Primary antiphospholipid syndrome: a unique presentation with multiple visceral aneurysms

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We present a unique case of a young woman with a proven primary type of antiphospholipid syndrome (APS) and multiple abdominal visceral aneurysms. Only one other case with such an association has been reported before to our knowledge. The presence of visceral aneurysms poses a therapeutic challenge because the anticoagulation treatment may be catastrophic in view of the risk of aneurysm rupture and abdominal bleeding.

A 38 year old woman was transferred from the department of obstetrics and gynaecology of the hospital, because of peripheral oedema. Two days earlier she had had a third trimester pregnancy loss. She had a history of four unexplained deaths of morphologically normal fetuses at the third trimester, during the past 10 years. She was the mother of a healthy 7 year old child. A diagnosis of primary APS was made based on clinical and serological criteria. Anticardiolipin IgG antibodies were present at a moderate level (48 GPL units; normal, <19 GPL). There was no evidence of a concurrent systemic disease as documented in all detailed laboratory examinations performed for almost 1 year. Computed tomography of the abdomen disclosed multiple partially thrombosed and calcified visceral aneurysms affecting the splenic, hepatic, and both renal arteries, which were further documented with selective angiography (fig 1). The course of the patient’s disease was uneventful for 3 years, but progressive pulmonary, renal, and hepatic malfunction then started to develop. She progressively deteriorated and died from multiorgan failure. Postmortem examination confirmed the presence of the splachnic aneurysms without any evidence of rupture.

APS is one of the most important causes of hypercoagulability. About 50% of patients with APS do not have an associated systemic disease and are labelled as cases of primary APS. The association of APS and arterial aneurysms is controversial and poses a critical therapeutic dilemma. Lifelong anticoagulation remains the fundamental treatment for APS and may obviously be hazardous in the presence of multiple aneurysms. Although in most cases of secondary APS the presence of arterial aneurysms can be attributed to the underlying systemic disease, the pathogenesis of such aneurysms in primary APS—such as in our case—remains unclear.

Kong et al reported a case of a young man with systemic lupus erythematosus and secondary APS who presented with acute abdominal pain owing to a ruptured right hepatic artery aneurysm. He was also found to have aneurysms of the left hepatic artery and splenic artery on necropsy. The aetiology of these aneurysms according to the authors and based on histological examination of the aneurysmal wall, was found to be systemic lupus erythematosus vasculitis.

Dongola and Foord described a case of primary APS presenting with varied arterial abnormalities. These included the presence of a large number of micro- and macroaneurysms of hepatic, renal, and mesenteric arteries. There was insufficient evidence to merit a concurrent diagnosis of polyarteritis nodosa or other associated systemic condition. The authors suggested that the arterial abnormalities in this patient might have been inherent to the syndrome itself and that APS can present protean vascular abnormalities, which represent a wide spectrum without associated vasculitis.

Our case is a further example of the unusual presentation of APS without any association with other syndromes, as shown by all laboratory examinations and documented by postmortem histological examination of the diseased arteries. Based on a literature review, we did anticoagulate the patient because there was serious concern about thromboembolic disease, despite the presence of multiple intra-abdominal aneurysms. We also followed all the other treatment protocols, including steroids and plasmapheresis, with the intention of provoking regression of the aneurysms. Such a regression was noted in a case of APS associated with polyarteritis nodosa, with a significant decrease in both the number and size of splachnic aneurysms after intensive treatment. In our case this treatment was unsuccessful because the postmortem examination showed the presence of the aneurysms, albeit without any evidence of aneurysm rupture or internal bleeding.

Despite the fact that the patient received all the appropriate supportive treatment, her disease progressed and she...
eventually died from multiorgan failure. Oral anticoagulation probably prevented the development of major arterial and venous thromboembolic disease, without causing the rupture of any of the pre-existing aneurysms. However, anticoagulation did not prevent the progression to multiorgan failure, which can be attributed to alterations in the microvascular circulation.

In conclusion, we think that multiple splanchic aneurysms probably represent part of the spectrum of vascular abnormalities of primary APS. If such aneurysms are identified, lifetime anticoagulation should still be considered as the preferred treatment in order to prevent deep venous thrombosis and/or pulmonary embolism, despite the risk of bleeding complications.

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A family with diffuse idiopathic skeletal hyperostosis
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We report a family with diffuse idiopathic skeletal hyperostosis (DISH). The most striking occurrence was severe cervical disease without extensive dorsal involvement. From the tissue typing results of our two sibling patients, it appears less likely that, if there is a hereditary component, it is linked to HLA status. It remains to be seen whether this is a new disease entity or an unusual familial variant of DISH. We are unaware of a similar published report.

A 23 year old man was referred with a painful stiff neck of 3 years’ duration. On examination, all movements of his cervical spine were restricted. Other spinal movements were normal. Inflammatory markers were normal and HLA-B27 was negative. An x ray examination of the sacroiliac joints, thoracic and lumbar spine were unremarkable. However, the cervical spine radiograph showed gross anterior osteophytosis (fig 1A).

This man’s 24 year old sister had been seen 7 years previously. She described a 6 year history of worsening neck pain and stiffness. On examination, movements of the cervical spine were severely limited in all directions, with mild limitation of the thoracic spine. An x ray examination and inflammatory markers were normal and HLA-B27 was negative. Five years later, the clinical findings had scarcely changed. However, although the sacroiliac joints were still normal, there was now marked osteophytosis around the hip joints with gross osteophytosis and ankylosis of the cervical spine (fig 1B). Two years later, this advanced cervical pathology precipitated cervical myelopathy.

The father of these patients was first seen at 52 years of age despite having a “30 year history of ankylosing spondylitis”. He had a strong family history of the disease, with brother, sister, and mother affected. On examination, all spinal movements were markedly reduced. Movements of both hips were severely restricted and bilateral elbow fixed flexion deformities were present. Inflammatory markers were normal and HLA-B27 was negative. An x ray examination showed normal sacroiliac joints, advanced osteophytosis and degeneration of the hip joints, and ankylosis of the cervical spine (fig 1C). His hip disease required prompt replacement surgery.

All these patients had radiological changes suggestive of DISH. Two of this patient’s siblings also had the disease, as do his other two offspring (they are receiving care at different hospitals). The first two patients described here were tissue typed: these siblings only shared alleles at DRB3 and the C locus, which occur frequently in the general population.

DISH is an ossifying, non-inflammatory, non-erosive enthesopathy favouring the dorsal spine but sparing the sacroiliac joints. By contrast, ankylosing spondylitis is an inflammatory condition with enthesopathies facing joints, always affecting the sacroiliac joints. DISH affects 3–6% of the population over 40 years of age and 11% aged over 70 years. It is twice as common in men and occurs more frequently in certain racial groups: it is common in Japanese and Pima Indians but rare in black and Asian races. Other causes of hyperostosis or bony excrescences include spondylitis deformans, ankylosing spondylitis, trauma, fluorosis, treatment with retinoids, ochronosis, acromegaly, hypoparathyroidism, and x-linked hypophosphataemic osteomalacia, but there was nothing in the history, physical examination, or the investigations to suggest that our three patients had any of those conditions.

In the cervical spine, ossification of the posterior longitudinal ligament (OPLL) is commonly seen. This phenomenon is often called “Japanese disease” owing to its predominance in the Japanese population. OPLL displays a strong genetic component with high concordance in twins and families. Various modes of inheritance have been suggested, including HLA linkage. In DISH, however, although there are racial differences, no strong familial tendency has been demonstrated. Neither is there a proven