Adamantiades-Behcet’s disease: the past, the present and the future

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Abstract

Introduction
Adamantiades-Behcet’s disease is more common along the ‘Silk Road’ and among young adults with HLA-B51 allele. The aim of this review was to discuss the past, present and future of Adamantiades-Behcet’s disease.

Discussion
It is a chronic relapsing vasculitis characterised by recurrent oral and genital ulcers, cutaneous and ocular manifestations. Visual loss may occur in up to 20% of the affected patients. Arthritis, gastrointestinal and nervous involvement may occur. This vasculitis has a tendency for superficial and deep vein thrombosis.

Corticosteroids remain the mainstay of treatment, while other immunosuppressive agents, such as azathioprine, cyclophosphamide, anti-TNF-α, colchicine and thalidomide have been used successfully for its treatment. Anti-TNF-α agents seem to be very promising for severe central nervous system, ocular and gastrointestinal involvement.

Conclusion
Morbidity is mainly due to ocular lesions, while mortality is low and is due to CNS involvement, bowel perforation, pulmonary symptoms or thrombosis.

Introduction
The first description of Adamantiades-Behcet’s disease was attributed to Hippocrates in the fifth century BC. In 1931, the Greek ophthalmologist Benediktos Adamantiades described a patient with relapsing iritis and hypopyon and associated other clinical features such as: genital ulcers and arthritis as features of a single disease. In 1937, the Turk ophthalmologist Hulusi Behcet reported the classical triad of oral and genital ulceration together with ocular inflammation in a small number of patients. Adamantiades-Behcet’s disease is a multisystem, inflammatory disorder of unclear aetiology that is characterised by recurrent oral ulcers and two of the following: genital ulcers, skin lesions, a positive pathergy test and ocular involvement. Other manifestations include arthritis, thrombophlebitis, central nervous system disease and gastrointestinal ulcerations. This review discusses Adamantiades-Behcet’s disease.

Clinical presentation
Adamantiades-Behcet’s disease is most common along the areas crossed by the ‘Silk Route’ countries, from the Mediterranean sea to the Far East. Genetic factors known to be involved is the HLA-B51 allele, while environmental stimuli seem to participate in the initiation of symptoms among young adults. Cytokines, such as interleukin-1, interleukin-8, interleukin-17, TNF-α, heat shock proteins, macrophage activation and neutrophils chemotaxis seem to be involved in the pathogenesis of the disease.

Adamantiades-Behcet’s disease is a chronic, multisystem relapsing vasculitis that presents predominantly with recurrent oral and genital ulcers, skin lesions and ocular involvement. International criteria have been established for its diagnosis, which have a sensitivity of 85% and a specificity of 96%. These criteria include recurrent oral ulcers and at least two of the following: recurrent genital ulceration, eye lesions, skin lesions and pathergy test. These criteria are applicable only in the absence of other possible explanations. Oral ulcers are painful lesions with round, sharp, erythematous and elevated borders, which may appear on the tongue, pharynx, buccal and labial mucosal surfaces. They may start as a raised redness, around 1–3 cm and they may soon ulcerate. The surface is covered with a yellowish pseudomembrane. The lesions heal within about 10 days mostly without scarring. Genital ulcers affect 60%–65% of patients, have the same characteristics with oral ulcers, but are usually larger, deeper and tend to leave scars in 50% of the affected patients. Skin lesions can be divided into two main types: erythema nodosum and papulopustular/ acneiform lesions. The formal pathergy test involves intradermal pricking of the skin with a needle and it is considered positive if an erythematous papule or a pustule develops at the prick site within 48 hours, while the occurrence of a papule or pustule at the site injection is considered as an analog to the formal pathergy test. Ocular involvement is usually bilateral and occurs within the first two to three years of the onset of Adamantiades-Behcet’s disease. The most common ocular manifestations are relapsing remitting posterior uveitis, panuveitis and retinal vasculitis. Less common manifestations include scleritis, episcleritis, conjunctival ulcers and extraocular muscle paralysis. Visual loss occurs in up to 25% of the affected patients. Other manifestations such
as arthritis, involvement of the gastrointestinal tract, superficial and deep venous thromboses and brain involvement may also occur.2–5

Gastrointestinal symptoms may include diarrhoea, nausea, abdominal pain and sometimes true perforation. Its distinction from inflammatory bowel disease may be very difficult, even in biopsy specimens. Lesions may be located throughout the gastrointestinal tract, from the oesophagus to the large intestines. Pancreatitis may rarely occur.6

Neurological involvement affects 20%–40% of patients. Usually, it is observed later in the course of Adamantiades-Behcet’s disease, even up to 10 years later.7 Central nervous system involvement more often manifests as an attack rather than a mild progressive disease. Headache, meningitis, meningoencephalitis, seizures, hemiplegia or cranial nerve paralysis may occur. Psychosis or personality changes may be observed, which may be difficult to differentiate from iatrogenic side effects of therapy.8,9 Cerebral venous thrombosis or benign intracranial hypertension is non-parenchymal disorders due to thrombosis.10 Multifocal areas of demyelination of the white matter are a feature of multiple sclerosis, but it can also be seen in Adamantiades-Behcet’s disease with involvement of the central nervous system (Figure 1).21,24

Arthralgia and/or arthritis of the knees, wrists, elbows and ankles may occur in up to 45% of the cases and it usually precedes years before the other manifestations.11 Arthritis is usually non-erosive, inflammatory, symmetric or asymmetric oligoarthritis, although polyarthritis or monoarthritis may rarely occur. Among patients with Adamantiades-Behcet’s disease there is tendency for superficial and deep venous thrombosis, which is associated with this vasculitis. Thrombosis in the dural sinuses, superior and inferior vena cava and Budd–Chiari syndrome carry a poor prognosis.25

Apart from venous thromboembolism, arterial involvement has been documented in 2%–3% of the patients. Arterial involvement may be in the form of thrombosis or aneurysms. Other very rare manifestations such as cardiac involvement in the form of myocarditis, myocardial infarction, endocarditis or pericarditis or pulmonary involvement such as aeurysms, infarction, haemorrhage may result in death among patients with Adamantiades-Behcet’s disease. Renal involvement is very rare and may occur as glomerulonephritis. Haematological involvement, such as haemophagocytic syndrome may also occur.6

Discussion

Treatment

Corticosteroids remain the mainstay of treatment in Adamantiades-Behcet’s disease. They can be applied topically or systematically in the cases of Neuro-Behcet’s disease and in cases of ocular involvement. After the initial 1 g methylprednisolone for three days intravenously, corticosteroids may be reduced with caution after four weeks of therapy. Relapses are frequently seen after discontinuation of corticosteroids. Immunosuppressive drugs have been proved to be effective, such as azathioprine, cyclophosphamide,

Figure 1: (a) A brain magnetic resonance imaging depicting Neuro-Behcet’s disease with demyelinating lesions. (b) This is a thoracic CT scan of a patient with Adamantiades-Behcet’s disease, who has superior vena cava syndrome due to the tendency of this vasculitis for deep venous thrombosis.
cyclosporine, methotrexate and anti-TNF-a agents, the latter especially in cases of severe uveitis, central nervous disease or severe gastrointestinal involvement. Anti-TNF-a agents seem to be very promising for the severe attacks of Adamantiades-Behcet’s disease. Plasmapheresis, intravenous immunoglobulins and alpha-interferon have been also efficacious in severe cases. Colchicine and thalidomide have been used successfully in mucocutaneous symptoms, together with other agents. Colchicine is usually given at doses of 1–2 mg daily and seems to decrease the frequency and size of mucocutaneous lesions. Dapsone is helpful for mucocutaneous lesions at a dose of 50–150 mg daily alone or in combination with colchicine. Topical corticosteroids or tacrolimus may also be applied. In severe mucocutaneous disease, which does not respond to topical treatment or colchicine alone or plus dapsone thalidomide may be used. As an alternative, a low dose prednisone and low dose methotrexate (2.5–25 mg weekly) may be administered. Furthermore, interferon-a may be used for severe mucocutaneous disease and some systemic manifestations at a dose of 9 million units three weekly initially and afterwards in 3 million units three times weekly as a maintenance therapy.

Conclusion
The main cause of morbidity in Adamantiades-Behcet’s disease is an ocular disease, while mortality is generally low and is attributed to Neuro-Behcet’s disease, pulmonary involvement, thrombosis and bowel perforation.

References