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Systemic Nocardia infection in a patient with Behçet’s disease

Sir, Behçet’s disease is an inflammatory disease of unknown cause, characterized by recurrent oral aphthous and genital ulcers, uveitis and skin lesions [1]. Gastrointestinal symptoms and central nervous system, large vessel or ocular involvement might necessitate the use of high-dose corticosteroids and other immunosuppressive agents [2]. Infections with Nocardia species are rare and generally seen in immunocompromised subjects [3]. N. asteroides is the most frequent offender in humans; it is mostly associated with skin, lung, and brain abscesses [4]. We present a patient with Behçet’s disease who used corticosteroids and immunosuppressives for a long time, and who died from systemic nocardial infection not responding to therapy.
In December 1999, a 29-yr-old man was admitted to our hospital with fever, chills, cough, sputum and abdominal pain. He reported inability to move his left upper and lower extremities for 6–7 days. He had had blurred vision, oral aphthous and genital ulcers, acneiform skin lesions, and erythema nodosum of the lower extremities for the last 5 yr. He was diagnosed 5 yr ago as having Behçet’s disease. He had used a variety of immunosuppressive agents, including high-dose systemic corticosteroids, azathioprine and cyclosporine in order to suppress recurrent attacks of uveitis, progressive visual loss and refractory skin lesions. On admission, his temperature was 38.7°C. He had a cushingoid appearance, with many striae and acneiform lesions. On the right upper quadrant of the abdomen, there was the opening of a fistulizing tract from which pus was draining. Neurological examination revealed a left-sided hemiparesis: there were no signs of meningeal irritation. The erythrocyte sedimentation rate was 132 mm/h. C-reactive protein was 19.8 mg/dl (normally <0.5), leucocyte count 14 300/mm³ and glucose 325 mg/dl. Anti-HIV and hepatitis serologies were negative. The lumbar puncture showed no cells and a slightly elevated level of protein (67.2 mg/dl). A computed tomography (CT) scan of the cranium demonstrated cerebral oedema and multiple ring-enhancing lesions, the largest measuring 2 cm in the cranio-caudal direction (Fig. 1). CT of the chest revealed an abscess surrounded by an area of consolidation in the right upper lobe. In the abdominopelvic CT, there were two abscesses with largest diameters of 2.5 and 1.2 cm in the iliac and iliopsoas muscle regions, which had fistulizing tracts to the skin.

Examination of the sputum specimen and pus obtained after opening of the fistula in the abdomen revealed acid-fast, branching gram-positive rods consistent with Nocardia species. Three days after inoculation, white-coloured, chalky rough colonies were present on chocolatized agar and agar supplemented with 5% sheep’s blood. Blood cultures remained sterile. An E-test (Epsilometer test; AB Biodisk, Solna, Sweden) indicated that the bacterium was susceptible to ceftriaxone and trimethoprim–sulphamethoxazole (TMP-SMX). Subspecies identification was not performed. Therapy with intravenous TMP-SMX (400 mg/2000 mg every 6 h) and ceftriaxone (2 g daily) was initiated. After 3 weeks of therapy, no regression of the abscesses in the brain, right lung and abdomen was seen on CT scans. Drainage of the cranial abscesses was planned, but the patient’s clinical situation deteriorated and he died after 6 weeks of hospitalization.

Nocardiosis is primarily an opportunistic infection [5]. Disseminated nocardial infection in Behçet’s disease has not been reported until now. Although neutrophil hyperfunction and lymphocyte function abnormalities have been reported, no significant immune dysfunction has been demonstrated in Behçet’s disease [2]. We assume that the cause of the disseminated nocardial infection was immunosuppressive therapy rather than the primary disease itself. The diabetes mellitus which developed after steroid use might also have played a role by disrupting cellular immunity [6].

As Nocardia species grow in cultures of sputum and pus from the fistula, it is almost certain that it was also the causative agent in the cerebral abscesses. It is known that haemocultures are rarely positive in nocardiosis [7].

The most effective therapy in cerebral nocardiosis is TMP-SMX. In patients with immunosuppression, combining it with imipenem or third-generation cephalosporins is advised [5]. In immunocompromised patients with large, multiloculated abscesses, craniotomy and surgical excision might be needed [8]. In some patients, successful results may be obtained with stereotactic needle aspiration and antimicrobial therapy [9]. In our case, surgical operation could not be performed because of the patient’s deteriorating clinical condition.

Neurological involvement may be present in 5% of patients with Behçet’s disease. It may present as brainstem and pyramidal symptoms, intracranial hypertension, aseptic meningitis and medullary symptoms [10]. Findings of lumbar puncture are not specific, but the most important diagnostic method is cranial CT and MRI [11]. High-dose steroids are used for treatment. Neurological symptoms in patients with Behçet’s disease, especially in young males, should alert one to the presence of neurological involvement in this disease. However, central nervous system involvement by opportunistic infective agents such as Nocardia spp, may cause similar neurological presentations. For this reason, cerebral imaging is advisable before administration of immunosuppressive agents. MRI is the method of choice to diagnose both neurobehçet and Nocardia abscesses. Although the relation between nocardiosis and immunosuppression is well known to our knowledge this is the first case of disseminated nocardial infection in a patient with Behçet’s disease.

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Fig. 1. Cranial CT showing two abscesses with surrounding oedema in the right lobe of the brain.
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