Rare disease

Progression of coronary disease in a Behcet's patient in remission

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Summary

Behcet's disease is characterised histologically by vasculitis. In the heart this can lead to aneurysm formation and thrombosis. There is also accelerated atherosclerosis, the mechanism of which is unclear. Patients with external disease from Behcet's disease are treated with immunosuppression. The authors present a case of aneurysmal disease in a Behcet's patient. This case demonstrates that coronary disease may progress in Behcet's patients despite external disease remission. Therefore, internal disease may progress in the absence of external symptoms when immunosuppressive therapy is usually stopped. This case raises the issue of whether immunosuppression should be continued in Behcet's patients with coronary disease to suppress disease progression or included in a treatment protocol for patients with Behcet's related coronary disease. Clinical trials on the use of immunosuppressive therapy for coronary disease in Behcet's patients are needed.

BACKGROUND

Behcet's disease is diagnosed by the presence of recurrent oral and genital ulceration, skin lesions and ocular involvement.¹ This is a rare disease with a prevalence of between 0.3 and 6.6 cases per 100 000.² The prevalence is highest in the Middle-East, China and Japan. Histopathology shows perivascular inflammation. In the heart this can lead to aneurysm formation of the coronary arteries. Also a hypercoagulable state can cause thrombosis of the coronary vessels. These manifestations may lead to myocardial infarction in patients with Behcet's disease.³ There may also be accelerated atherosclerosis through the prolonged use of steroids or directly due to the disease but this has not yet been clearly demonstrated.

The management of Behcet's patients following myocardial infarction may involve treatment with revascularisation either by coronary artery bypass graft or percutaneous coronary intervention (PCI). There is an increased risk of complications in these patients due to the propensity for aneurysm formation. With bypass grafting there can be aneurysm formation in the graft.⁴ Post-PCI there may be aneurysm formation at the site of catheter insertion and following balloon angioplasty.⁵ Due to these complications some opt for conservative management where symptoms can be controlled with medication.

There is however, considerable variability in the use of immunosuppressive regimes. In previous case reports, immunosuppression has been used alone or in combination with revascularisation to treat patients with apparent success in the resolution of symptoms and even reduction in the size of aneurysms.^{5–8} In the case presented we demonstrate that even in the absence of external ulceration when immunosuppression is usually stopped, internal coronary disease can progress. This case therefore raises the issue of the role of immunosuppression in the management of internal coronary disease when external disease is in remission.

CASE PRESENTATION

A 73-year-old lady, known to have Behcet's disease in remission and ischaemic heart disease, presented with acute onset shortness of breath and chest tightness. Her only cardiovascular risk factor was a smoking history of four pack years.

On the basis of her clinical history, a raised troponin T level, non-specific T wave changes on ECG and changes on echocardiogram demonstrating reduced left ventricular function (ejection fraction 35–40%) and hypokinesis of the left ventricular wall, she was diagnosed with a non-ST elevation myocardial infarction (NSTEMI). A CT scan of her chest performed to exclude pulmonary embolism (PE) showed probable pulmonary fibrosis, but no evidence of PE.

Her Behcet's disease was first diagnosed at the age of 34 with the occurrence of multiple recurrent and painful ulcers primarily affecting her mouth and vaginal mucosa. She took prednisolone for many years which failed to control the development of the ulcers. In 1999, she was started on a course of chlorambucil in addition to her steroid therapy. This was effective and within 3 years her disease had settled to such an extent that it was possible to stop all her immunosuppressive therapy. Since 2001 she has taken no further immunosuppressive therapy as her symptoms had remained under control.

She first developed anginal chest pain in 1999. She had a positive dobutamine stress echocardiogram and was started on atenolol which controlled her symptoms. Her chest symptoms progressively worsened and in 2006 she had a coronary angiogram which showed severe three vessel disease. The left anterior descending artery was occluded mid-vessel with TIMI 1 flow and 70% ostial stenosis in D1. The circumflex was atherosclerotic with 70% stenosis in the mid-segment and 70% ostial stenosis in OM1. The right coronary was also atherosclerotic with a long 70% stenosis proximally and a further 60% stenosis mid-vessel.

Given the severity of her disease she was referred for coronary bypass surgery.

Although she was considered a candidate for surgery, she declined as she was apprehensive about the effects surgery could have on her Behcet's disease. Her coronary disease was therefore managed with medication.

Given the diagnosis of NSTEMI on this admission we discussed whether she would consider surgery however, she remained apprehensive about proceeding with this route. She was however, prepared to have PCI and stent insertion if necessary. In order to determine if she would benefit from revascularisation a cardiac MRI was performed to investigate the viability of the myocardium. This concluded near transmural infarction of the apex. The distal left anterior descending territory was non-viable. However, the right coronary and left circumflex territories were viable and possibly hibernating.

Based on the results of her cardiac MRI we repeated her angiogram to assess for potential targets for stent insertion. Her angiogram showed persisting and worsening atherosclerosis. Coronary aneurysms which were not noted on the 2006 angiogram had developed in the right coronary and left circumflex arteries. A comparison of

the aneurysms seen on the 2006 and 2011 angiograms is shown in figures 1 and 2. This progression of Behcet's disease was despite being in remission during this period and off immunosuppressive therapy.

Her case was discussed in our local multi-disciplinary meeting and a decision was made to proceed to stenting of the lesions in both the right coronary and circumflex arteries. We inserted stents to the circumflex artery. A stent was inserted into the aneurysm as well as along the stenosed mid-segment of the vessel in order to avoid mismatch (figure 2). She had a second procedure to the right coronary artery with balloon angioplasty to the stenosed vessel; stent insertion was technically not possible. The patient has not had a recurrence of symptoms and remains well after 6 months.

DISCUSSION

This case demonstrates progression over a 5-year period of aneurysmal disease (seen in figures 1 and 2) while this Behcet's patient was off immunosuppressive therapy. Despite being in remission and off immunosuppressive therapy this patient had progressive coronary disease. It appears even if active disease is in remission externally in

Figure 1 Progression of disease in the right coronary artery over 5 years. Significant enlargement of the aneurysm has occurred.

Figure 2 The circumflex artery in 2006 and in 2011 pre and poststenting. There is a small amount of aneurysm formation beyond the stenosis. Stenting into this segment was performed too ensure no mismatch beyond the distal end of the stent.

the form of oral or genital ulceration, coronary disease may still be progressive.

This causes a dilemma as to whether a patient should be on immunosuppressive therapy. There are several published case reports that suggest immunosuppressive therapy can be used to achieve regression of aneurysms and symptom control. In one previous case report following endovascular stent insertion and combined immunosuppression consisting of high dose prednisolone and azathioprine, after 3 months a coronary aneurysm was seen to regress.⁶ The same method of combining stent insertion with a similar immunosuppression regime is also advocated by Kwon *et al* who report that a 5×5 cm left anterior descending artery aneurysm regressed to only a vestige after 6 months.⁶ In another case report regression of an ascending aortic aneurysm was seen with immunosuppressive therapy consisting of methylprednisolone followed by oral prednisolone.⁷ An improvement in angina chest symptoms was also noted. Sonia *et al* also report an improvement in cardiac symptoms with immunosuppression consisting of a 3 day course of intravenous cyclophosphamide and methylprednisolone followed by a reducing course of prednisolone.⁸ However, not all previous case reports have shown benefit with immunosuppression. Arishiro *et al* used a short course of high dose prednisolone but saw no difference in the size of the aneurysm after 6 months.⁵ The immunosuppression regime used was relatively modest however, compared with the levels used in other case reports where success has been reported.

The clinical trial data is very limited. In a study of 25 patients where vascular surgery has been performed on aneurysm disease in Behcet's patients, postoperative corticosteroids were associated with a lower rate of recurrence of disease following surgery.⁹

Our case establishes that coronary disease may progress in Behcet's patients off immunosuppression. It may be that Behcet's patients with coronary disease would benefit from immunosuppressive therapy however, there is a need for clinical trials to establish the efficacy of this therapy.

Learning points

- Behcet's disease can lead to the development of coronary artery disease including: aneurysm formation, thrombosis and atherosclerosis.
- Behcet's patients receive immunosuppression to control external disease.
- This case shows that internal Behcet's disease may be progressive in the absence of external symptoms. This raises the question of the role of immunosuppressive therapy in the management of Behcet's related coronary disease.

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Competing interests None.

Patient consent Obtained.

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