CASE REPORT

Rapidly progressive coronary artery disease as the first manifestation of antiphospholipid syndrome

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Accepted 9 March 2014

SUMMARY

Antiphospholipid syndrome (APS) is an autoimmune multisystem disorder characterised by high incidence of arterial and venous thrombosis. Cardiovascular manifestations also include valvular heart disease, ventricular thrombi and higher risk for coronary artery disease (CAD). In this case report, we describe a 61-year-old woman who had no significant risk factors for CAD, and presented with aggressive disease in native and graft vessels that required multiple coronary interventions. The extent of her aggressive CAD could not be explained by her risk factors profile. Therefore autoantibodies screening was carried out and showed a strongly positive anticardiolipin and β_2 glycoprotein-I antibody, and hence a diagnosis of antiphospholipid syndrome was made.

BACKGROUND

Antiphospholipid syndrome (APS) is an autoimmune multisystem disease. It occurs secondary to another autoimmune disorder, but majority of cases are primary. It usually presents with recurrent miscarriages or recurrent thromboembolic disease. Cardiovascular complications include valvular heart disease, but aggressive coronary artery disease is rare.¹ To the best of our knowledge, APS presenting solely with multiple acute coronary syndromes that necessitated coronary artery bypass grafting (CABG) and multiple percutaneous coronary interventions (PCI) to native vessels has not been reported previously.

The condition results from the formation of autoantibodies against phospholipids and β_2 glycoprotein-I. Failure of macrophages to clear apoptotic cell membranes, histones and nuclear material leads to the deposition of debris in the lymphoid tissues and prevents their uptake by antigen presenting cells. T cells recognise these self-antigens and stimulate B-cell response and subsequent autoantibody formation, with deposition of immune complexes in endothelial cells, monocytes, platelets and trophoblasts. This alters the functioning of these cells leading to classical features of APS.²⁻³ Persistent positive lupus anticoagulant test and antiphospholipid antibodies are required for diagnosis.⁴ These include anticardiolipin and anti β_2 glycoprotein-I antibodies.

Inflammation has long been postulated as a key factor in atherosclerosis, and research is still ongoing to define its relative role.⁵ In this report we describe an association of aggressive coronary artery disease with APS.

CASE PRESENTATION

A 61-year-old woman presented with aggressive coronary artery disease as an unusual first manifestation of antiphospholipid syndrome.

The patient had no risk factors for coronary artery disease (CAD) or history of hormone replacement therapy. She did have one miscarriage in her first pregnancy but subsequent five pregnancies were uneventful. Her initial presentation was with a non-ST segment myocardial infarction (NSTEMI). Urgent coronary angiography demonstrated left main stem (LMS) 70% ostial stenosis, proximal left anterior descending (LAD) stenosis of 50%, right coronary artery (RCA) mid 95% lesion, small left circumflex artery (LCX) and mildly reduced left ventricular function with inferobasal akinesis. The patient was referred for CABG.

Eight months after her CABG, she presented with unstable angina. Coronary angiography and a graft study revealed unchanged severe native vessel disease, patent saphenous vein graft (SVG) to RCA and patent SVG to first diagonal branch. Left internal mammary artery (LIMA) angiography revealed an 80% lesion at the LIMA-LAD anastomosis. Intensification of medical therapy was recommended at this stage.

The patient re-presented to the hospital for the third time 2 months later with acute coronary syndrome and high cardiac troponin. On this occasion, the coronary angiogram showed progression of her native disease over this short period. Her RCA is now 100% occluded at mid-segment ([figure 1](#)). There was a new 70% narrowing in posterior

Figure 1 Right coronary artery total occlusion.

To cite: Abdullah AS, Yagoub H, Kiernan TJ, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2013-203499

Figure 2 Posterior descending artery critical stenosis.

Figure 4 Posterior descending artery stent after balloon angioplasty.

descending artery branch (PDA) of the RCA, a new tight ostial LCX stenosis and LAD stenosis of 70%. At this point, a decision was made to perform a PCI to the RCA and its PDA branch with a drug eluting stent placed in each vessel. The patient continued to suffer from ongoing angina at rest and was brought for further intervention. This time, a successful PCI was performed for her LAD. She tolerated the procedure very well.

One month later, she re-presented with another NSTEMI. An angiogram showed patent SVG graft to PDA, but 90% in-stent restenosis of the PDA branch stent, a new 100% occlusion of the native RCA proximally ([figure 2](#)) and critical LIMA-LAD anastomosis site stenosis ([figure 3](#)). A balloon angioplasty was successfully performed for the PDA in-stent restenosis ([figure 4](#)) and a stent was placed in the LIMA-LAD stenosis.

Again, the patient presented with NSTEMI in 6 months' time and angiogram showed a new 100% LMS lesion at the origin, RCA blocked, good SVG to RV branch with a new 90% in-stent restenosis within the PDA stent, LIMA to LAD occluded and SVG to diagonal was patent. EF at this time was 28%. A decision was made to continue medical treatment which included aspirin, clopidogrel, statin, β -blocker and ACE inhibitor.

Figure 3 Left internal mammary artery to left anterior descending anastomosis site stenosis.

INVESTIGATIONS

As this was a very unusual course of events with very rapidly progressing coronary lesions, the question of an underlying systemic cause for her CAD was raised. A homocystine level was negative and an autoantibody screening showed negative anti-nuclear antibody, extractable nuclear antigen, antineutrophil cytoplasmic antibody, antidouble-stranded DNA, and a positive β_2 glycoprotein-I. A repeat autoantibody screen again confirmed a high titre of anti- β_2 glycoprotein-I and anticardiolipin antibody. This was repeated after 12 weeks with similar results.

TREATMENT

The patient was seen in the coagulation disorders clinic and a diagnosis of antiphospholipid syndrome was made based on the immunological profile, previous miscarriage and evidence of arterial thrombosis. She was then started on long-term warfarin and was to remain on aspirin for life, and clopidogrel was stopped after 6 months.

DISCUSSION

This is a very unusual report of APS diagnosed in a 61-year-old woman with recurrent acute coronary syndrome. It is unique because of the age of the patient and the nature of thrombotic events. APS usually presents with recurrent venous and arterial thrombosis. First presentation with CAD is extremely rare and only a few cases have been reported.⁶

In patients with systemic lupus erythematosus (SLE), the presence of secondary APS is an independent factor for increased cardiovascular risks.⁷ A Swedish cohort of 182 patients with SLE had also shown a very high prevalence of CAD among those who had APS. In that study, a positive antiphospholipid was independently related to the time to the first cardiovascular event.⁸ This is probably a reflection of increased endothelial cell activation and damage. This case is more unique because of the extent and speed of the disease progression.

This endothelial dysfunction was assessed at the molecular level in patients with APS. Pro-inflammatory cytokines IL2, IL6 were found to be significantly higher in patients with APS coronary artery disease and this correlated directly with markers of endothelial dysfunction.⁹

The association between the presence of antiphospholipid antibodies and the risk of cardiovascular events was studied in 2001

within the Honolulu heart programme. Anti- β_2 glycoprotein-I was associated with increased risk of stroke and myocardial infarction.¹⁰ In another cross-sectional study, sequential patients admitted with suspected coronary artery disease were tested for the presence of APS antibodies. Patients with angiographically documented CAD had higher incidence of positive antibodies and those with positive antibody profile had more severe disease.¹¹

Learning points

- ▶ Consider antiphospholipid syndrome (APS) as a possible cause of aggressive coronary artery disease.
- ▶ Further research is needed to fully understand the extent of association of APS and proinflammatory mediators and atherosclerosis.
- ▶ More studies are needed to elaborate on any causal relationship between β_2 glycoprotein-I antibodies and coronary artery disease.

Contributors ASA wrote the original script and edited the final manuscript. HY and TJK and CD participated in literature review and writing the manuscript. CD participated in literature review and writing the manuscript and is the principal physician in patient care.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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