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A Child With Multiple Sclerosis Manifested as Central Nervous System Tumour

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Abstract Multiple sclerosis (MS) is rare in paediatric population. The diagnosis is always difficult as the presentations can be very diverse and can mimic a tumour. A case of MS was discussed, which initially presented as central nervous system (CNS) tumour. On further investigations, the diagnosis of MS was made.

Key words Multiple sclerosis; Tumour

Introduction

Multiple sclerosis (MS) is a chronic disease of the central nervous system (CNS), characterised by discrete areas of demyelination and axon injury associated with inflammatory activity.[1] MS usually appears between 20 and 40 years of age, with a peak onset at around 30 years and a female to male ration of 2:1.[2] The percentage of MS patient who presented before 10 years of age, before 15 years of age and before 21 years of age are 0.2% to 0.7%,[3] 3% to 5%[4,5] and 17%[6] respectively. Clinical presentations of MS may involve motor system, sensory system and optic nerve. Cerebellar system and sphincter system are involved sometimes. A key-defining feature of MS is that lesions are disseminated in both space and time, i.e. they occur at more than one site and developed on more than one occasion.[1] On the other hand, tumour is just progression. We presented a case of MS, which manifested as a CNS tumour initially. On follow-up and investigations, the diagnosis of MS was made.

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Case Report

A 9-year-old boy who enjoyed good past health, except glucose-6-phosphate dehydrogenase deficiency, presented with fever and upper respiratory tract infections symptoms followed by one month history of on and off four limbs weakness. Prior to admission, physical examination showed generalised weakness and upper motor neuron signs of all extremities. Sensation was intact. Visual acuities were 20/25 on both eyes. Fundi were normal. There was no evidence of cranial nerves involvements. Bowel and bladder control were normal. CT brain done in Alice Ho Miu Ling Nerthersole Hospital was unremarkable. Patient was transferred to Prince of Wales Hospital for further management.

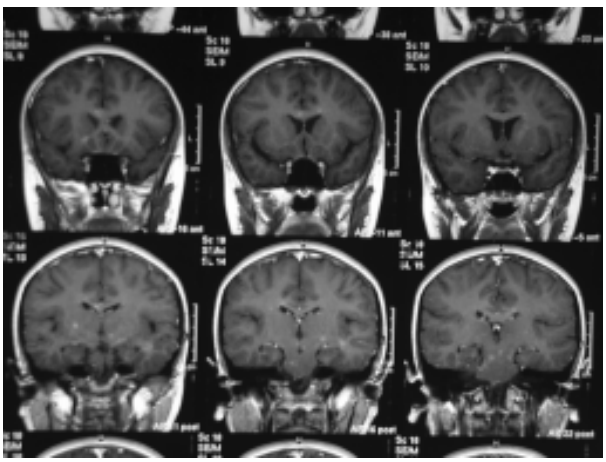
Urgent MRI spine and brain showed generalised and multiple ill-defined lesions with abnormal contrast enhancement in the cerebral peduncles, corpus callosum and periventricular regions of the lateral ventricles (Figure 1). The findings were highly suggestive metastatic pattern favouring a "medulloblastoma". Lumbar puncture was performed after the MRI with opening pressure of 16 cmH_2O. The protein of CSF was 0.25 g/L and glucose was 2.9 mmol/L with plasma glucose 4.4 mmol/L. The WCC of the CSF was 18 X 10E6/L with 96% of lymphocytes. Cytology did not showed any evidence of malignancy. Blood for alpha-fetal protein, B-HCG were normal. CXR and USG of abdomen did not show any evidence of tumour. In view of the MRI report, spinal cord tissue biopsy was performed but the histology did not show

any evidence of malignancy nor any inflammation.

Because of the lack of evidence of malignancy, diagnosis of tuberculosis infection or sarcoidosis was suspected. ESR was 70. MT 2 was negative. CXR was normal. Histology was reviewed but there were no evidence of TB infection or sarcoidosis. Early morning urine and sputum were collected for TB culture. The second lumbar puncture was performed with opening pressure of 12 cm H_2O. Biochemistry of CSF was normal and the culture of CSF did not show any growth of bacteria. CSF for PCR was negative for TB infection. Lyzozyme level in CSF and serum were 35 and 318 (150-500) unit/ml respectively. In view of the high prevalence rate of tuberculosis in our locality, standard anti-TB treatment including isoniazid, pyrazinamide, ethambutol and rifampizine, were started empirically while waiting for TB culture result. A total of eight weeks anti-TB treatment was given.

However, the condition of the patient did not improve. Second MRI brain and spine were performed one month afterwards, which showed reduction in size of the old lesions with development of new lesions with similar characteristics in left frontal-parietal lobe and right cerebral peduncle (Figure 2). In view of the waxed and waned nature of the lesions which were showed by the serial MRI, overall features were more in favour of inflammation or demyelinating disease. Third lumbar puncture was performed and CSF for oligoclonal band protein was negative and CSF myelin basic protein was also negative. As inflammation disease such as MS was one of the differential diagnosis, visual evoked potentials (VEP) was performed and showed bilateral prolonged VEP although clinically the patient had no features of papillitis.

With the evidence of abnormal bilateral visual evoked potentials, the waxed and waned of the CNS lesions on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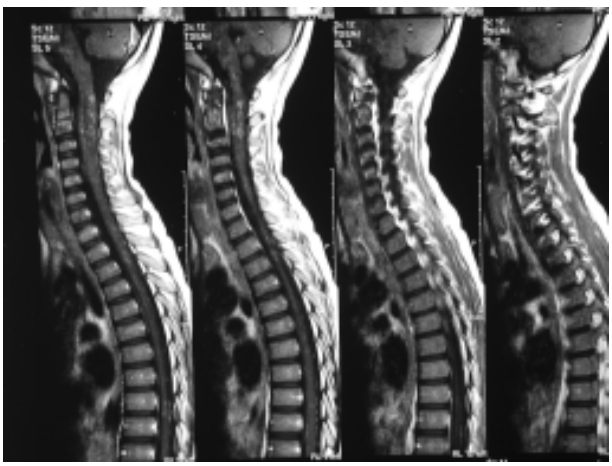
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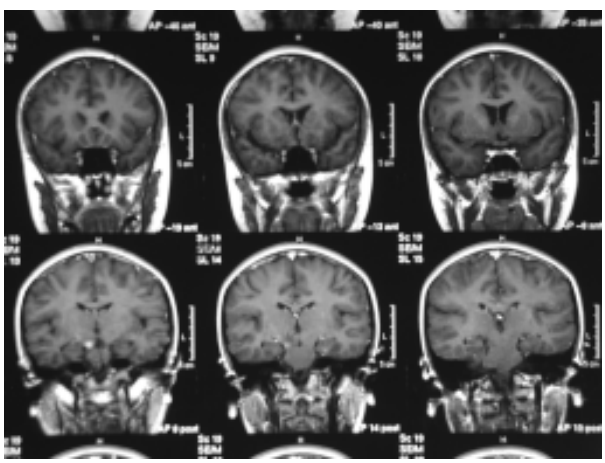
Figure 1 There were multiple ill-defined lesions in the brain and the spinal cord.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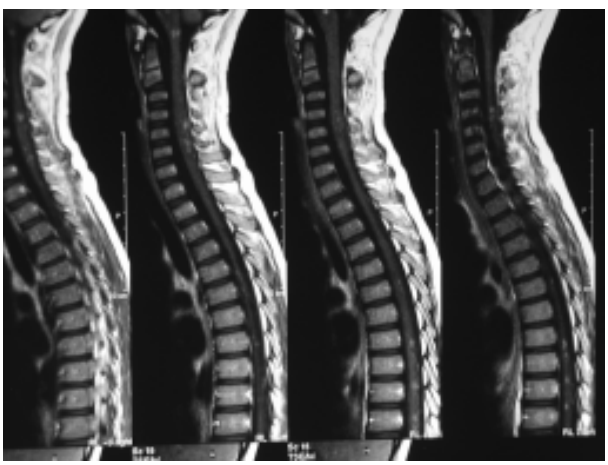
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Figure 2 There were new lesions and some of the old lesions reduced in size.

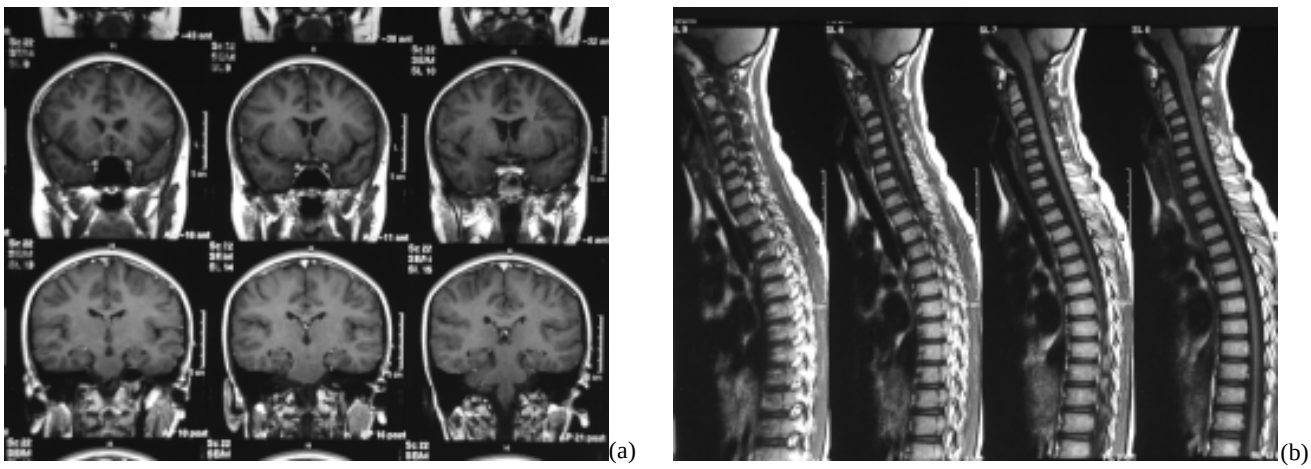
MRI and the course of the disease, MS was diagnosed. He was treated with pulse iv methyprednisolone (15 mg/kg/day) for 5 days. Power of the 4 limbs was almost fully recover after 5 days of treatment. Steroid was gradually taped off in 6 days. He was again noticed to have increasing four limbs weakness 2 weeks later. A second 5 days course of methyprednisolone was given. Power was regained again after the treatment. Third MRI brain and spine showed almost complete resolution of the enhancing cerebral and spinal nodules (Figure 3).

Unfortunately, patient suffered from another major deterioration 3 months later when the family did not bring the patient back for pulse steroid treatment. At that time, parents were scared by the complication of steroid treatment for SARS resulting in avascular necrosis in some SARS victims that had been over-emphasis in mass media. As a result, the patient had suffered severe neurological deficit resulting in complete paraplegia and was subsequently wheel chaired bound. Prophylactic IVIG was given monthly over the past one year in order to reduce relapse frequency. Monthly IVIG will be continued in the coming 12 months for a total of two-year course. On follow up assessments, patient had no clinical deterioration even though MRI follow-up scan still showed active disease.

Discussion

The diagnosis of MS is always difficult. The differential diagnosis of myelitis includes connective tissue disease (e.g. SLE), viral infection (e.g. Epstein-Barr virus), bacterial or mycobacterial infections, demyelinating and dysmyelinating disease (e.g. multiple sclerosis, acute disseminated encephalomyelitis (ADEM)), neoplasm (e.g. leukemia), sarcoidosis and etc. MS is a rare disease in paediatric population and Asian population. The most important factor in diagnosis of MS is time because of the relapsing and remitting natural course of MS as indicated in this case. MRI provides a very useful tool for diagnosing and monitoring the progress of disease. Initial imaging may provide a false impression of CNS tumour. Follow-up imaging is very useful as illustrated in this case. CNS tumour will not regress without any treatment but MS may be. TB infection should always be considered, as it is relatively common in our locality. In this case, PCR is negative for TB and makes the diagnosis of TB infection very unlikely. Sarcoidosis is rare in Chinese but should be considered. CSF lyzozyme is not very useful for differentiating TB infection, sarcoidosis, inflammatory disease or CNS tumour as all the conditions can increase the level.[7] Lyzozyme level was performed in our case to look for evidence of sarcoidosis because tumour and TB infection have been almost excluded by biopsy and PCR. It is always difficult to differentiate ADEM and MS in the initial phase. But with the multiple relapses and severe neurological consequences, MS should be the diagnosis rather than ADEM.

So far, there are no randomised control studies on the management of MS in children because of its rarity. Most of approved treatments are registered for use in patients greater than 18 years of age. Therapy of acute relapse of MS follows the recommendations for adults. Treatment includes 15-20 mg/kg/day iv over 5 days. IVIG may also



(a) (b)

Figure 3 There were almost complete resolution of the enhancing cerebral and spinal nodules. Residual left frontalparietal and cervical intramedullary lesions were also showed in the MRI.

be beneficial to patient with remitting-relapsing MS by reducing the relapse rate and arresting the disease progression.[8] The dosage was 0.4 g/kg/day for 5 consecutive days, with a booster dose of 0.4 g/kg every 6 weeks for a period of 2 years. Interferon β is also proved to be effective in reducing the rate and severity of relapses, slowing the progression. However, side effects are not well tolerated. Other agents such as cytotoxic drugs (e.g. mitoxantrone and cyclophosphamide) are seldom used in children because of severe toxicity and long-term complications. Other treatment modality such as plasmapheresis has seldom been tried in children and the effectiveness in adult is unknown.

The prognosis of MS in children is no worse than in adults.[9] The problem of early onset VS late onset is the risk of earlier disabling but not the aggressiveness of the disease.

In conclusion, diagnosis of MS in children is always difficult. The presenting features could be very variable. MS should be considered as one of the differential diagnosis even through MRI brain and spine were suggestive of tumour as illustrated in our case. Invasive procedures (such as spinal cord biopsy) should be considered cautiously. Follow up MRI imaging would definitely give the crucial clue for diagnosis.

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