Pediatr Nephrol (2001) 16:148–150

BRIEF REPORT

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Severe renal impairment in the case of classic polyarteritis nodosa

Received: 15 February 2000 / Revised: 28 August 2000 / Accepted: 30 August 2000

Abstract A 14-year-old boy with classic polyarteritis nodosa (cPAN) and a clinical picture resembling rapidly progressive glomerulonephritis (RPGN) is described. He had severe hypertension, malaise, weight loss, fever, myalgia, and rapid deterioration of renal function. Renal biopsy revealed acute necrotizing vasculitis. Angiography showed small saccular aneurysmatic dilatations in the intrarenal branches of the right renal artery and the intrahepatic branches of the hepatic artery. cPAN was diagnosed and pulse methylprednisolone (MP), pulse cyclophosphamide (CYC) and subsequently oral prednisolone were given. Clinical and laboratory findings improved dramatically and remission was attained rapidly. The patient has remained in remission for the last 11 months. cPAN should be considered in patients who present with severe systemic symptoms and hypertension. Progressive renal insufficiency can occur during the acute course of cPAN due to renal vascular involvement without glomerulonephritis. Prompt and aggressive corticosteroid and cytotoxic therapy is essential to suppress disease activity and to maintain remission.

Keywords Classic polyarteritis nodosa · Progressive renal failure · Pulse steroid · Cyclophosphamide · Children

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Introduction

Polyarteritis nodosa is a multisystem disease characterized by inflammation and necrosis of medium-sized muscular arteries leading to aneurysm formation [1]. The clinical features are tissue infarction, hemorrhage, and organ dysfunction, typically affecting the gastrointestinal tract, nervous system, muscles and soft tissue. Fever, malaise, weight loss and hypertension are common [2, 3]. Renal involvement may present with loin pain and hematuria and occasionally renal impairment due to renal ischemia [2]. Rapidly progressive glomerulonephritis (RPGN), the clinical reflection of necrotizing and crescentic glomerulonephritis, is the main clinical feature of microscopic polyarteritis (mPA) but not of cPAN. Furthermore, mPA was clearly distinguished from cPAN in the Chapell Hill Consensus based on the presence of glomerulonephritis and p-ANCA positivity [3–6].

The case of a 14-year-old boy presenting with the clinical features of RPGN in whom subsequent studies disclosed cPAN is described below.

Case report

A 14-year-old boy was admitted to a local hospital with malaise, weight loss, fever, and myalgia. He was transferred to our hospital with severe hypertension and rapid deterioration of renal function. The urea nitrogen (urea) and serum creatinine (Cr) concentrations increased to 175 mg/dl and 3.2 mg/dl respectively from normal values within 7 days. The family history and past medical history were unremarkable. Blood pressure (BP) was 170/110 mmHg and temperature 38.5°C. There were no pathologic clinical findings. Laboratory findings were: hemoglobin (Hb) 9.4 g/dl, WBC 18,750/mm^3, erythrocyte sedimentation rate (ESR) 71 mm/h, and C-reactive protein +++. Urinalysis showed a specific gravity of 1010, pH 6, and protein: trace. On microscopic examination there were 7–8 WBCs and 10–12 erythrocytes/HPF. Blood chemistry results included: urea 220 mg/dl, Cr 3.9 mg/dl, uric acid 8.2 mg/dl, AST 144 U/l, and ALT 146 U/l. Serum electrolytes, calcium, alkaline phosphatase, and protein levels were within the normal limits. Complement levels were normal. ANA, anti-DNA, ANCA and hepatitis markers were negative. A renal biopsy revealed acute necrotizing vasculitis (intimal medial fibrinoid necrosis, mixed

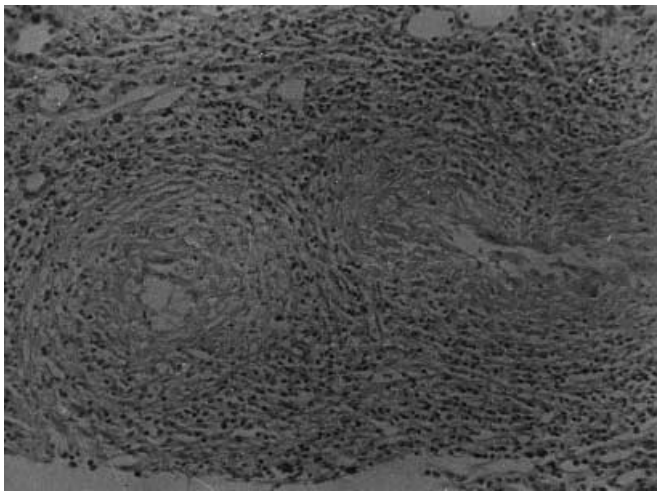

Fig. 1 Acute necrotizing vasculitis in renal biopsy. HE. ×30

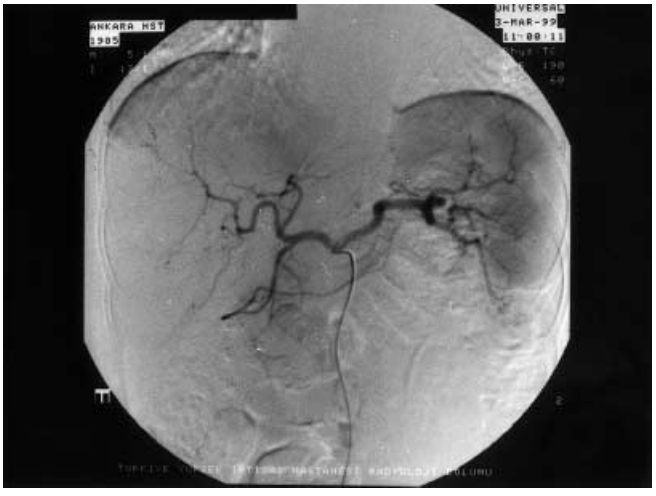

Fig. 2 Intrarenal saccular aneurysms in renal angiography

leukocyte infiltration and fibrin deposition in the arterial wall and luminal narrowing of the artery) in a medium-sized artery similar to an interlobular artery (Fig. 1). The glomeruli were intact. The immunofluorescence microscopic examination was negative. These histopathologic findings were interpreted as cPAN. On angiographic examination, small saccular aneurysmatic dilatations were detected in the intrarenal branches of the right renal artery and in the intrahepatic branches of the hepatic artery (Fig. 2). cPAN was confirmed on the basis of these clinical and laboratory findings. After controlling his BP, pulse MP at a dose of 30 mg/kg per day (maximum 1 g) was given for three consecutive days, then pulse CYC at a dose of 500 mg/m^2 was administered. Subsequently, oral prednisolone (60 mg/day) was commenced with conversion to alternate day therapy after the 1st month. On the 15th day of therapy, renal function tests improved significantly (urea 40 mg/dl, Cr 1.4 mg/dl). At the end of 4 weeks all systemic symptoms subsided, the urine was clear and the acute phase reactants and liver function tests returned to normal (Table 1). After 2 months, the renal functions were normal (urea 45 mg/dl, Cr 0.9 mg/dl). Therefore, clinical remission was attained and the alternate-day prednisolone dose was gradually tapered by 5-mg decrements every month. The patient has remained well for the past 11 months.

Table 1 Clinical and laboratory findings on admission and in the 1st month of therapy (*RBC* red blood cell, *CCr* Cr clearance)

Clinical and laboratory findings	On admission	First month of therapy
Malaise	+++	–
Fever (°C)	38	36
Myalgia	++	–
BP (mmHg)	170/110	120/70
Hb (g/dl)	9.4	11.9
WBC (per mm^3)	18,750	13,200
ESR (mm/h)	71	27
C-reactive protein	+++	–
Urinalysis	10–12 RBCs, trace protein	Normal
Urea (10–50 mg/dl)	220	71
Cr (0.8–1.2 mg/dl)	3.9	1.1
CCr (ml/dak/1.73m^2)	52	92
AST/ALT (U/l)	144/146	36/24

Discussion

Systemic vasculitides are not homogeneous and comprise distinct groups. After the nomenclature of systemic vasculitis was proposed at the Chapel Hill Consensus Conference, difficulties and confusion in the classification or differential diagnosis decreased. The most important distinguishing feature is the presence of vasculitis in small vessels (arterioles, venules, and capillaries) in mPA and its absence in cPAN. By this definition, cPAN has no involvement of microscopic vessels and therefore no glomerulonephritis [4]. In contrast, patients with mPA have predominant involvement of glomerular capillaries and present with or develop RPGN [5, 6]. Progressive renal impairment may occur during the course of cPAN in occasional cases. In these instances necrotizing arteritis and arterial aneurysms leading to renal ischemia give rise to renal impairment without glomerulonephritis [2, 3]. In our patient, an uncommon renal presentation resembling RPGN was of particular interest. A renal biopsy revealed acute necrotizing arteritis without glomerular involvement. Therefore, it was thought that progressive deterioration of renal function resulted from renal ischemia. This is due to necrotizing inflammation and following aneurysmatic dilatation of the renal artery. The same changes in the hepatic artery lead to elevated liver enzymes.

Overall prognoses of PAN improved due to earlier diagnosis, rapid initiation of accurate treatment, and careful treatment monitoring. As renal insufficiency is indicated as one of the major independent factors associated with a poor prognosis, early diagnosis and prompt treatment are of particular importance [7]. A renal biopsy was performed on our patient on his admission day. Due to severe systemic involvement and the rapid course of renal disease, pulse MPs were immediately commenced and a pulse CYC was added. A dramatic clinical response was observed within several days and a considerable improvement of renal function was attained in the subsequent weeks.

Corticosteroids and CYC are frequently used in the treatment of systemic vasculitis in order to induce remission of the active disease and to maintain remission [4, 8, 9]. However, there is still uncertainty as to the dosage and the duration of these drugs. Overtreatment leads to drug toxicity and has deleterious effects whilst undertreatment leads to relapses or organ damage from vasculitis [3, 8, 10]. Remarkable therapeutic responses have been reported with pulse MP and CYC in severely affected patients or in those who failed to respond to oral steroids [3, 8, 9, 11–13]. In addition, it has been well documented that increased survival by using steroids alone has been further prolonged by adding CYC [8, 9, 14]. Due to its rapid action and relative safety, the usage of pulse CYC is now encouraged in systemic necrotizing vasculitis [3, 8, 11, 15, 16]. Even though an optimal duration of treatment has not been well established in PAN, treatment is usually given for approximately 1 year [3, 10, 15, 17]. The disease activity was controlled in our patient with pulse MP and pulse CYC. Then oral prednisolone was used for a further 11 months and the patient remains well. We believe he benefited remarkably from pulse MP and pulse CYC therapy.

In conclusion, the main interest of this case was the uncommon renal presentation. The presence of a rapidly progressive renal disease associated with necrotizing arteritis, instead of necrotizing and crescentic glomerulonephritis, was highly significant. In spite of the difficulty in making a differential diagnosis between cPAN and mPA, renal biopsy and angiographic findings gave us the opportunity to clarify the diagnosis. After the definitive diagnosis of cPAN, the use of urgent and aggressive immunosuppressive/cytotoxic therapy was found to be beneficial. The prognosis of PAN is closely correlated with the severity of renal involvement; therefore, immediate and accurate therapy is vital.

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