CASE REPORT

Transient neonatal Behçet's disease

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marilina@doctors.org.uk**SUMMARY**

A term neonate with a transient form of Behçet's disease (BD) is described. The mother had a 3-year history of BD treated with corticosteroids, which remained in remission during pregnancy. On day 1 of life, the neonate was noted to have papulopustular lesions of the labia and perineum. She remained clinically well and bacterial and viral infection screens were negative. The lesions disappeared within 3 weeks without scarring. No recurrence has been reported.

of the neonate. No lesions were seen on the oral mucosa or elsewhere.

The baby's mother had a history of polycystic ovarian syndrome, vitamin D deficiency and BD. She had a 3-year history of BD characterised by severe recurrent orogenital ulceration and arthritis. She was treated with intramuscular hydrocortisone at presentation and the disease had been in remission for 1 year. Remission was maintained during pregnancy without the need for immunosuppressive treatment.

BACKGROUND

Behçet's disease (BD) is a recurrent systemic vasculitis of unknown aetiology, characterised by recurrent oral and genital ulcers and ocular inflammation. Other clinical manifestations include arthritis, skin lesions, neurological, gastrointestinal and vascular abnormalities. No laboratory diagnostic test is available and the diagnosis remains clinical. The International Study Group on BD has reached agreement on a set of diagnostic criteria (box 1).¹

Infectious agents, immune mechanisms and genetic factors are implicated in the aetiopathogenesis of the disease.² The principal finding on microscopy of most sites of active BD is of an immune complex occlusive vasculitis.³

The occurrence and transient nature of neonatal BD provide supporting evidence for the autoimmune pathogenesis of the disease. There are only a limited number of case reports in the literature.

INVESTIGATIONS

The patient was clinically well with vital signs within normal range. Inflammatory markers were not raised: C reactive protein <1 and white cell count $11.5 \times 10^9/l$ with normal differential. Blood cultures revealed no growth at 48 h. PCR of serum and vesicle fluid was negative for herpes simplex virus. A positive pathergy test was noted at the site of venepuncture.

Autoimmune screen was not performed. However, in reported cases of severe orogenital ulceration secondary to neonatal BD autoimmune screen has revealed raised IgG and IgM concentrations with normal complement levels.⁴

In a separate case report with a similar presentation, biopsy of the skin lesions revealed perivascular neutrophilic infiltration and necrosis of the epidermis consistent with the histopathological findings in BD.⁵

CASE PRESENTATION

A 3326 g girl was delivered at term to 29-year-old primiparous mother. The baby was born by spontaneous vaginal delivery in good condition with Apgar scores 9 at 1 min and 10 at 5 min. At 8 h of life, genital lesions were noted by the mother. Medical review confirmed multiple 1–2 mm pale papulopustular lesions on the labia and perineum

DIFFERENTIAL DIAGNOSIS

Disseminated infection due to herpes simplex and staphylococcal disease must be excluded, before a diagnosis of neonatal BD can be made. Immunodeficiency disorders secondary to defects of leucocyte and bacterial phagocytic function such as chronic granulomatous disease can have a similar presentation, although they tend to present at an older age. Leucocyte function tests to assess

Box 1 The International Study Group of Behçet's disease diagnostic criteria (1990)

Recurrent oral ulceration
At least 3 times in one 12-month period

Minor apthous, major apthous or herpetiform ulceration

Plus 2 of the following:

Recurrent genital ulceration
Eye lesions
Skin lesions
Positive Pathergy test

Uveitis, Retinal vasculitis, Cells in vitreous
Erythema nodosum, Folliculitis, Acneiform lesions,
Papulopustular lesions

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bactericidal activity and nitroblue tetrazolium test can be considered.

TREATMENT

The patient was admitted for observation until day 2 of age and remained haemodynamically stable. The ulceration did not progress and no further lesions developed.

In reported cases, the treatment of neonatal BD is supportive and observation. Intravenous broad-spectrum antibiotics such as third-generation cephalosporins and acyclovir were started empirically until primary or superimposed disseminated staphylococcal and herpetic diseases were excluded.^{4–6} One case was reported of life-threatening disease where intravenous hydrocortisone was administered followed by oral prednisolone.⁷ Glucocorticoids have been used as first-line treatment to achieve remission as they are the least toxic treatment regimen. The use of cytotoxic drugs and cyclosporine used to treat adult BD is inappropriate in neonates.

OUTCOME AND FOLLOW-UP

The patient's lesions disappeared in 3 weeks, with no evidence of scarring. In reported cases, the lesions disappeared within 6 weeks but healed with scarring.^{4–5} No recurrence of orogenital ulceration has been reported.

In view of the resolution of symptoms and the transient nature of the disease further investigations were not deemed appropriate on follow-up.

DISCUSSION

A transient form of BD may develop in a neonate of a mother with this disease. The available scientific literature is limited, mainly consisting of level III and II-3 evidence. In previously reported cases, the clinical features of neonatal Behçet's occurred within 1 week of birth and resolved by the age of 8 weeks. In each of the cases, diagnosis of maternal Behçet's predated pregnancy and in all cases mothers had orogenital ulceration during the pregnancy.^{4–7}

The most common features of neonatal BD include orogenital ulcerations and pustulonecrotic skin lesions that present in a spectrum of severity in terms of depth of ulceration, extent of spread and presence of associated pyrexia. A case of transient neonatal BD with life-threatening complications has also been reported.⁷ This patient developed pyrexia, bloody diarrhoea and extensive oral and pharyngeal ulcers, resulting in progressive inspiratory stridor and subsequent respiratory arrest. Generalised seizures secondary to cerebral ischaemia and haemorrhage into ischaemic areas have also been reported.⁸

In the antenatal period, Clausen and Bierring⁹ reported aortic lesions—oedema of the subendothelial space and of the luminal part of the tunica media—in a 16-week-old fetus of a mother with BD. Association of maternal BD with fetal IUGR has also been reported.¹⁰

Little is known about the influence of Behçet's on the outcome of gestation. A retrospective analysis conducted by Marsal *et al*¹¹ in 61 pregnant women with BD, of which 23 had active disease, concluded that BD does not represent major risk during pregnancy. However, two cases were reported where one woman suffered Budd-Chiari syndrome in the puerperium and another developed cerebral thrombosis at 31 weeks of gestation. The mechanism is thought to be a combination of the reduced fibrinolytic activity in addition to a vasculitic process in BD and the hypercoagulable state of pregnancy.

Pathogenesis

The mode of transmission from the mother to the fetus is unclear. It is thought to be transmitted by an immune mechanism similar to the mechanism of neonatal lupus and myasthenia gravis; however, the causative autoantibodies for neonatal BD have not been identified.¹²

Indeed, neonatal BD is thought to be a transplacentally acquired disease characterised by the passage of immune complexes or autoantibodies giving rise to transient illness. Supporting evidence for transplacental transmission is found in cryoglobulins and circulating immune complexes that have been identified in the maternal sera of neonates who had the disease.⁵ In addition, Hwang *et al*¹³ reported necrotising inflammation in placentas and decidua from two patients with BD: both placentas showed focal necrotising villitis with neutrophil-dominant infiltration, similar to BD in other organs.

BD and pregnancy

In this case the mother of the patient has a history of polycystic ovarian syndrome (PCOS). Although PCOS and BD are conditions with distinct pathophysiology, they both carry a prothrombotic risk which could complicate future pregnancies.

Melis *et al*¹⁴ reported that the risk of deep vein thrombosis is elevated fivefold to sixfold during pregnancy and twofold to threefold during the puerperium. This hypercoagulable state is present for 6 weeks postpartum, and can be explained by venous stasis or changes in the haemostatic system with increasing pro-coagulant factors and platelet adhesiveness.

There is little information about an increase in thrombotic events during the last months of pregnancy and puerperium in BD patients. Marshal *et al*¹¹ reported the case of a 26-year-old woman with known BD who developed Budd-Chiari syndrome in the puerperium. One report of cerebral venous thrombosis at 20 weeks of gestation in a BD patient has also been published.¹⁵

A reduced fibrinolytic activity in addition to a vasculitic process has been suggested as an explanation for venous thrombosis in BD. During pregnancy, a reduced fibrinolytic activity coupled with the coexistence of two hypercoagulability conditions might further increase the risk of thrombotic events.¹⁶

PCOS is associated with increased risk of cardiovascular events. The mechanisms of potential disturbances of the haemostatic system in women with PCOS are unknown. There is evidence that plasma levels of several haemostatic factors are altered by hyperglycaemia, insulin resistance with compensatory hyperinsulinaemia, pro-inflammatory agents and dyslipidaemia, all of which are typical in PCOS.¹⁷

We could argue that BD should always be considered as a prothrombotic risk factor, especially during pregnancy and puerperium. For this reason, prophylactic anticoagulant therapy might be considered depending on the presence of further risk factors.

Learning points

- ▶ Transient neonatal Behçet's disease (BD) is a rare secondary neonatal autoimmune disease.
- ▶ It should be considered and treated after disseminated staphylococcal and herpetic disease is excluded.
- ▶ The likely transplacental mode of transmission and transient nature of the neonatal disease support an autoimmune pathogenic mechanism of BD.

Competing interests None.

Patient consent Obtained.

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