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Case Report

Neuro-Behçet – Clinical and radiological findings in a Patient of Sub-saharan African origin ☆☆☆

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ABSTRACT

Behçet's disease is a rare, systemic variable vessel vasculitis mostly seen in patients from the Middle East, Northern Africa and Central Asia. Neuro-Behçet disease (NBD) is often diagnosed in patients with known Behçet's disease who present with neurological symptoms and radiological features of central nervous system involvement. There are very few cases with neuro-Behçet reported from Sub-Saharan Africa in the literature. We report a case of severe parenchymal neuro-Behçet with pseudo-tumoral brainstem lesions in a young male patient of South African origin.

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Introduction

Behçet's disease is a rare, systemic variable vessel vasculitis mostly seen in patients from the Middle East, Northern Africa and Central Asia. The condition is named after Turkish dermatologist, Hulusi Behçet, who characterized the main features of oral and genital ulcers and eye involvement in 1937 [1]. The disease may present with attacks affecting only skin, mucosa or eyes at separate intervals [1], making the diagnosis

challenging. If other organs are primarily affected or the disease occurs in geographical areas where it is rare, the diagnosis may be delayed or missed.

While involvement of the gastrointestinal system, cardiovascular organs and joints are common, pulmonary and central nervous system (CNS) complications are very rare [1]. Neuro-Behçet disease (NBD) is often diagnosed in patients with known Behçet's disease who present with neurological symptoms and radiological features of central nervous system involvement. It affects more commonly young male patients [2] and is associated with a higher mortality. Two dif-

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☆☆ Telephonic consent: As the patient lives a long distance away from the hospital, telephonic consent was obtained. The patient will sign consent on the next follow up visit Institutional ethics approval was granted under these conditions No patient details are identifiable on the submission

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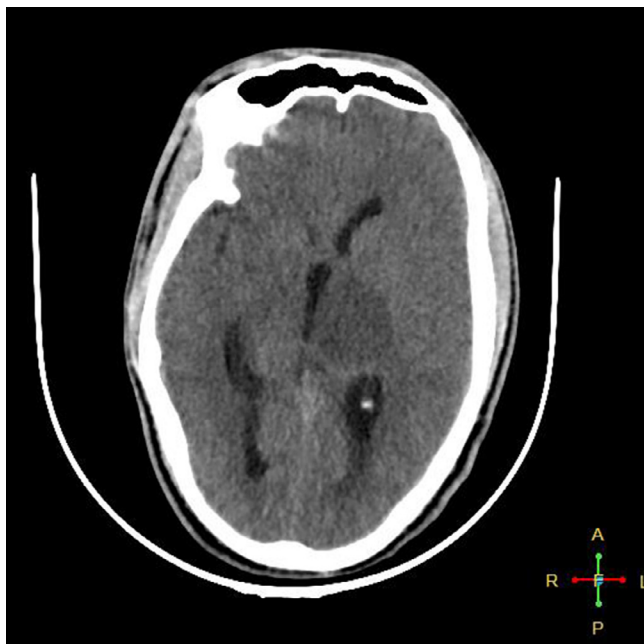


Fig. 1 – Axial CT scan of the brain (A) pre-contrast at the level of the basal ganglia demonstrating low density in the left thalamus and (B) pre-contrast at the level of the midbrain and (C) delayed post contrast at a similar level demonstrating low density with patchy enhancement



Fig. 1 – Continued

ferent CNS manifestations are described with parenchymal lesions on the one hand and non-parenchymal on the other hand. While parenchymal lesions can affect the hemispheres and spinal cord, there is some evidence that brainstem manifestations are more common [3]. Non-parenchymal lesions are vascular and can affect venous and arterial blood vessels of the brain with cerebral venous sinus thrombosis more often encountered than arterial stenosis or aneurysms [3].

There are very few cases with neuro-Behçet reported from Sub-Saharan Africa in the literature. The largest cohort comes from a French study and included 50 patients of families originating from Sub Saharan countries seen in a hospital in Paris over a time period of 36 years [4]. In an African study from Senegal, the manifestations of 16 patients with neuro-Behçet from Dakar were reported [5]. To our knowledge, no previous cases with neuro-Behçet were reported from South Africa.

We report a case of severe parenchymal neuro-Behçet with pseudo-tumoral brainstem lesions in a young male patient from South Africa. The rarity of the disease in Southern Africa as well as the high burden of other diseases associated with HIV that may mimic the clinical findings in Behçet's disease potentially makes the diagnosis challenging.

Case study

An 18-year-old male of African origin presented to the emergency unit with right sided hemiparesis. His family reported a gradual onset of symptoms over an 8-to-10-day period with



Fig. 1 – Continued

headaches and right sided numbness affecting his arm and leg. On the day before admission, he developed right-sided weakness and his level of consciousness deteriorated. The family reported that he was previously healthy and that he had not been exposed to any illicit drugs or toxins.

On examination 2 ulcers (0.5cm and 1cm) were detected on the scrotum. No other clinical signs to argue for Behçet's disease were detected. On neurological examination he had a Glasgow Coma Scale of 11/15 without signs of meningism. The

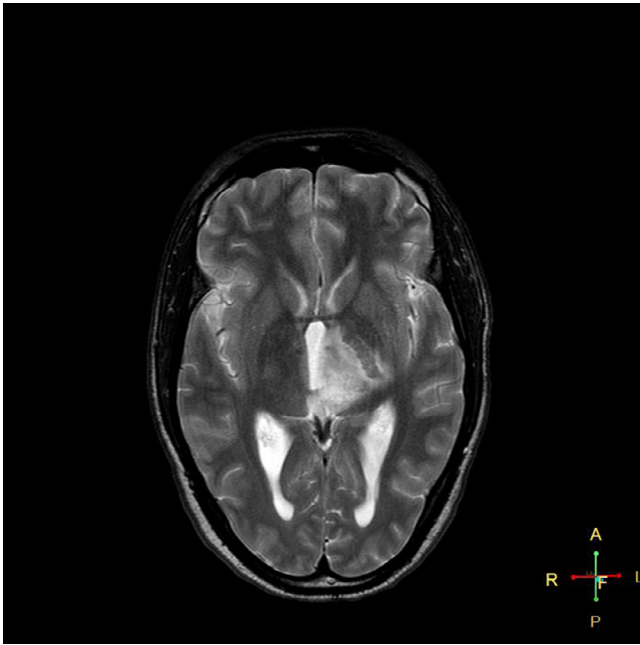


Fig. 2 – Axial T2W sequences (A) at the level of the basal ganglia and (B) at the level of the midbrain demonstrating hyperintense signal in the left thalamus, posterior limb of the internal capsule, posterior lentiform nucleus and left midbrain

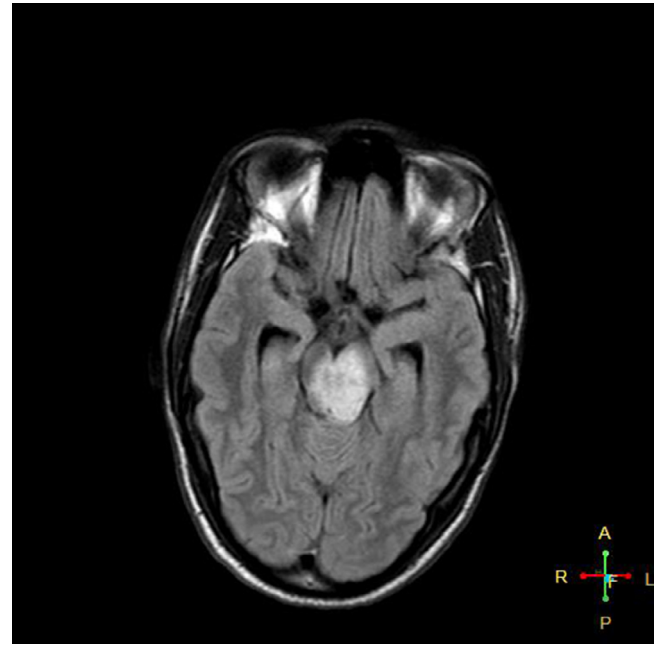


Fig. 2 – Continued

cranial nerve examination revealed anisocoria with a dilated and non-reactive right pupil, limited adduction of the right eye and a discrete skew deviation. No uveitis was noted. He had a severe, right sided hemiparesis with facial nerve involvement. The muscle tone was spastic with increased reflexes, including patellar clonus and up-going plantar response on the right side. Furthermore, we found a severe left sided limb ataxia. These findings were suggestive of an extensive brain stem lesion or multiple lesions with brainstem involvement.

An urgent computer tomography (CT) of the brain revealed ill-defined, hypodense lesions in the left thalamus (Fig 1A), posterior limb of the internal capsule, midbrain and pons (Fig 1B) and, in addition, in some cortical and subcortical regions of the right frontal lobe. Some of these lesions demonstrated patchy enhancement (Fig 1C) on delayed contrast administration. The ventricle system was mildly enlarged with prominent temporal horns in keeping with an early hydrocephalus resulting in cerebral edema. As initial differential diagnosis we considered infectious diseases and autoimmune conditions like acute demyelinating encephalomyelitis (ADEM).

On further inquiry about preceding ocular or oral symptoms, the family confirmed recurrent oral ulcers in the previous 12 months, locally treated with antiseptic mouthwash. No history of previous pustulosis or erythema nodosum was reported. A skin pathology test performed was negative. Under the assumption of possible Behçet's disease with neurological involvement, magnetic resonance imaging (MRI) of the brain was requested. T1W, T2W and FLAIR sequences, as well

as diffusion, susceptibility and post contrast sequences were performed.

The T2 (Fig 2A and B) and FLAIR sequences demonstrated hyperintense signal changes, affecting the left thalamus, posterior limb of the internal capsule, posterior lentiform nucleus, left midbrain and bilateral pons. The characteristic 'waterfall' or 'cascade' appearance (Fig 3) on coronal views further supported the diagnosis of neuro-Beçet. These lesions were low on T1W and did not demonstrate any restricted diffusion. The spinal cord showed no abnormalities on MRI.

To evaluate for extra-cerebral manifestations, a CT scan of the chest and abdomen including CT-angiography was performed. Circumferential mural thickening of the terminal ileum and large bowel was demonstrated (Fig 4) and further strengthened our differential diagnosis. Pulmonary arterial emboli or aneurysms were excluded.

All basic blood tests were normal with the exception of an initial white cell count of $22 \times 10^9/l$ with neutrophilia and a CRP of 66 mg/l. HIV and Syphilis serology were negative. CSF analysis showed an acellular liquor cerebrospinalis with normal glucose levels and a mildly raised protein of 0.57 g/l. Gram staining, India Ink, Cryptococcal latex antigen, bacterial antigen testing and Mycobacterium tuberculosis PCR as well as bacterial and fungal cultures were negative. Anti-neuronal antibodies on CSF were normal. Vitamin B12 levels were normal, antinuclear antibodies (ANA), antineutrophilic cytoplasmic antibodies (ANCA), and rheumatoid factor were also absent.

He was treated with high dose intravenous steroid pulse therapy for 5 days followed by oral steroids. In addition, he received sodium valproate for intermittent, involuntary and rhythmical movements of his right arm and shoulder that were suspicious of focal seizures. An electro-encephalogram showed diffuse slowing, indicating a moderate to severe gen-

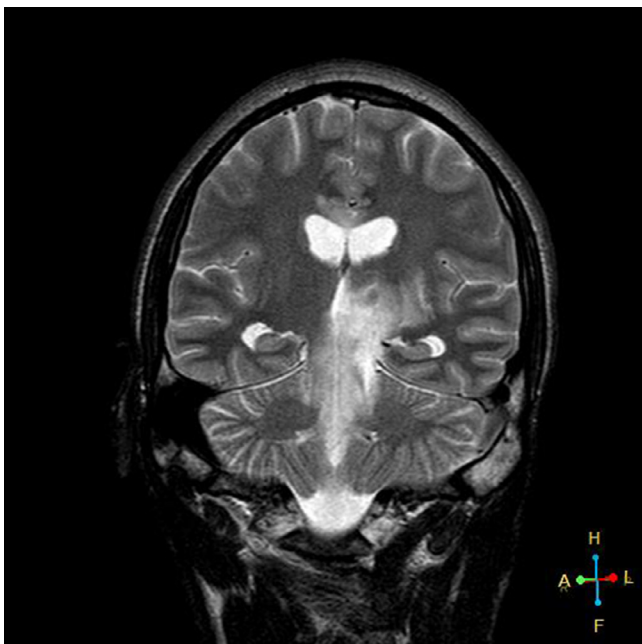


Fig. 3 – T2W coronal sequence demonstrating hyperintense signal in the left thalamus, left midbrain, bilateral pons with a characteristic ‘waterfall’ or ‘cascade’ appearance, supporting the diagnosis of neuro-Behçet



Fig. 4 – (A) Axial and (B) coronal post contrast CT scan of the abdomen demonstrating circumferential mural thickening of the terminal ileum and large bowel, compatible with Behçet's disease

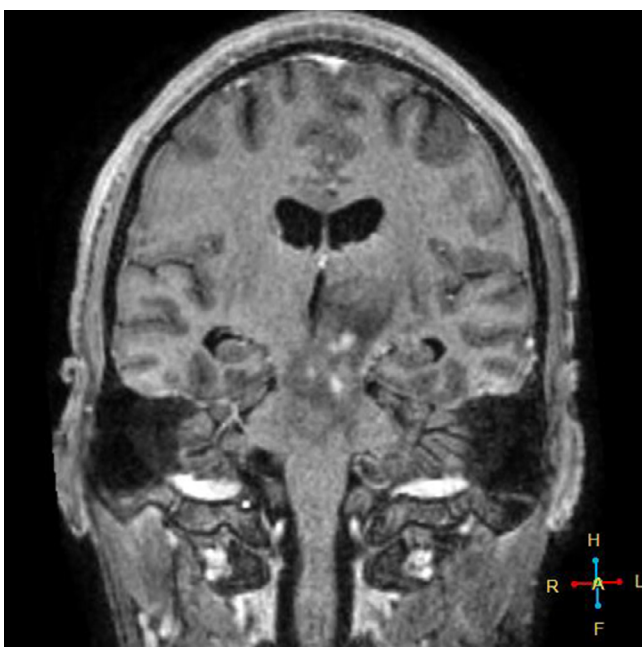


Fig. 3 – Continued



Fig. 4 – Continued

eralized cerebral dysfunction but no focal or epileptiform abnormalities.

During the first week of admission, he deteriorated further, resulting in a soporose state and bilateral ptosis. Steroid treatment was continued and because of unavailability of intravenous cyclophosphamide, he was treated with oral cy-

clophosphamide. Over the following 2 weeks he slowly improved, regaining a full level of consciousness and partial improvement of his left sided ataxia. He started to communicate non-verbally and was able to eat. Due to concerns of toxicity of oral cyclophosphamide his treatment was then changed to Azathioprine.

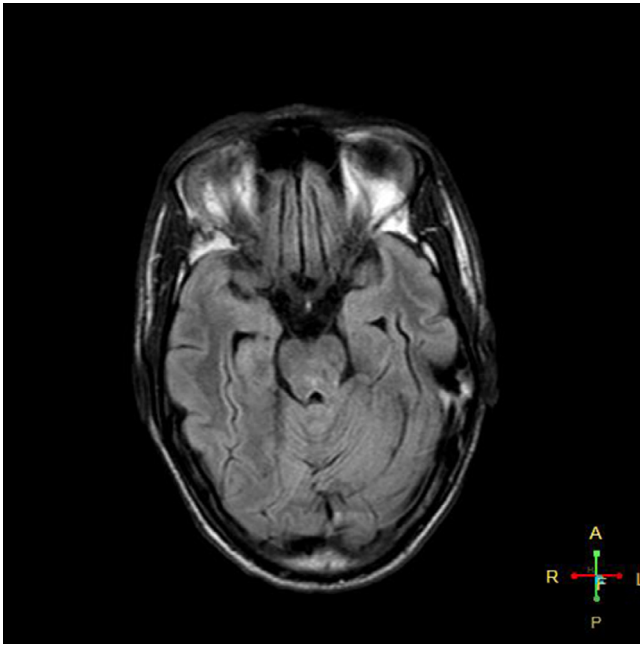


Fig. 5 – T2W coronal sequence of the follow-up MRI done 4 months later revealed mild residual hyperintense signal in the left thalamus and brain stem

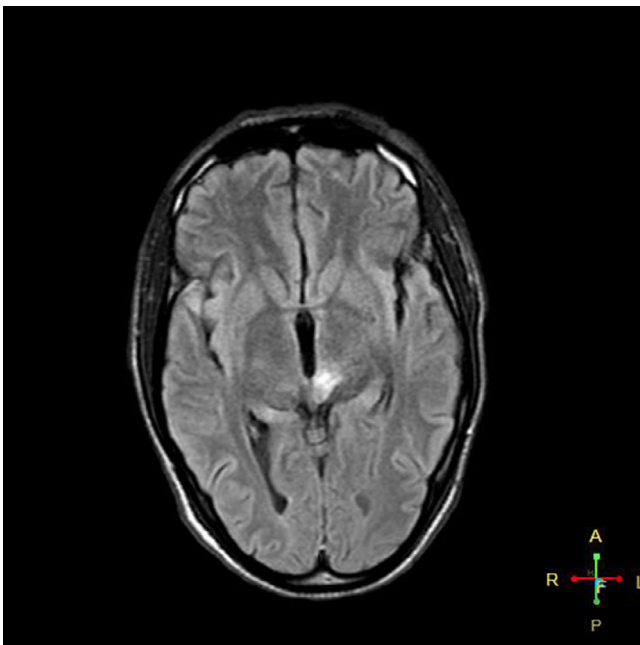


Fig. 5 – Continued

A follow up MRI after four month showed marked improvement of the extensive brainstem lesions and only mild residual gadolinium enhancement (Fig 5). The patient was discharged into a local rehabilitation facility for continuation of physiotherapy, occupational therapy and speech therapy.

Discussion

The radiological features of Behçet disease can be categorized according the systems involved, namely: central nervous system, chest and cardio-vascular system, gastro-intestinal system and musculoskeletal system. As this is a multi-system disease, radiological findings involving more than one system may be encountered simultaneously.

Neuro-Behçet disease:

NBD can be subdivided into parenchymal and non-parenchymal involvement. Parenchymal NBD typically involves the brainstem, basal ganglia and spinal cord. Non-parenchymal involvement includes aseptic meningitis, intracranial hypertension, cranial nerve lesions and vascular lesions (e.g. arterial dissection, aneurysms and dural venous sinus thrombosis) [6]. The most common acute and sub-acute NBD lesions occur at the meso-diancephalic junction (MDJ) with a pattern of asymmetrical involvement, extending inferiorly along fiber tracts with sparing of the red nuclei. Subsequent reversibility might be demonstrated on follow-up MRI with residual central lesions [7]. The thalamus, cerebral peduncle, midbrain, pons and posterior limb of the internal capsule are common sites on involvement as in our case [6–10].

Following brainstem involvement, asymmetrical lesions of the basal ganglia are the second most common sites for NBD. Subcortical lesions are also encountered, however less frequently. Parenchymal involvement may present as pseudotumors on imaging [8].

On MRI, parenchymal NBD lesions typically present with foci of increased signal intensity on T2W and FLAIR imaging, often with adjacent edema. The corresponding T1W signal intensity in these lesions is hypo- to iso-intense. The shape of parenchymal NBD lesions is very variable [11], however, a classic configuration extending from the thalamus inferiorly into the midbrain and cascading down the brainstem has been described as the ‘cascade sign’ of meso-diancephalic involvement and was seen in our patient [9,10].

Spinal cord lesions occur rarely in NBD and are usually multi-focal and non-contiguous [11]. Two distinct MRI patterns of the spinal cord have been described in NBD, namely the “bagel sign” and the “motor neuron pattern”. The ‘bagel sign’ is characterized by a central cord lesion with central hypo-intensity and a hyper-intense rim. The motor neuron pattern shows symmetrical anterior horn cell involvement [13]. No spinal cord lesions were detected in our patient.

Contrast enhancement pattern of neuro-Behçet lesions are highly variable and can be irregular, circular or curvilinear [9]. Reversibility is an important feature of NBD and is seen as decrease in the extent of lesions, presence of edema or enhancement on follow-up imaging [11], as noted in our patient. Typically, NBD lesions do not demonstrate restricted diffusion, however atypical lesion may exhibit restricted diffusion and, thereby, indicate non-reversibility [9]. On MR Spectroscopy, NBD lesions present with a reduced NAA/Cr ratio [9]. No restricted diffusion was noted in the patient described and MR Spectroscopy was not done.

Multiple sclerosis (MS) is an important differential diagnosis for NBD. However, lesions in MS are more typically located

at the periventricular and calloso-septal interface and, if the brainstem is affected, the floor of the fourth ventricle and the middle cerebellar peduncles more commonly favor MS, compared to the confluent brainstem involvement seen in NBD [11,12].

Cardiovascular and pulmonary Behçet disease:

The most common thoracic manifestation of Behçet's disease is pulmonary vessel vasculitis however, mediastinal, lung parenchyma and pleural involvement are also described. While CT is the primary imaging modality for detection and evaluation of the chest [14], MR angiography is an accepted alternative modality, but provides limited information about the lung parenchyma.

Chest radiographs may demonstrate non-specific lung changes and hilar enlargement due to pulmonary artery aneurysms [14].

Vasculitis can occur in vessels of any size and overall, venous involvement is more common than arterial disease, typically in the form of thrombophlebitis. [10] Mural thickening of the aorta and superior vena cava (SVC) indicating vasculitis, is detectable on CT [13–15]. Pulmonary vasculitis with infarction and hemorrhage may be visualized on CT as areas of consolidation and focal high attenuation within the lung parenchyma [14].

On CT angiography, the most common findings of Behçet's disease are vascular occlusions and aneurysms. Behçet's disease is the most common cause of pulmonary arterial aneurysms and, if present, they are associated with a poorer prognosis [14]. The main pulmonary arteries and their branches are most commonly affected [15], but, rarely, aortic, coronary and subclavian aneurysms may also occur [13].

Primary pulmonary arterial thrombosis, as well as intracardiac thrombi have occasionally been described [14]. The superior vena cava (SVC) may become occluded and cause the clinical picture of a SVC syndrome [15]. If pleural and pericardial involvement occurs, it presents as effusions and nodules on CT chest. Reactive mediastinal lymphadenopathy or an inflammatory mediastinal mass on CT can indicate mediastinal involvement [14]. In our case, there were no feature of intrathoracic disease.

Gastro-intestinal (GI) Behçet disease:

Similarly to the findings in the thorax, involvement of the GI tract is caused by a vasculitis. Here the mural vessels of the bowel, in particular the venules, are affected and the terminal ileum and caecum are the predominant anatomic sites. Less commonly, the upper gastro-intestinal tract, including the stomach and esophagus may also be involved [8,16].

Pathologically, Behçet disease of the GI presents as ulcers - either focal, more common at the ileo-caecal region, or diffuse often in the colon. There is significant overlap and similarity in the radiological features of Behçet disease and Crohn disease - however, the latter is associated with more surrounding inflammation, lymphadenopathy and fibro-fatty proliferation, which is rare in Behçet's disease. Similarly to Crohn's disease, discontinuous multi-focal involvement and deep penetrating ulcers may be encountered with complications including perforation, fistulas, hemorrhage and peritonitis [8,16].

Polypoid lesions and significant fold and mural thickening of the bowel can also be seen on CT. Occasionally, a large (up to 10cm) inflammatory mass lesion may be demonstrated at the ileo-caecal region and can be difficult to differentiate from a neoplasm. Aneurysmal dilatation of distal ileum has also been described [8,16].

Ulcers may be demonstrated classically as punched-out lesions on double contrasted barium studies. However, contrast enhanced CT is the preferred modality, because evaluation of extra-intestinal extension and potential complications is wanted [8,16]. In our case, we found significant concentric and nodular bowel wall thickening of the terminal ileum, caecum and ascending colon on CT abdomen, indicating severe GIT involvement.

Conclusion

Here, we present a case of Behçet disease in a young male of African origin. Characteristic radiological features suggestive of neuro- Behçet disease, in particular, the classic "cascade" configuration of lesions extending from the thalamus inferiorly into the brainstem facilitated the diagnosis in a setting, where this disease is rare. In addition, concentric mural thickening of the terminal ileum and large bowel was present, providing further radiological evidence and supporting the diagnosis.

The knowledge of radiological hallmarks of Behçet's disease and close collaboration between the radiologist and clinicians are essential, in order to promptly establish a diagnosis and avoid delay in treating patients with this potentially devastating disease.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:[10.1016/j.radcr.2021.11.046](https://doi.org/10.1016/j.radcr.2021.11.046).

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