A case of recurrent tumefactive demyelination or tumefactive multiple sclerosis

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Introduction

Tumefactive demyelinating lesion (TDL) is defined as a solitary demyelinating lesion larger than 2 cm[1]. Many patients have a history of multiple sclerosis (MS)[2]. It might present with intracranial space occupying lesion (SOL) like effects[3]. Magnetic resonance imaging (MRI) is important for diagnosis and it can be confirmed on histology via biopsy[4]. Tumefactive lesions should be differentiated from other causes of SOL in the brain for appropriate management. Both tumefactive demyelination (TD) and tumefactive multiple sclerosis (TMS) are very uncommon in children. We report a case of TD or TMS in an adolescent girl who developed recurrent central nervous system (CNS) symptoms over a span of 1.5 years. Though the first episode was treated as a tuberculoma, we are speculating that it is a case of recurrent TD or TMS.

Case report

A 12 year old right handed female, born of a non-consanguineous marriage, was admitted with the chief complaints of inability to speak since 2 months and weakness of both upper and lower limbs since 2 months. This patient was apparently well one and half years prior to admission when she had a episode of generalised tonic clonic convulsions lasting about 20 minutes followed by weakness of the left side of the body more pronounced in the upper limb. This was at another centre where an MRI of brain was done which was suggestive of ring enhancing lesions (Figure I). Tuberculoma was diagnosed provisionally and the child was started on oral prednisolone 2mg/kg/day with 4 anti-TB drugs (isoniazid, rifampicin, ethambutol and pyrazinamide) for 3 months followed by 6 months of 2 anti-TB drugs (isoniazid and rifampicin). However, there was no contact history of TB, there were no clinical features of TB and the BCG vaccination scar was present. Gradually, child started improving and started to go to school after two months of starting treatment. For around 14 months, the child was well except for minimal residual weakness in the left arm.

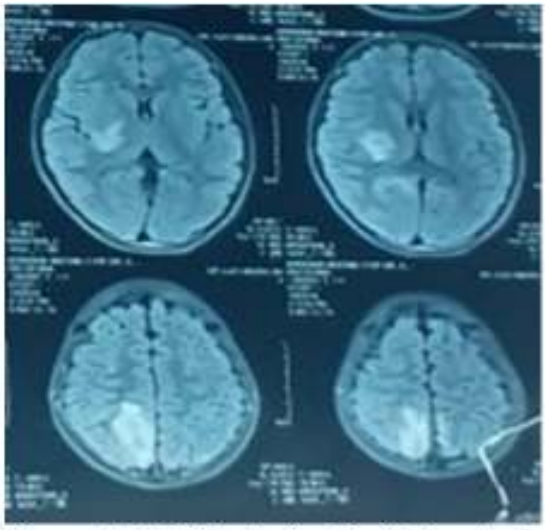

Figure I: ***MRI brain for the first episode showing ring enhancing lesions***

Then suddenly, one evening around two months prior to current admission, mother noticed that child's speech had become slurred followed by complete loss of voice over a few days. Along with the speech difficulty, the child also had loss of power in all four limbs simultaneously which was progressive. It was more on the right side compared to the left. After 3-4 days, child became bed ridden and was not able to hold up her neck. She also had loss of bowel and bladder control. She used to pass large amounts of urine infrequently. She had drooling of saliva and was not able to chew and swallow food.

On examination, she had spontaneous eye opening but was constantly staring towards the left side and not responding when called. Her pulse, blood pressure and respiration were normal. The child

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had gross wasting with the body mass index (BMI) 11.6 kg/m^2 indicative of undernutrition.

Fundoscopy showed bilateral early papilloedema. Measures to manage raised intracranial pressure were taken including use of hypertonic saline. Dynamic contracture in the tendo-achilles on the right side was noticed. On CNS examination, child did not respond when called, did not recognise parents, was constantly looking towards the left side and preferred to move left hand. She was unable to move her eyes to right (right sided conjugate movements were absent). Otherwise her cranial nerves were normal. Motor examination showed spasticity with grade 1 power in all four limbs. Deep tendon reflexes were exaggerated, with ankle clonus which was well sustained on the right side. Plantars were extensor on both sides. No meningeal signs were present.

MRI of brain showed multiple ill-defined variable sized altered signal intensity lesions in left parieto-temporal, basal ganglia, right parietal region appearing hypointense on T1/FLAIR, hyperintense on T2, showing linear and incomplete ring (open ring towards cortical grey matter), also signs of perilesional oedema causing mass effect in the form of midline shift towards left suggestive of demyelination most probably tumefactive demyelination (Figure 2). Screening spine MRI showed multiple well defined short segment hyperintense lesions involving cervical and upper dorsal region. The spine MRI was done by the Radiology Department and the images are not available.

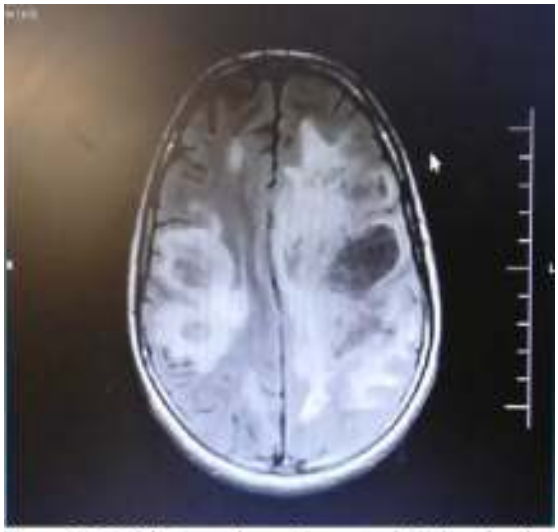

Figure 2: ***MRI brain at time of current admission showing changes of tumefactive demyelination***

After managing the raised intracranial pressure, lumbar puncture was done and the CSF showed 30 cells/mm^3 (60% polymorphs, 40% lymphocytes), elevated protein (115 mg/dl) and normal sugar. Oligoclonal bands and IgG index in CSF were not done because of economic constraints. Child was started on pulse therapy of methyl prednisolone (30 mg/kg/day) for 5 days followed by oral prednisolone 2mg/kg/day for 2 weeks, tapering over the next 2 weeks. After starting pulse therapy, child started to show improvement in the form of response to sound and interest in surrounding and the improvement continued. At the time of discharge, the patient was able to lift her left hand and leg (power - grade 4), was able to move her right hand and leg against gravity (power - grade 3). Patient was able to sit without support and stand with support. She started responding to commands. Patient was able to communicate with hand and eye movements and could make eye contact with parents. She was able to chew the food slowly and there was no drooling of saliva.

MRI of brain was repeated before discharge and again showed multiple areas of demyelination in both parietal areas but with significant decrease in size, oedema and enhancement (Figure 3). We speculate this child to be a case of recurrent TD or TMS.

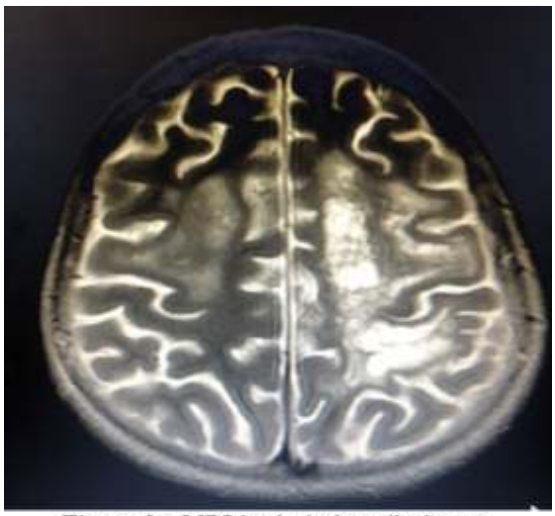

Figure 3: ***MRI brain before discharge***

Discussion

Tumefaction is an uncommon cause of demyelination and can be missed in the absence of clinical suspicion. The prevalence of TD is estimated to be approximately 1–2 per 1000 cases of multiple sclerosis[5]. The age groups affected are the second and third decade, although paediatric and elderly are reported. Role of B cell-mediated immunity is proposed although exact pathogenesis is not clear[6]. There is a potential role for inflammatory cytokines such as TNF-α and IL-1β. They both are toxic to myelin and oligodendrocytes[7]. TDL lesions can also be seen in malignancy (e.g. renal cell carcinoma), immunosuppressed states (e.g. HIV), autoimmune disorders (e.g. Sjogren syndrome, systemic lupus

erythematosus (SLE), Behcet disease and neuromyelitis optica) and drugs (tacrolimus) [8-16].

Clinical presentation of TD typically can be subacute to chronic[17]. Patients may present with altered level of consciousness and cortical signs and symptoms. They may present with signs of raised intracranial pressure suggesting an intracranial mass. In one study where TD was proved on biopsy the symptoms seen were motor in half the cases. Cognitive symptoms were seen in 43% patients and sensory disturbances in 36%[19]. A large number of cortical and cognitive signs were described, which included aphasia (17%), apraxia (4%), visual field defects (10%), Gerstmann syndrome (4%), memory dysfunction (17%), delirium (19%), and seizures (6%). Paediatric age usually presents with headache and vomiting due to increased intracranial pressure[20]. Severe cases may progress to stupor and coma because of severe raised intracranial pressure requiring urgent decompressive hemicraniectomy[21].

Our case was a 12 year old girl with clinical features progressing over weeks. She also had a polysymptomatic onset. Though she did not have frank symptoms of raised intracranial pressure, she had early papilloedema. The weakness of all 4 limbs during the initial presentation may be because demyelinating lesions were present bilaterally although more pronounced on the left side. The apparent response to the anti-TB drugs on the first occasion may really have been a response to the oral steroids which were given simultaneously. MRI brain has a major role in making the diagnosis of TD. Immediate differential diagnoses are neoplasm, abscess and inflammatory granulomas. Frontal and parietal lobe involvement with well circumscribed lesions suggests tumefaction. Perilesional oedema causing mass effect is seen in TD lesions but generally it is not as prominent as that seen in malignant lesions[19]. In most lesions size ranges from 2 to 6 cm. Gadolinium enhances lesion. It appears as open ring with the incomplete portion of the ring on the grey matter side of the lesion. This is an important clue to suggest a diagnosis of tumefactive lesion. Other features include a T2 weighted hypointense rim, peripheral restriction on diffusion weighted imaging. In MRI brain of our patient, characteristic features were present. Acute disseminated encephalomyelitis is unlikely as the size of the lesion was over 2 cm.

Treatment of TD requires special considerations. In the acute stage, the patients respond to pulse corticosteroid and in some cases require plasma exchange. In a clinical series of TD, mean time to relapse was approximately 16 months and the majority of patients showed good clinical recovery, similar to our patient. Good clinical evidence on long-term treatment of such patients is not present. Azathioprine, mycophenolate mofetil, cyclophosphamide, and methotrexate have been used effectively in relapsing-remitting TD[6]. In our patient recurrence is suspected but not proven and hence we have not planned any long term therapy as of now. We would like to highlight the importance of keeping TD in the loop when dealing with ring enhancing lesions. TD is rare in the paediatric age group. It has a polysymptomatic onset which can be subacute to chronic. Early steroids seem to have favourable response and the long term prognosis seems to be good. In this patient, TMS cannot be ruled out since oligoclonal bands (bands of immunoglobulin seen when a patient's blood or CSF is analysed), which would have helped to distinguish between TD and TMS, was not done.

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