Vanishing Brain Lesions in a Patient with Vision Loss and Ataxia: A Case of CNS Lymphoma with Corticosteroid Related Regression

Dear Editor,

A 46-year-old man presented at another centre with headache and 15 days later ataxia and diplopia developing over a week. He was evaluated with magnetic resonance imaging (MRI) of the brain [Figure 1]. A provisional diagnosis of primary CNS demyelinating illness was made based on imaging and was started on intravenous methylprednisolone followed by a short course of oral prednisolone with which his symptoms resolved. No other tests were performed as the patient recovered completely. Three months later, he developed complete vision loss in the right eye over 1 week. He had features of retinal necrosis - a diagnosis of cytomegalovirus (CMV) retinitis was made at another centre and was treated with valacyclovir and intravitreal triamcinolone. Vision improved partially to 6/36 over the next 3 months, when he developed complete vision loss in the left eye. This was also treated with valacyclovir and corticosteroids and there was a partial improvement in vision to 5/60. Seven months later, he again developed ataxia, dysarthria and headache. Brain imaging was repeated [Figure 2] which showed a contrast enhancing well-demarcated lesion in cerebellar vermis which was hyperintense on FLAIR and was diffusion restricting, while the cerebellar hemispheric lesions seen in the previous imaging [Figure 1] had resolved. Once again, he received injectable methylprednisolone. He had transient improvement over the next 2 weeks, followed by recurrence of symptoms. Imaging was repeated [Figure 3] which revealed FLAIR hyperintense lesions in the subcortical white matter and in the left cerebellar hemisphere which were diffusion restricting and contrast enhancing. With the third

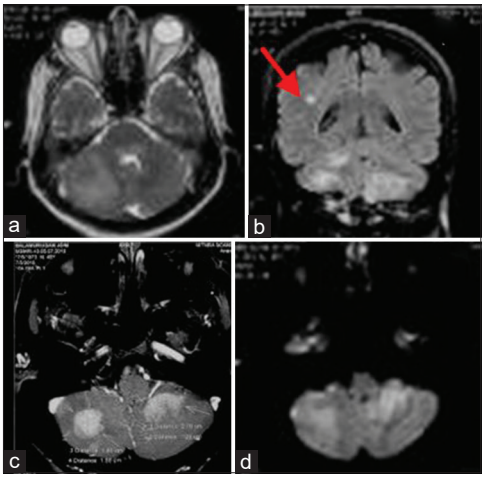

Figure 1: Axial T2 (Figure 1a) and Coronal FLAIR (Figure 1b) showing hyperintense lesions in both cerebellar hemispheres and parietal subcortical white matter (1b, red arrow). The lesions are avidly enhancing on T1 post contrast (Figure 1c) and are diffusion restricting (1d)

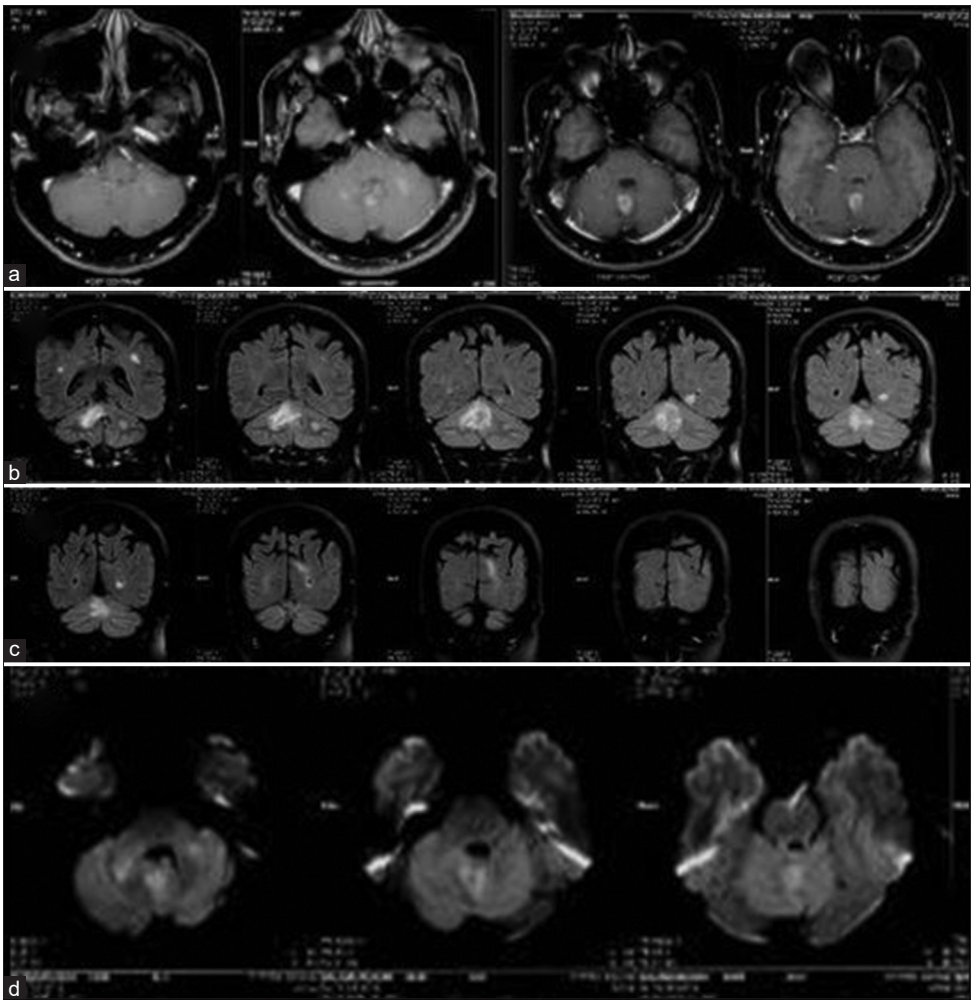

Figure 2: Post contrast axial T1 weighted imaging (Figure 2, row a) showing contrast enhancing lesions in both the cerebellar hemispheres and vermis. Coronal FLAIR imaging (Fig 2 row b and c) showing hyperintense lesions in the subcortical white matter and the cerebellar vermis which are also diffusion (Fig 2 row d) restricting

imaging, he was referred to our institute with a diagnosis of 'multiple sclerosis'. On review of history, it was found that the patient had sensory loss over the dorsum of the right foot and difficulty in gripping footwear for one year. Examination revealed bilateral cerebellar signs more on the left side and restriction of abduction of both eyes.

Differential Diagnosis

Vanishing or relapsing-remitting brain lesions could be due to various aetiologies such as demyelinating illnesses such as MOG (anti-myelin oligodendrocyte glycoprotein) associated demyelination, Neuromyelitis optica spectrum disorder (NMOSD), multiple sclerosis, recurrent acute demyelinating encephalomyelitis (ADEM); inflammatory diseases such as sarcoidosis, Behcet's disease; autoimmune diseases such as lupus, Anti-phospholipid antibody (APLA) syndrome; Lymphoma, granulomas and infections such as neurocysticercosis with post-inflammatory recurrent demyelination, mitochondrial lesions, toxic and metabolic causes such as hypoglycaemia, hepatic encephalopathy, uraemia, drugs such as vigabatrin, metronidazole and methotrexate.[1]

In the above patient, given the clinical presentation of symptoms developing over days and slowly recovering over weeks, demyelination, inflammatory conditions and lymphoma were high on the cards which are known to respond to steroids.[2,3]

CSF examination revealed one lymphocyte/mm3, with normal glucose (99 mg/dL) and slightly raised protein (98 mg/dL). There were no oligoclonal bands or malignant cells. CSF lactate was within normal limits. Hemogram, peripheral smear, liver and renal functions, serum electrolytes including calcium were normal as were the serum angiotensin-converting enzyme levels. Serum testing for anti-aquaporin 4 antibodies, myelin oligodendrocyte glycoprotein, antinuclear antibodies, extractable nuclear antigens and anti-nuclear cytoplasmic antigen (ANCA) were negative. Biopsy of the left cerebellar lesion was performed which revealed a

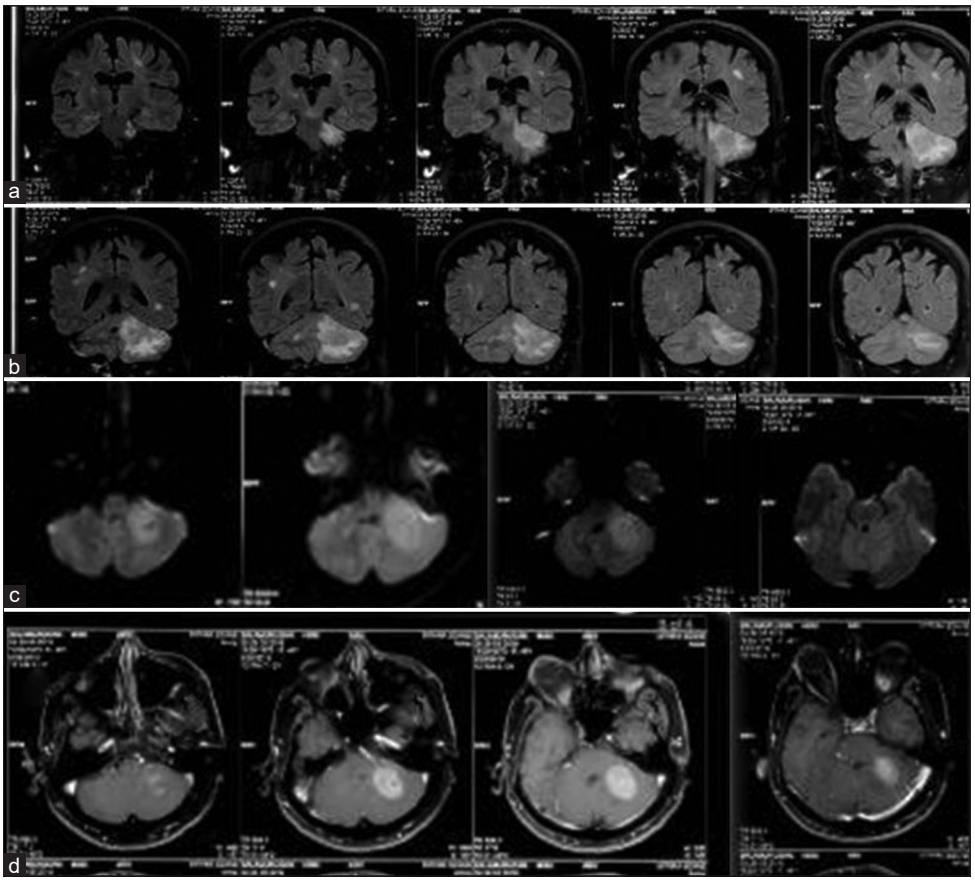

Figure 3: Coronal FLAIR (Figure 3 row a, b) showing hyperintense lesions in the subcortical white matter and in the left cerebellar hemisphere which are diffusion restricting (row c) and contrast enhancing (row d)

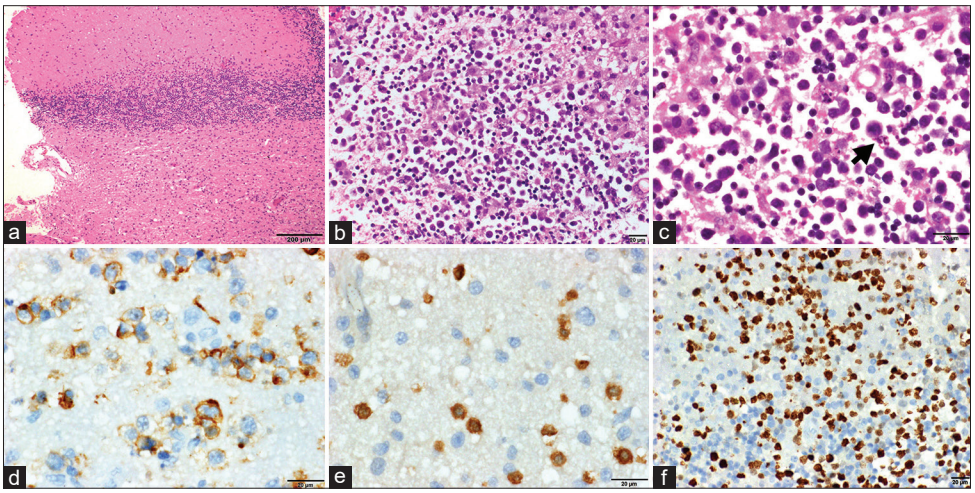

Figure 4: Photomicrographs show cerebellar parenchyma with increased cellularity (a, H and E, ×40) as a result of infiltration by atypical lymphoid cells (b, H and E, ×100) with hyperchromatic nuclei and apoptosis (arrow, c, H and E, ×400). The large atypical B lymphoid cells are labelled by CD20 (d, ×200), reactive T cells are labelled by CD3 (e, ×200) and the proliferation is high in the tumour cells (f, MIB-1, ×100)

high grade non-Hodgkin's B cell lymphoma. There was no evidence of systemic involvement or bone marrow infiltration. HIV serology, Hepatitis B surface antigen and anti-Hepatitis C antibodies were negative. The biopsy from the cerebellar tissue showed a high grade B cell non-Hodgkin's lymphoma [Figure 4]. The patient was treated with modified de Angelis' protocol for primary CNS lymphoma with Rituximab, methotrexate, procarbazine, vincristine and prednisolone. After 6 cycles of chemotherapy and two fractions of whole brain radiotherapy, he was completely asymptomatic except for gaze-evoked nystagmus at 18 months follow up. At 20 months follow up, patient was found to have recurrent disease. He was

planned for stem cell transplantation, however, before finding an appropriate match, the patient succumbed to the disease.

There are a few case reports and series of CNS lymphomas which vanish spontaneously or in relation to administration of corticosteroids.[4-10]

Firstly, even though primary demyelinating disorders such as tumefactive demyelination is a possibility in our case, other aetiologies should always be kept in mind and a detailed workup performed including anti-MOG, AQP4 antibodies and autoimmune profile. CSF examination if performed, should always be evaluated for the presence of malignant cells in addition to oligo-clonal bands.

Secondly, in our patient, sequential vision loss occurred which partly improved with corticosteroids. Important to mention here is the fact that the patient had some retinal lesions which were diagnosed as CMV retinitis. We did not have access to the patient's fundus pictures. Though the diagnosis of CMV retinitis is possible in this case, in retrospect, it is more likely that the patient had vitreo-retinal lymphoma, which presented with vision loss. In patients with suspected CNS lymphoma, careful slit-lamp examination is essential because the anterior chamber may have lymphoma cells forming a pseudo-hypopyon.[11] In such cases sampling the aqueous humour or iris biopsy can be diagnostic. Vitreous can also have lymphomatous cells suspended and if found, a vitrectomy will yield a definitive diagnosis and the need for CNS lesion biopsy may be obviated.[12] In a patient with fluctuating brain lesions and retinal lesions, it is very important to consider lymphoma as a differential. Retinal lymphoma is a differential in cases with acute retinal necrosis or progressive outer retinal necrosis and a prompt vitrectomy with viral PCR and histopathologic examination would clinch the diagnosis

Thirdly, some with CNS lymphoma, may respond dramatically to steroids and even a single dose can lead the tumour to melt away. So in patients with suspected tumefactive demyelination, if a biopsy is planned, it should be done before the administration of steroids.[7,12] If steroids are administered, it may be impossible to differentiate lymphoma from demyelination.[13] In a patient with multiple sclerosis, usually, though the administration of corticosteroids leads to good functional recovery, near complete disappearance of lesions rarely occur. Imaging follow up studies of patients with multiple sclerosis have revealed that up to 17% of patients may have complete resolution of the index T2 hyperintense lesion on MRI.[14,15] The plaques of demyelination remain, and later may form black holes. On the other hand, in CNS lymphoma, the lymphoma cells get lysed due to corticosteroids leading to near complete disappearance of the lesion. This distinction is important to remember.

Fourthly, all the images should be reviewed in sequential order before embarking on a diagnosis and management plan. In some instances, there is a tendency to see the first imaging and the last one alone. In this patient, another observer reviewed the first and third imaging [Figures 1 and 3] and had come to a conclusion that the lesion in the first image had partly resolved in the right cerebellar hemisphere while the left cerebellar lesion had become more extensive, and both the images [Figures 1 and 3] done with an interval of around a year between them showed similar contrast enhancement of the left cerebellar lesion. However, careful re-assessment of the second imaging [Figure 2] done 17 days prior to the third imaging shows interesting findings. There is near-total disappearance of the cerebellar lobar lesions while there was a new contrast-enhancing T2/FLAIR hyperintense lesion in the vermis. Figure 3 reveals a complete disappearance of this contrast-enhancing mass in the vermis and new contrast enhancement in the left cerebellar hemisphere. This rapid waxing and waning in the absence of therapy strongly suggested lymphoma.[6]

Non-Hodgkin's lymphoma is an enigma with a huge variation in their natural history. There have been instances with spontaneous remissions that are durable and some cases in the other extreme can be fatal. In this patient, clinically, the history of suboptimal visual recovery after the very first episode of vision loss, presence of retinal lesions and on imaging, large areas of diffusion restriction in the posterior fossa with a waxing and waning course pointed strongly towards CNS lymphoma. In retrospect it is very easy to make a diagnosis of CNS lymphoma in this case. However, a high degree of suspicion leading to early biopsy before administering steroids is essential to make a diagnosis of CNS lymphoma and initiate treatment for a good outcome.

Patient consent

Obtained.

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Conflicts of interest

There are no conflicts of interest.

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