Case Report

Systemic fibromuscular dysplasia masquerading as polyarteritis nodosa

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Introduction

The diagnosis of systemic diseases, such as vasculitis, may be difficult because of an uncharacteristic clinical presentation or the inability to obtain histopathological confirmation. Classification criteria for the systemic vasculitides have been composed as a guide for the diagnostic process. If polyarteritis nodosa (PAN) is strongly suspected histological confirmation is not mandatory for the diagnosis [1]. Characteristic angiographic findings such as visceral microaneurysms provide strong support for the diagnosis of PAN. In the present case the angiographic findings were considered to be typical of PAN but the clinical course and autopsy findings revealed another systemic vasculopathy.

Case report

A 43-year-old caucasian woman was referred to our hospital because of severe hypertension. During recent months the patient had experienced progressive and severe fatigue, diffuse myalgias, intermittent headaches, and abdominal pain. She had lost 7 kg of weight. The patient's medical history consisted of cervical dysplasia for which she had undergone conization and no hypertension. On physical examination the blood pressure was 210/110 in both arms and the pulse rate was 100. Ophthalmoscopy revealed grade I hypertensive retinopathy. A loud systolic bruit was heard in the upper abdomen.

Laboratory investigations revealed an ESR of 24 mm (normal (N), <25 mm), a normochromic normocytic anaemia of 8.4 g/dl (N,12.0–16.0 g/dl), normal leukocyte and thrombocyte counts, normal coagulation parameters, sodium 135 mEq/l (N,136–144 mEq/l), potassium 3.0 mEq/l (N,3.6–4.8 mEq/l), creatinine 1.1 mg/dl (N,0.8–1.5 mg/dl), urea nitrogen 15 mg/dl (N,7–21 mg/dl), lactate dehydrogenase 883 U/ml (N, <160 U/l) and normal liver enzymes. Urinalysis demonstrated a proteinuria of 4.7 g/24 h and the sediment contained >15 erythrocytes, 0–5 leukocytes, and many erythrocyte casts per high-power field. Serological examinations for hepatitis B surface antigen, antineutrophil cytoplasmic antibodies, antinuclear factor, cryoglobulins, and anticardiolipin antibodies were negative.

Because glomerulonephritis was suspected the patient was admitted for an ultrasonic guided renal biopsy. On admission, 1 week after the first visit, no abdominal bruit was heard, a slight hydrops of the left knee was noted, and the serum creatinine had increased to 1.6 mg/dl. Neither leukocytes nor crystals could be found in the synovial fluid. Ultrasonic investigation demonstrated that the size of the right kidney was decreased (8 cm) and the left one was of normal size. The next day a left hemiplegia and somnolence developed. Computerized tomography demonstrated oedema in the territory of the right middle cerebral artery, compatible with an ischaemic infarction. Magnetic resonance imaging of the brain confirmed the presence of an infarction of the territory of the right middle cerebral artery. No signs of raised intracranial pressure were found. Since a systemic vascular disease was still suspected, an abdominal angiogram was performed. Selective percutaneous angiography of the coeliac trunk demonstrated multiple microaneurysms of the splenic and hepatic arteries (Figure 1). In addition the origin of the right renal artery was found to be occluded and the left renal artery was normal. Subsequently the diagnosis classic polyarteritis nodosa was made on the basis of the patient’s weight loss, the presence of diffuse myalgias and hypertension, the visceral microaneurysms, and the elevated serum creatinine [1]. The patient was treated with intravenous methylprednisolone 1000 mg and cyclophosphamide 200 mg daily after a biopsy of the quadriceps muscle had been obtained. The next day the patient had a respiratory arrest and assisted ventilation was begun. Neurological examination demonstrated complete brainstem dysfunction and intracranial hypertension. Hereafter the ventilatory support was withdrawn and the patient died.
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Fig. 1. Two microaneurysms of the splenic artery on percutaneous selective angiography of the coeliac trunk.

Pathological findings

The renal biopsy on review contained too few glomeruli to reach a definite judgement. The muscle biopsy was normal and in particular the arteries showed no evidence of vasculitis. Post-mortem examination demonstrated fibromuscular dysplastic lesions in the right renal, the splenic, the right middle cerebral, the hepatic, the superior mesenteric and the coronary arteries (Figure 2). All lesions were of the medial type. Both the right renal and the middle cerebral arteries were occluded by thrombi. The right frontal and parieto-occipital cortex showed extensive necrosis. The brain furthermore showed signs of raised intracranial pressure. Autopsy, too, could not demonstrate any signs of vasculitis or glomerulonephritis. Immunofluorescence microscopy of the kidneys could not demonstrate deposition of immunoglobulins or complement components.

Discussion

The patient presented a systemic and rapidly progressive fatal illness, which had characteristics of arterial involvement at multiple sites. The disease caused impairment of organ function with signs of vasculitis, which led us to the diagnosis of classic PAN. Our patient fulfilled five of the ten classification criteria for this rare disease [1].

The clinical features of PAN are caused by either infarction or haemorrhage of tissues and organs. Both are caused by a necrotizing vasculitis of small or medium-sized muscular arteries, which tends to be segmental [2]. Clinical features include constitutional symptoms such as fever and weight loss. Organ involvement in PAN is represented by hypertension, renal impairment, peripheral neuropathy, abdominal pain, and involvement of the musculoskeletal system. Less frequently, skin involvement and cerebral vascular accidents can occur [3,4]. The course of disease in PAN is almost inevitably lethal if not treated [5]. Therefore the avoidance of unnecessary delays during the evaluation of patients is vital. The classification criteria consist of clinical and non-clinical items. Of the latter, the finding of multiple aneurysmal dilatations up to 1 cm in size on visceral angiography is considered to be virtually pathognomonic of PAN, even in the absence of histological evidence of the disease [3]. The specificity of the characteristic angiographic findings was found to be 95% [1]. A muscle biopsy has been considered to have an even greater specificity and predictive value [6].

Post-mortem examination of our patient revealed that a systemic vascular disease was present, but of a different nature than had been anticipated during life. Generalized fibromuscular dysplasia (FMD) was diagnosed. FMD is a non-inflammatory and non-atherosclerotic disease which, like polyarteritis nodosa, affects small and medium-sized arteries and whose pathogenesis is unclear [7]. It is a well-recognized cause of hypertension in young caucasian women when the renal arteries are involved [8]. However, other vascular beds may also be involved in 28% of patients with FMD [9]. Dysplastic lesions of the cerebrovascular, visceral, iliac, and brachial arteries have been described. The clinical manifestations of FMD are determined by the artery involved and by the degree of impairment of arterial blood flow. Hypertension and cerebrovascular symptoms are the most common manifestations. The extrarenal sites of systemic fibromuscular dysplasia may remain asymptomatic. The histopathological classification of FMD is based on the location of the major lesion within the vessel wall [10]. As in our patient, medial FMD has been found in 85% of the cases. In the minority of cases dysplastic lesions were found in the intima or in the perimedial layers. The artery wall is alternately thickened by dysplastic lesions, giving rise to stenosis, or attenuated by disruption of the internal elastic lamina, giving rise to aneurysmic dilatation of the artery. The diagnosis of FMD is made by angiography or histopathology. The characteristic lesions on angiography, especially the 'string of beads' appearance, are considered to be pathognomonic of the disease [11].

Follow-up of patients by angiography has demon-
strated that FMD is a progressive disease [12]. Treatment of fibromuscular dysplastic lesions is only recommended in symptomatic cases and is either surgical or by percutaneous transluminal angioplasty [9,13].

PAN and FMD may both be diagnosed by angiography without histopathological confirmation, as was the case in this patient. This raises the question of whether the arteriographic manifestation of these diseases are truly pathognomonic and characteristic. The present case demonstrates that the finding of visceral aneurysms may cause confusion between the two diseases. Anecdotal cases have been reported of visceral aneurysms, resembling those found in PAN, in systemic lupus erythematosus, drug abusers, and bacterial endocarditis [4]. In another case, in which an aneurysm of one renal artery was found, the initial diagnosis PAN was corrected to FMD after the histopathological diagnosis had been obtained by nephrectomy [14]. Another feature that led us to the diagnosis PAN in our patient was the presence of proteinuria and microscopic haematuria. These two laboratory results, together with an increased lactic dehydrogenase, are, however, also compatible with renal blood flow impairment [15].

The presented patient demonstrates that FMD may present as a systemic vascular disease and may mimic PAN. Visceral angiography is an important diagnostic tool, said to be pathognomonic in both rare diseases, but failed to be so in our patient. Since PAN and FMD may both have a serious clinical course and require different treatments, it is important to realise the limitations of angiography in the diagnosis of these diseases.

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References


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