The Maritime Silk Road: case report of Neuro-Behçet's disease from Somalia with positive HLA-B51 haplotype

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Abstract

Behçet's Disease (BD) is a multisystemic inflammatory disorder that commonly presents with oral and genital ulcers and uveitis, and can involve the nervous system i.e. Neuro-Behçet's Disease (NBD). We present the first reported case of Neuro Behçet's Disease (NBD) in a patient of Somali origin. A 34-year-old female from Somalia who had initially presented with headaches and Generalized Tonic-Clonic Seizures (GTCS) but was lost to follow-up. She represented with additional headache, neuropathic leg pain and ulcerated leg swellings with genital itching. Physical examination revealed hyperpigmentation and erythema nodosum on the lower limbs. Laboratory investigations revealed elevated ESR, positive HLA-B51 and a positive skin pathergy test. MRI brain scan revealed non-enhancing white matter hyperintensities in the right meso-diencephalic junction classical for NBD. She was commenced on immunosuppressive therapy with good response at one month. In conclusion, NBD is rare in sub-Saharan Africa. Our case report highlights that the disease is prevalent also on the Maritime Silk Road which includes Somalia.

Key words: Behçet's disease, Neuro-Behçet's disease, Sub-Saharan Africa, Somalia

Introduction

Behçet's Disease (BD) is a multi-systemic inflammatory disorder that usually affects those aged between 20 to 50 years[1]. The prevalence has traditionally been thought to be highest in regions along the ancient 'Silk Road' trading route from the Middle East, but BD is now known to occur in populations far outside this geographical area[2], including along the seldom-known maritime route which extends to the Horn of Africa. The point-based diagnostic criteria for BD include: recurrent oral and/or genital ulceration; ocular lesions; mucocutaneous lesions; vascular lesions; and/or a positive pathergy test[1]. Neurological involvement can occur in approximately 5% of patients with BD i.e. Neuro-Behçet's Disease (NBD), and is defined as BD with additional neurological symptoms in clinical patterns known to occur in BD[3]. NBD usually occurs in the first 5 years of established BD, and can involve the central and/or the peripheral nervous system(s)[3].

Little is known about NBD in indigenous African populations. Severe meningo-encephalitis was found to be more common in Afro-Caribbean patients in the Guadaloupe archipelago[4]. In multi-ethnic European countries, NBD is found to be more common in males with BD from North Africa[5,6], these findings have been consistently shown in indigenous cohorts e.g. from Tunisia and Morocco, where the commonest manifestation of NBD was cerebral venous sinus thrombosis[7,8]. A study from Libya showed that neurological involvement occurs earlier and more frequently in BD patients[9].

There are very few reports of NBD from sub-Saharan Africa (SSA), but they show similar findings of male preponderance. A case series from Senegal found the majority with NBD had parenchymal complications of rhombencephalitis[10], similar to the Caribbean study; however, headaches are also the main presenting feature in NBD from West Africa[10,11]. The only published reports from East Africa come off the coast from Comoros: in addition to echoing findings from the rest of the continent, one-third had severe disability or death due to NBD[12]. Over-arching all these reports from Africa is the significant absence of the HLA-B51 haplotype, which has the highest genetic susceptibility and is associated with more severe BD[13]. There are no published reports of HLA-B51 positive individuals from the East Africa region.

We present the first reported case of NBD in a patient of Somali origin, who also carried the HLA-B51 haplotype, who we diagnosed and managed at our tertiary regional referral centre in Nairobi, Kenya.

Case report

A 34-year-old female from Somalia first presented to our facility five years before with headache. Magnetic Resonance Imaging (MRI) of the brain was reported to show non-specific White Matter Hyper-intensities (WMHs). She was commenced on medication but was very soon lost to follow-up when she returned to her home country.

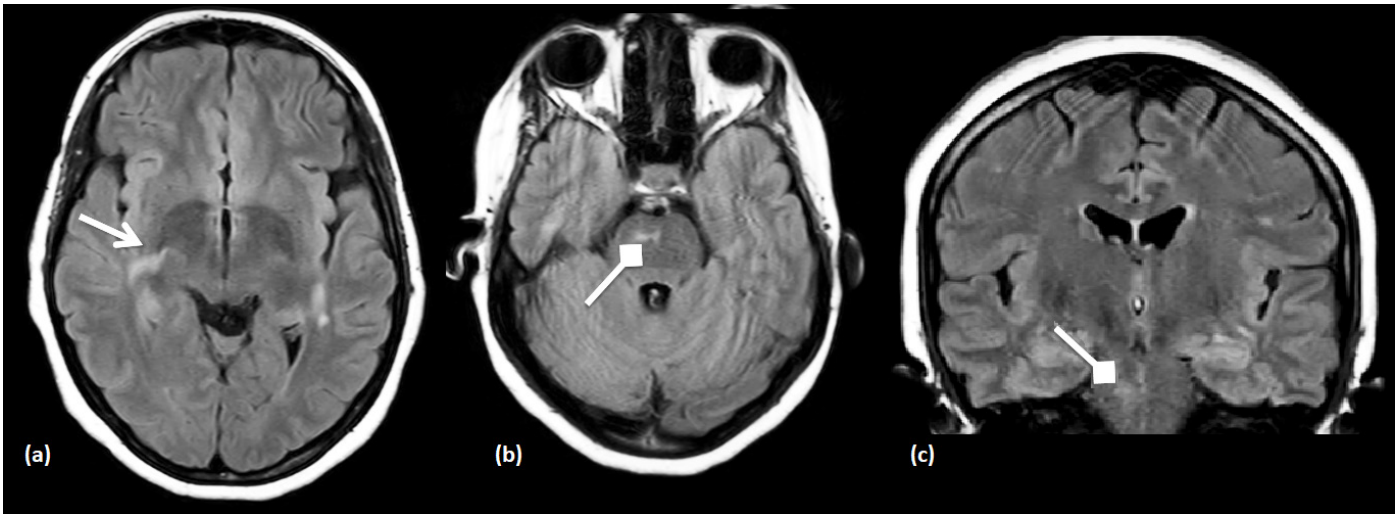
Five years later, she was admitted to our hospital as an emergency due to one year of worsening headaches, but also frequent Generalised Tonic-Clonic Seizures (GTCS), new pains in her lower limbs and depressed mood for six months. On further clinical evaluation, she also confessed to having ulcerated swellings of the lower limbs for six months, genital itching, and occasional mouth ulcers. She commented that she would develop large blisters on her hands following intravenous cannulations in Somalia when she was admitted sometimes for GTCS.

Physical examination revealed erythema nodosum on the shins. Neurological examination demonstrated reduced reflexes in the lower limbs with stocking distribution loss of sensation to the mid-shin level, in keeping with peripheral neuropathy. Gynaecological examination confirmed vulvo-vaginal ulcers. Ophthalmological examination was normal.

Blood tests, including full infective, metabolic, vasculitic and auto-immune panels, were all normal except for raised white cell count of 12.9 x 10^9/L, elevated Erythrocyte Sedimentation Rate (ESR) of 130 mm/h (normal <20) and C-Reactive Protein (CRP) of 109.6 mg/L (normal <5). Chest radiograph was normal.

We suspected BD, and proceeded to do a skin pathergy test which was positive, and further requested for HLA-B51 haplotyping which also came back positive, confirming the diagnosis. We did not organise neurophysiological testing due to the leg ulcerations and pain. Repeat MRI brain scan showed worsening WMHs, but now with involvement of the right meso-diencephalic junction and pons without vascular involvement (Figure 1), all pathognomonic of NBD.

Figure 1: Fluid-Attenuated Inversion Recovery (FLAIR) MRI sequences of the brain: (a) coronal, (b) axial, and (c) coronal slices showing meso-diencephalic junction (open arrow) and pontine (diamond arrows) white matter hyper-intensities pathognomonic of neuro-Behçet's disease.



For NBD we initiated immunosuppressive therapy with azathioprine at 2.5mg/kg/day, prednisolone at 1mg/kg/day, and colchicine 0.25mg three times a day. Her seizures were controlled with carbamezapine 200mg twice a day, which we slowly increased to 300mg twice a day after a week, and her neuropathic pain was controlled with pregabalin 150mg twice a day. She was reviewed by the inpatient psychiatry team and commenced on mirtazapine 15mg nocte for her depression. She also underwent inpatient physiotherapy and counselling.

We reviewed her as a Multi-Disciplinary Team (MDT) after one month. She was remarkably better with resolution of most of her debilitating symptoms. She had no more headaches and had had no more seizures, and her skin lesions healed had healed well. Repeat ESR and CRP were now in normal range.

Discussion

This case fulfilled the international diagnostic criteria for NBD[3]. She presented with headache, seizures and neuropathic pains almost in tandem with the new diagnosis of BD. This contrasts with the average time usually taken from onset of BD to NBD[7,14]. It is possible that the first presentation to our facility with headaches could have been the onset of NBD, and the systemic features were not clinically evident. Primary headache disorders are common in NBD patients[15], and up to 20% of BD patients can first manifest as NBD, which is a possibility for our patient too[16]. Cutaneous manifestations were important in clinching the diagnosis clinically in our patient; erythema nodosum is more prevalent in female patients with BD[13] but can often be missed.

The HLA-B51 allele positivity in our case is unique when compared to the overwhelming number of negative cases reported across SSA[4,10]. Putatively, the proximity of Somalia to the traditional Silk Road could explain this finding. Having this haplotype is also associated with more severe disease as presented in our case[3].

The MRI findings in our patient were also pathognomonic for NBD. Studies from North Africa have shown that deep white matter and subcortical structures are most affected, followed by the brainstem and pons, and then the spinal cord[17]. We did not manage to scan the spinal cord of our patient, although clinically she did not have a myelo- or radiculo-pathy. Some patients with NBD in SSA have been reported to have more tumefactive lesions mimicking brain tumours, including of the pons[18,19].

Our patient had good outcomes as treatment was directed by the MDT, and therapy followed the international guidelines for the management of NBD[20]. In our case, given the moderate burden of disease, we added azathioprine on top of the usual regimen of corticosteroids and colchicine. We kept in mind the child-bearing age of the patient in our choice of immunosuppression, otherwise we would have considered more efficacious treatments such as infliximab.

In conclusion, our case is unique in the published literature of NBD in SSA in that she was a female, from a lesser-known part of the Silk Road, had positive HLA-B51 haplotyping, and had both central and peripheral nervous system involvement. Additionally, the MRI brain findings and cutaneous manifestations were important in making the timely diagnosis so as to allow immediate and appropriate treatment, which led to good outcomes.

Declarations

Ethics approval and consent to participate

This manuscript fulfilled our institutional criteria for exemption from full Institutional Ethics Review Committee evaluation. The patient gave informed written consent for her anonymised case history and images to be published, and this consent form is filed in her medical file.

Availability of data and materials

Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.

Competing interests

The authors declare that they have no competing or conflicts of interests.

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