated changes in blood flow. **FMRI** (4)
12. The history of trepanation dates back to the **Neolithic** period. (9)
13. A dopaminergic agonist **Cabergoline**. (11)
14. The intracranial tumor most likely to be encountered in a middle-aged man with AIDS is **Lymphoma**. (8)

The Fortis Network

Amritsar


Anandapur, Kolkata

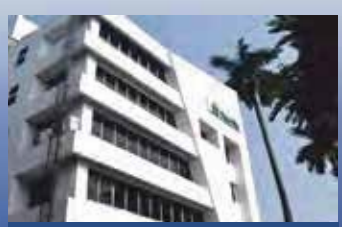

Bannerghatta Road, Bangalore

Chirag Enclave, New Delhi


Cunningham Road, Bangalore


Faridabad


FEHI, New Delhi


FHKI, Kolkata


FLF Greater Kailash, New Delhi


FMRI, Gurugram


Jaipur

Kalyan


Ludhiana


Malar, Chennai


Mohali


Mulund, Mumbai


Nagarbhavi, Bangalore


Noida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SL Raheja, Mumbai

Vadapalani, Chennai


Vasant Kunj, New Delhi


Vashi, Mumbai

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clinical.connect@fortishealthcare.com