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CASE REPORT

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Mature ovarian teratoma as a possible cause of fever and clinical exacerbation in Behçet's disease: a case report

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Abstract Behçet's disease (BD) is a chronic relapsing systemic vasculitis of unknown etiology. BD is very rarely associated with neoplastic diseases. We report the case of a 39-year-old woman who had been treated for BD for 3 years. She presented with relapsing oral and genital lesions and persistent high-grade fever which had lasted for 1 month. The possible cause of the exacerbation of BD and fever in this patient was a mature ovarian teratoma. To our knowledge this is the first report of a patient with BD associated with a ovarian teratoma.

Key words Behçet's disease · Teratoma

Introduction

Behçet's disease (BD) is a chronic relapsing systemic vasculitis in which orogenital ulceration is a prominent feature. BD has a undulant clinical course with relapses and remissions.[1] The coexistence of a neoplasm with BD is quite rare. The case presented was a 39-year-old woman who was diagnosed as having BD 3 years ago. In the last month before admission her oral and genital lesions suddenly flared up, and a high and persistent fever appeared. The exacerbation of the disease was investigated, and a mature ovarian teratoma (MOT) was found which was believed to be the underlying cause. To our knowledge, this is the first case of BD associated with MOT.

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Case report

A 39-year-old woman, a known Behçet's disease patient, came to our haematology department in May 1999 complaining of relapsing orogenital ulcerations and high-grade fever that had been present for 1 month. She had been on colchicine therapy for the last 3 years. On admission, her vital signs were as follows: blood pressure 120/70 mmHg, pulse 100/min, fever 39.5°C, and respiratory rate 25/min. The patient had many painful oral and genital ulcerations and papulopustular lesions on the face and trunk. There was no organomegaly or peripheral lymphadenopathy (LAP). An ophthalmological examination was normal. The genital ulcers did not respond to treatment. Her temperature remained above 39°C, and antipyretic (paracetamol) therapy did not control it. The fever was thought to be due to the activation of BD, and interferon α-2a (IFN) (3 MU every other day) was added to the colchicine treatment. At this time, her WBC count was 13.2×10^6/l, the hematocrit value was 28.5%, and the erythrocyte sedimentation rate (ESR) was 94 mm/h. A peripheral smear showed neutrophilia with a left shift. The lactic dehydrogenase level was high (530 U/dl). Urinalysis and chest X-rays were normal. C-reactive protein (CRP) was positive. With latex fixation, antibodies to nuclear antigens and neutrophils were not detected. Blood, urine, and bone marrow cultures were all negative. The Mantoux test for tuberculosis was negative. Bone marrow aspiration and biopsy were normal. Tumor markers were within normal limits, except for elevated CA 15-3 level (43.5 IU/ml). Mammography showed no abnormality. Echocardiography revealed minimal pericardial effusion. Abdominal computed tomography (CT) demonstrated multiple LAP's extending from the retroperitoneal region to both parailiac areas, and also a large cyst containing both calcification and fat in the right adnexal area (Figs. 1 and 2). For diagnosis and treatment, a right oophorectomy

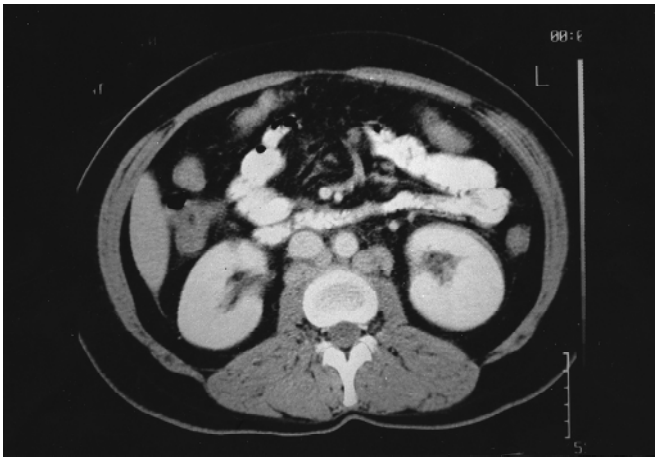

Fig. 1. Axial contrast-enhanced CT image through the level of the kidneys showing multiple lyphadenopathy filling the paraaortic and paracaval spaces

Fig. 2. Axial contrast-enhanced CT image through the pelvis showing the dermoid cyst in the right adnexa containing calcification and fat

was performed, and samples of the enlarged lymph nodes were taken.

Macroscopical examination of the oophorectomy material revealed a thick-walled cystic partially solid lesion, 7 cm in diameter, with an encapsulated white-to-grey external surface. Yellow sebaceous material and hair filled some of the cysts, the others contained a colourless watery fluid. Microscopic sections showed a cystic teratoma with a wide variety of fully mature tissue components. The cysts were lined with keratinizing stratified squamous epithelium (Fig. 3a). Skin appendages were present. Mature fat, neural tissue, bone, cartilage, thyroid gland, serous–mucinous acini, respiratory epithelium, and smooth muscle, mostly arranged in an organoid fashion, were also detected (Fig. 3b). In the surrounding tissues, histiocytic reactions and lymphocytic infiltration were observed, suggesting a response to the escape of the contents of the cyst into the adjacent stroma (Fig. 4). The lymph nodes were reactive. Table 1 shows the clinical course of the fever and the treatment given.

On the first day after the operation, the fever disappeared. There were no postsurgical complications, and the patient was discharged 7 days after the operation. One month later, at a routine check-up, she was completely healthy, and the oral and genital lesions had healed. Total blood count, liver and renal functions, CRP, ESR, and tumor markers were all normal, and there were no signs or symptoms of BD. IFN was then stopped.

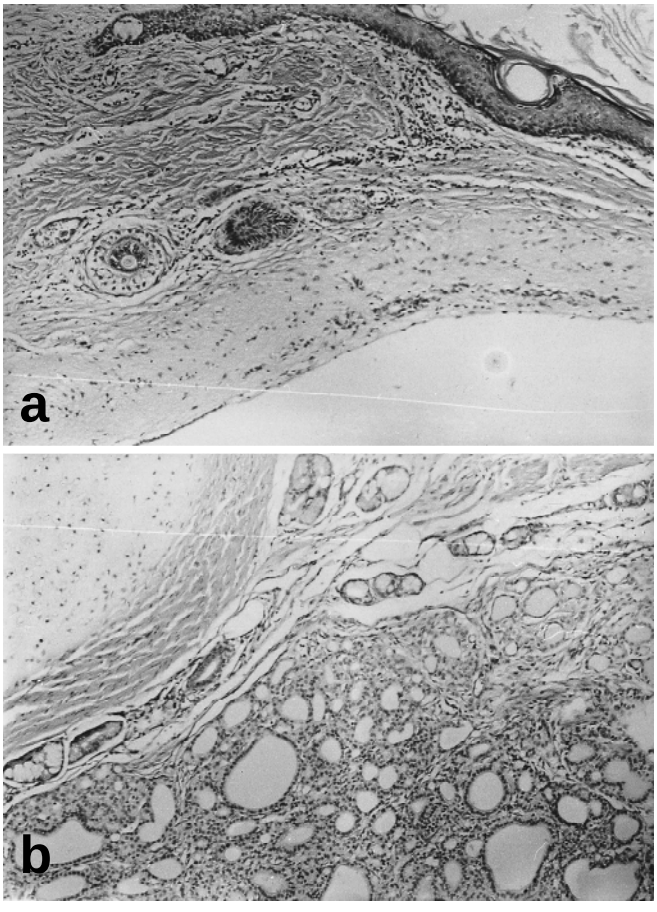

Fig. 3. **a** Cysts were lined with keratinizing stratified squamous epithelium and contained a wide variety of fully mature tissue components. **b** Skin appendages such as mature fat, neural tissue, bone, cartilage, thyroid gland, serous–mucinous acini, respiratory epithelium, and smooth muscle were present, and were mostly arranged in an organoid fashion

Discussion

BD has been described by Hulusi Behçet, a Turkish dermatologist, as a triple-symptom complex of recurrent orogenital aphteous ulcerations and relapsing iritis with hypopion.[1] Although the underlying etiopathogenesis has not been identified precisely, the main underlying pathological event is vasculitis.[2] Because of the clinical heterogeneity of BD and the lack of specific diagnostic laboratory or

Table 1. Clinical course of the patient and the treatment given

Date	Symptoms and signs	Diagnostic findings	Treatment
Presentation	Relapsing orogenital ulcerations, high-grade fever (39.5°C), papulopustular lesions on the face and trunk	Leucositosis, anemia, ESR elevation, neutrophilia with a left shift on peripheral smear, CRP (+), lactic dehydrogenase level high	Colchicine + paracetamol
1 week later	High-grade fever	Minimal pericardial effusion on echocardiography	Interferon alpha-2a added to the colchicine + paracetamol
2 weeks later	High-grade fever	Elevated CA 15-3 level, abdominal CT showed multiple LAPs in the abdomen and a large cyst in the right adnexal area	Right oophorectomy and sampling of enlarged lymph nodes
First day after operation	No fever	–	Colchicine + interferon
Seventh day after operation	No fever	–	Colchicine + interferon
One month later	No fever, oral and genital lesions were healed	Complete blood count, CRP, ESR, and tumor markers were normal	Colchicine

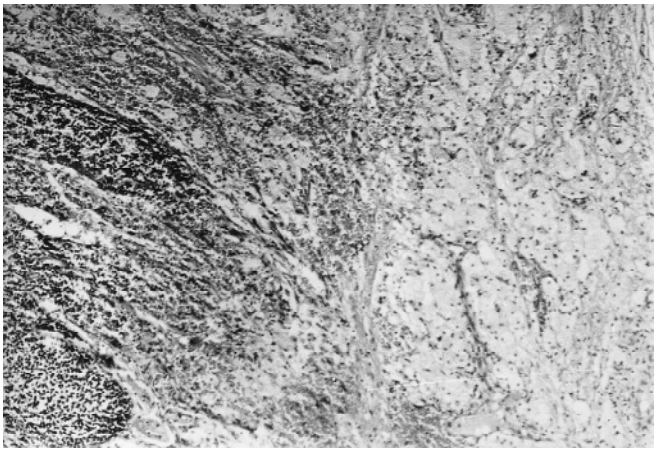

Fig. 4. Histiocytic reaction and lymphocytic infiltration were observed in the surrounding tissues, suggesting a response to the escape of the contents of the cyst into the adjacent stroma

clinical tests, in 1990, the International Study Group for BD (ISG) published its universal criteria. These require the presence of recurrent oral ulceration plus any two of the following findings: recurrent genital ulceration, eye lesions, skin lesions (erythema nodosum, folliculitis, pustules), or a positive pathergy test.[3] Other clinical features have been left out of the diagnostic criteria because they are less specific.

The case presented was diagnosed as BD according the established ISG criteria. Although the patient had been having colchicine treatment for the last 3 years, her oral and genital lesions had flared up, and high-grade and persistent fever was added to these in the last month before admission. Although low-grade fever is also one of the systemic manifestations of BD and will generally respond to the colchicine therapy, high-grade and persistent fever is rare and may be due to any of the diseases which may complicate BD.[4–7] At first, IFN therapy was initiated to control this acute exacerbation of the disease. IFN has been shown to be effective in the treatment of BD.[8–10] In this case, all bacteriological cultures and serological markers of connective tissue diseases were negative, and the fever did not subside with IFN treatment. Abdominal CT showed a mass and multiple LAP in the lower abdomen which was consistent with a cystic teratoma. The result of a histopathological examination revealed a mature cystic ovarian teratoma with reactive LAP. On the first day after the operation, the patient's fever disappeared. Although it has been suggested that BD might give rise to postsurgical complications,[11] none were observed. The association of malignant disease with BD is quite rare. The autoimmune nature of the disease and/or the immunosuppressive drugs used in its management are regarded as probable causes of the malignant transformation in most of the cases.[12,13] In the present case, however, no immunosuppressive agents had ever been administered. Before this case, only five of our BD patients developed malignant tumors during the course of the disease; these were carcinoma of the breast (BC), chronic myelocytic leukemia, epidermoid carcinoma of the skin, and hepatocellular carcinoma in two patients.[13–15] Cyclophosphamide was only used as an immunosuppressive agent in the treatment of the patient with BC.

We think that the possible cause of the exacerbation of BD and the high-grade fever in this patient was the MOT. Infection, inflammation, and neoplasia are well-known classical pathobiological causes of acute-phase reactions. The exact mechanism triggering the attacks of BD is unknown. However, a large tumoral lesion (e.g., a teratoma) could be the underlying pathology leading to the active state (heightened inflammation) of BD by causing proinflammatory responses in this patient. To our knowledge, this is the first case of BD associated with MOT in the English literature.

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