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A Case of Neuro-Behçet's Presenting with Tumour-like Lesions and Responding to Rituximab

Running Head: Neuro-Behçet's causing hydrocephalus

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Abstract

We describe a case of neuro-Behçets disease (NBD) that presented with symptoms of raised intra-cranial pressure including papilloedema. MRI revealed tumour-like lesions which, on biopsy, confirmed the presence of an active vasculitis. Treatment was commenced with Prednisone and cyclophosphamide which proved unsuccessful with enlargement of the cerebral mass lesions. Infliximab and mycophenolate were trialled also without benefit. The patient required ventriculo-peritoneal shunts to relieve the symptoms of hydrocephalus. Rituximab was then commenced with significant symptomatic and imaging improvement. The case is unique in our experience in the need for shunting to relieve the symptoms of hydrocephalus related to vasculitis.

Manuscript

A 38-year-old female of European descent was reviewed in June 2010 with a history of generalised arthralgia and a tender, nodular rash on her lower limbs which developed over the preceding months. She had a background of four episodes of bilateral uveitis over the previous decade, and recurrent orogenital ulcers since her teenage years.

Her initial investigations showed an ESR of 21 (0-15mm/h) and a previously cleared hepatitis B infection. All other laboratory tests were unremarkable. Skin biopsy revealed an arteritis in the deep dermis with inflammatory infiltrate.

Based on this clinical presentation and the above investigations the patient was diagnosed with Behçet's disease (BD) with associated cutaneous vasculitis. She was started on 40mg of oral prednisone, 500mcg of colchicine daily and local steroid treatment for ongoing uveitis, which improved her symptoms.

Six months later the patient had a symptomatic relapse, with significant worsening of her vasculitic rash and development of an insidious onset frontal headache with associated nausea and vomiting. Ophthalmological examination revealed bilateral papilloedema.

An urgent brain magnetic resonance imaging (MRI) scan demonstrated abnormal intrinsic brain lesions. The largest measured 35x15mm arising from the choroid plexus of the temporal horn of the right lateral ventricle, with extension into the white matter, surrounding oedema and entrapment and enlargement of the right temporal occipital horns (Figure 1). The lesion had slightly decreased signal on T1 and T2 weighted imaging and marked enhancement with contrast. Thickening and enhancement of the choroid plexus of the left lateral ventricle was also noted. A further subtle area of abnormality, with increased signal on T2 weighted imaging, was seen within the right parafalcine gyri.

Cerebrospinal fluid (CSF) sampling revealed clear, colourless fluid with a high protein level of 0.82g/L (0.15-0.45), slightly low glucose level of 2.5mmol/L (2.8-4.4), red blood cells of $105 \times 10^6/L$ and white blood cells of $8 \times 10^6/L$, of which 63% were lymphocytes, culture was negative. CSF cytology demonstrated abundant lymphocytes, histiocytes and some polymorphonuclear leucocytes.

A biopsy of the temporal lobe lesion revealed perivascular cuffs of well differentiated lymphocytes with focal reactive germinal centre formation. The lymphocytic infiltrates were confined to the Virchow-Robin spaces and lymphocytes were also noted to infiltrate the vessel walls (Figure 2). Neither tissue necrosis nor granulomatous inflammation was noted and a Martius Scarlet Blue stain did not show fibrinoid necrosis. Immunocytochemistry performed on the tissue showed most of the lymphocytes within the perivascular cuffs were reactive B lymphocytes with reactivity seen for CD20 and Bcl2, with a scattering of CD23 positive lymphocytes. A lesser population of reactive CD3 and CD5 positive T lymphocytes were seen. No reactivity was seen for CD10 and cyclin D1. A scattering of CD38 and CD138 positive plasma cells were noted.

Based on the presentation, imaging and histopathology neuro-Behcet's Disease (NBD) was thought to be the most likely diagnosis.

The patient went on to have 1000mg of IV cyclophosphamide, initially fortnightly and then monthly, with concomitant oral prednisone. However, after four cycles of cyclophosphamide no clinical or radiological improvement was seen. No response was seen to infliximab or mycophenolate and the patient eventually underwent a bilateral temporal horn ventriculo-peritoneal shunt and right occipital horn reservoir placement with symptomatic relief and resolution of hydrocephalus (figure 3).

In March 2012 the patient was changed to IV rituximab (1000mg x2 six monthly) and 6 months of oral cyclophosphamide. Her symptoms and radiology improved and at last follow up, in May

2015, she remains asymptomatic and in full-time employment, while continuing oral azathioprine and six monthly rituximab.

Discussion

Our patient fulfils the ISG criteria for BD (1) and the recent consensus for NBD (2). To our knowledge, this is the second case in the literature describing hydrocephalus requiring a neurosurgical procedure in NBD (3), and the only case requiring permanent ventriculo-peritoneal shunting. It also highlights the potential role of rituximab in the treatment of refractory NBD.

Headache is common in BD but only represents true NBD in 10% of cases, and is more often a primary headache disorder (2). Our case highlights the importance of the recommendation that headache in a patient with BD needs to be investigated further if it has “red-flag” features; different in character, progressive, refractory, severe, or associated with other neurological symptoms and signs (4).

For parenchymal NBD, MRI brain typically shows hyperintense lesions on T2 weighted imaging, which are enhancing and have a predilection for the brain stem and basal ganglia (6). Linear high signal along the internal capsule is thought to be characteristic of acute NBD, and brain stem atrophy a more specific sign later in the disease (6-7). Our case is unusual in both the distribution of lesions and the fact the predominant lesion showed hypointensity on both T1 and T2 imaging, however the smaller lesion was T2 hyperintense.

The pseudo-tumoural presentation is rare; reported to occur in 1.8% of patients with NBD (4). There is often a greater degree of disability at presentation and usually a longer delay until diagnosis than classical NBD (4). The tumour-like lesions are often found in the capsulo-thalamic area and “typical” radiological findings are infrequently reported (4). Our patient’s headache resulted from the pseudo-tumours causing hydrocephalus and raised intracranial pressure (ICP).

Raised ICP is known to occur in patients with thrombotic NBD but almost never occurs with parenchymal involvement (6). Although symptoms of raised ICP are not recognised as a feature of parenchymal NBD in the ICR diagnostic criteria (4) there are a number of other case reports in the literature that describe this. Matsuo *et al* describe a patient with a decreased level of consciousness due to raised ICP from a NBD pseudo-tumour in the left basal ganglia (8). Noel *et al* report two patients, out of the 23 in their case series of pseudo-tumoural NBD, who underwent neurosurgical removal of the tumour-like lesions (5). Akman-Demir *et al* report one patient with raised ICP in the setting of parenchymal NBD in their review of 134 cranial MRI scans of patients with NBD (6). Only one other case, reported by Chi Long Ho *et al*, describes hydrocephalus in NBD requiring temporary ventriculostomy, secondary to compressive effects of a cerebral abscess (3). Our case adds to the literature supporting raised ICP as a rare feature of parenchymal NBD.

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Figures & Figure Legends:

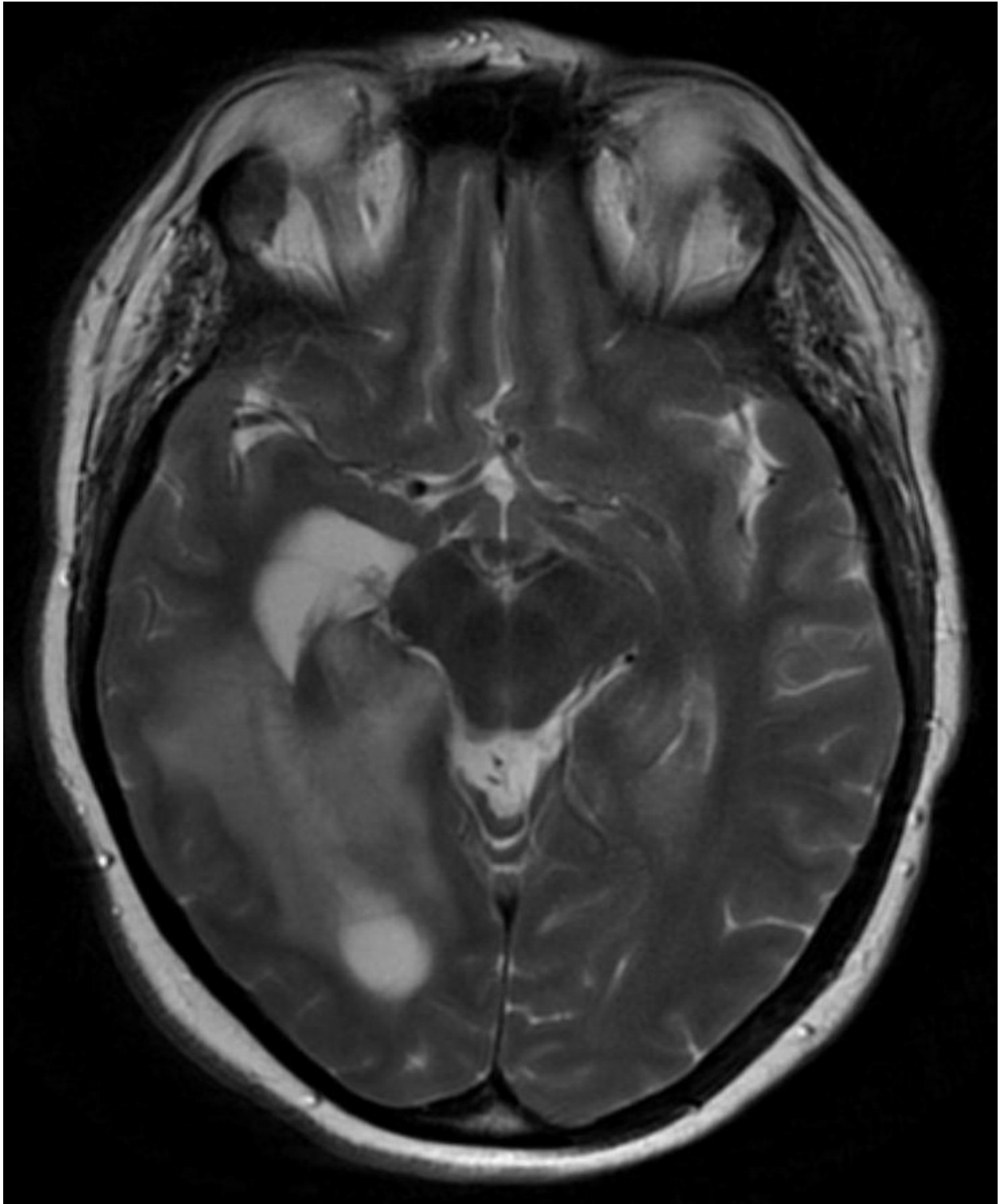


Figure 1: Brain magnetic resonance imaging (MRI) scan with contrast demonstrating largest contrast enhancing lesion measuring 35 x 15mm arising from the choroid plexus of the

temporal horn of the right lateral ventricle, with extension into the white matter, surrounding oedema and entrapment and enlargement of the right temporal and occipital horns.

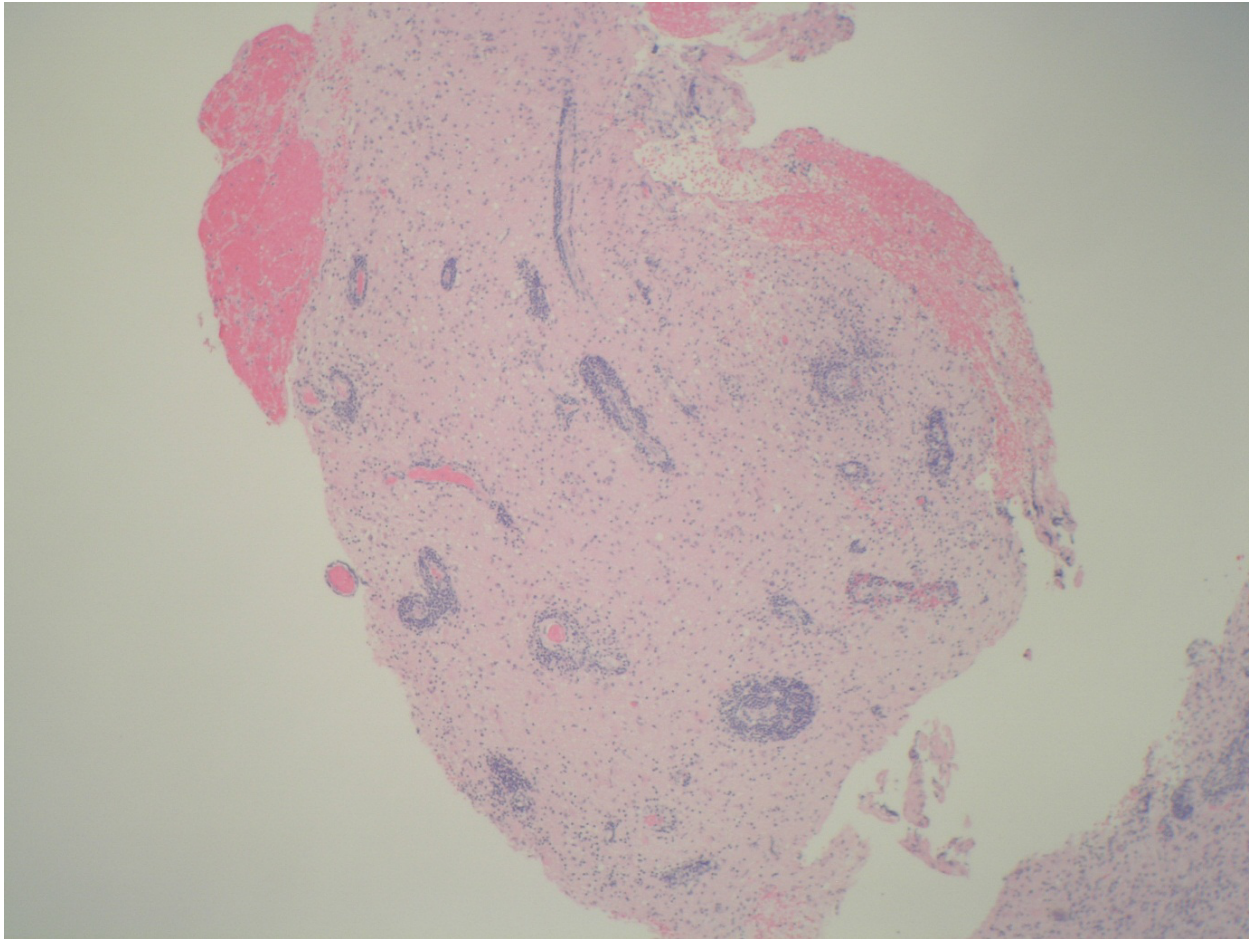


Figure 2: 40x Haematoxylin and Eosin stained section of cerebral tissue showing striking perivascular cuffs of lymphocytes around blood vessels. The lymphocytic infiltrates appear confined to the Virchow-Robin spaces. There is fresh haemorrhage on the edges of the biopsy fragments secondary to the surgical intervention.

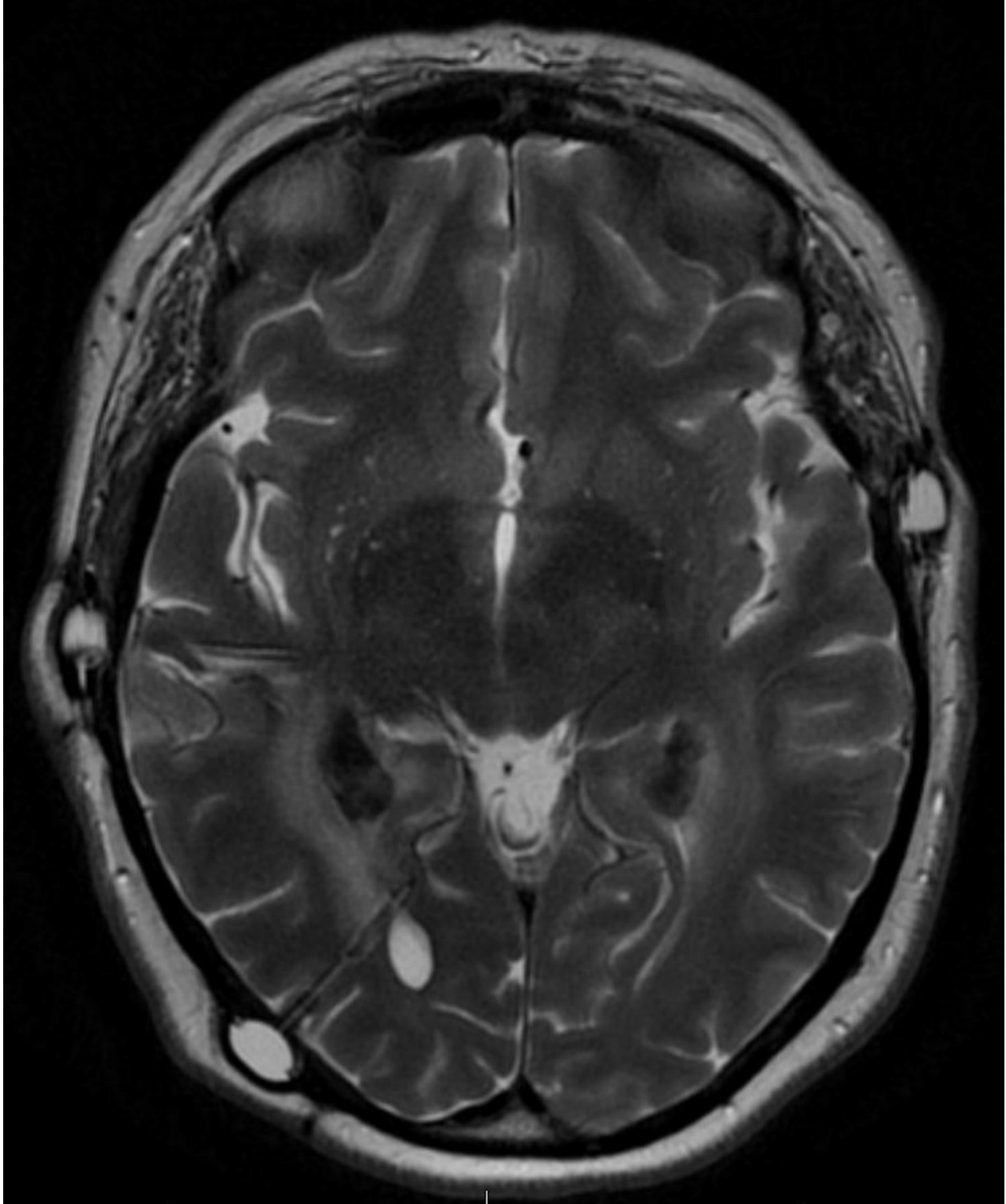


Figure 3. Brain magnetic resonance imaging (MRI) scan with contrast demonstrating ventriculo-peritoneal (VP) shunt entering from the right parieto -occipital region and traversing the

occipital horn of the right lateral ventricle and significant decompression of the loculated hydrocephalus is noted.