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CASE REPORT

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Spontaneous bilateral perirenal hematoma as a complication of polyarteritis nodosa in a patient with human immunodeficiency virus infection

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Abstract We present a 29-year-old man with polyarteritis nodosa (PAN) having human immunodeficiency virus (HIV) infection. This patient fulfilled the American College of Rheumatology (ACR) 1990 criteria for PAN, and the diagnosis was confirmed by typical arteriographic findings, including microaneurysms. Due to the rupture of microaneurysms, perirenal hematomas occurred in both kidneys. Unilateral nephrectomy was performed, and renal histology confirmed that aneurysm rupture was the etiology of the perirenal hematoma. The occurrence of renal hematomas is a usual complication of PAN. However, bilateral renal hematoma during the course of HIV-associated PAN is quite rare, and to our knowledge, this would be the second case reported in the literature. When compared with other viral agents, the association of HIV with PAN may be considered rare. However, as suggested by various reports in the literature, HIV infection should always be kept in mind while evaluating patients with PAN.

Keywords Human immunodeficiency virus · Polyarteritis nodosa · Renal hematoma

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Introduction

Polyarteritis nodosa (PAN) is a systemic necrotizing vasculitis of small and medium sized arteries involving mainly the skin, kidney, peripheral nerves, muscles, and gut [1]. Infectious agents, including various viruses, may contribute to the pathogenesis of PAN, either by inducing immune complexes or directly invading the endothelial cells [1, 2, 3]. Hepatitis B virus (HBV) infection is certainly the most well known infectious etiology in PAN. However, the association of human immunodeficiency virus (HIV) with PAN is also increasingly reported. Here we report a 29-year-old Turkish man with HIV infection presenting with PAN complicated by bilateral renal hematoma.

Case report

A 29-year-old man with fever, malaise, diffuse myalgias, intermittent left upper quadrant abdominal pain, and weight loss of 5 kg during the previous 6 months was admitted to hospital for further investigations. A year previously, he had had severe abdominal pain in his right lumbar region, and a perirenal hematoma had been diagnosed by ultrasound scan, followed by right nephrectomy. The histopathological examination of the nephrectomized kidney showed inflammation characterized by fibrinoid necrosis and pleomorphic cellular infiltration, with predominantly polymorphonuclear leukocytes. The histopathological examination also confirmed that the etiology of perirenal hematoma was aneurysm rupture. Intermittent left upper quadrant pain had arisen nearly 6 months after the operation. In the patient's physical examination, arterial blood pressure was 160/110 mmHg, heart rate was 92/min, and oral temperature was 37.8°C. Diffuse tenderness of extremity muscles on palpation and localized tenderness in the left upper quadrant of the abdomen were notable. The rest of the physical examination was unremarkable. Routine laboratory investigations revealed erythrocyte sedimentation rate (ESR) 65 mm/h, C-reactive protein (CRP) 45 mg/l, serum glutamic oxaloacetic transaminase (sGOT) 72 IU/l, serum glutamic pyruvic transaminase (sGPT) 43 IU/l, total bilirubin 1.9 mg/dl, and serum creatinine 1.7 mg/dl. Complete blood count showed WBC 12,000/mm^3 with a differential count of 78% neutrophils (9,360/mm^3), 12.6% lymphocytes (1,509/mm^3), 2% eosinophils (238/mm^3), 4.8% monocytes (575/mm^3), and 2.6% basophils (318/mm^3). Hemoglobin (Hb) was 11 g/dl, and platelets were 539,000/mm^3. Microscopic hematuria was also

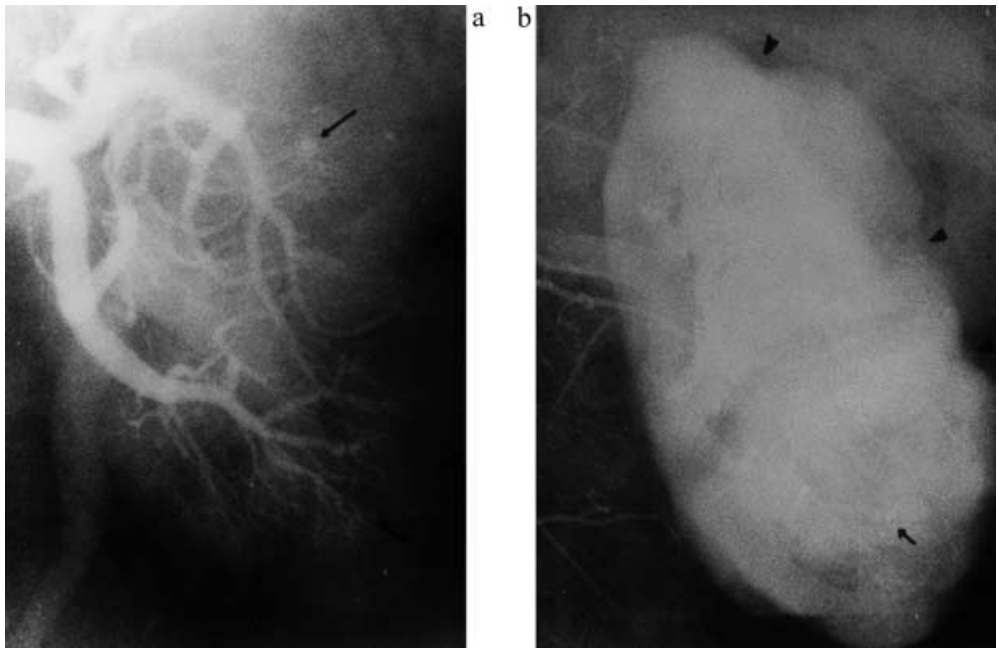

Fig. 1a, b. Left renal angiogram. **a** Multiple microaneurysms (*arrows*) in interlobar arteries. Parenchymal phase. **b** Renal contour irregularities due to multiple peripheric infarcts (*arrowheads*)

present, with five to six erythrocytes per high-power field. Antinuclear and antineutrophilic cytoplasmic antibodies were negative.

Ultrasound scan, which was performed to find out the etiology of the left upper quadrant abdominal pain, revealed an old subcapsular hematoma on the left kidney. Then selective renal and mesenteric angiography were done, revealing microaneurysms of 3–4 mm in diameter, especially in the branches of the left renal and hepatic arteries (Fig. 1, Fig. 2). Since there was a single kidney with microaneurysms, we could not do a renal biopsy. Unfortunately, the patient refused the muscle or sural nerve biopsy.

Viral serology including hepatitis A (HAV), HBV, hepatitis C virus (HCV), Epstein-Barr virus (EBV), cytomegalovirus (CMV), and parvovirus B19 was negative. Only HIV serology was found to be positive in this patient, and a confirmation test with Western blotting was also positive. CD4+ and CD8+ T lymphocyte counts were 583/mm^3 and 624/mm^3, respectively. The patient had no lymphadenopathies but only constitutional symptoms. According to the revised classification criteria of centers for disease control (CDC), he was classified as B1 due to the presence of constitutional symptoms [4]. However, one can not exclude the possibility that the constitutional symptoms might have alternatively resulted from vasculitis. The patient denied drug abuse and homosexuality, however he was sexually active and had had different partners in the past.

He was commenced on 32 mg/day of methylprednisolone and 300 mg/day of zidovudine. After discharge, he was lost to follow-up for the next 9 months. Then he was admitted to the emergency unit of our hospital with poor condition. He confessed that he did not receive his treatment regularly. The diagnosis of pneumonia and sepsis were made and, despite vigorous efforts, he died.

Discussion

Rheumatologic manifestations of HIV infection are protean and may be summarized as undifferentiated spondylarthropathies, Reiter's syndrome, psoriatic arthritis, HIV-associated arthritis, avascular necrosis of bone, septic arthritis, Sjögren's-like syndrome, and systemic vasculitis [5, 6]. With respect to vasculitis, HIV may cause various vasculitic syndromes such as systemic necrotizing vasculitis including PAN, hypersensitivity vasculitis, granulomatous angiitis, and primary angiitis of the central nervous system. So vasculitis types occurring during the course of HIV infection are heterogeneous in their clinical presentation, time of occurrence, histological findings, and etiological factors [5]. Human immunodeficiency virus vasculitis can involve vessels of any size but usually small ones [2]. Despite the persistence of virus in HIV vasculitis, the disease is limited to one flare [7].

The presence of weight loss, diffuse myalgias, diastolic hypertension, elevated serum creatinine level, microscopic hematuria, elevated acute phase reactants, leukocytosis, thrombocytosis, and histopathological findings of the nephrectomized kidney supported the diagnosis of PAN in this patient. Most importantly, the

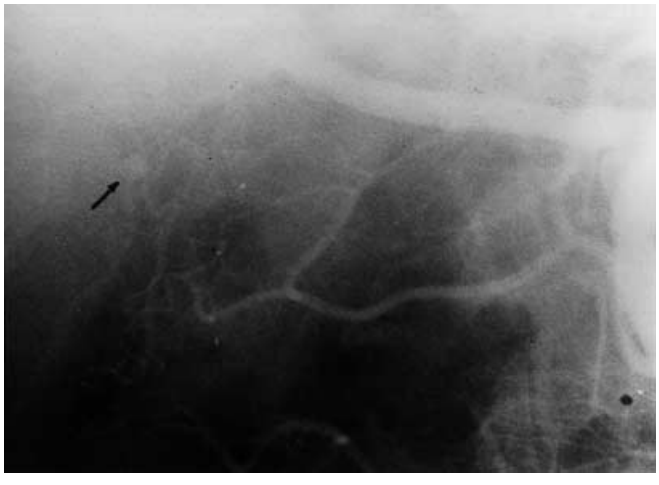

Fig. 2. Selective superior mesenteric (SMA) arteriogram. Microaneurysms (*arrows*) in distal branches of the right hepatic artery arising from the SMA

presence of typical microaneurysms in angiography confirmed the diagnosis of PAN. This patient also fulfilled five of the ten criteria described by the American College of Rheumatology (ACR) for the classification of PAN [8]. We do accept that, before claiming an association between HIV infection and systemic vasculitis, one should exclude the other possibilities. Various infectious agents such as HAV, HBV, HCV, EBV, CMV, and parvovirus may cause secondary infections in HIV-positive patients, and all these viral agents may also contribute to vasculitis etiopathogenesis. However, in our patient, the serology was negative for all these viruses, and HIV positivity was confirmed by Western blot assay. Neurological, renal, pulmonary, and cardiac manifestations of HIV infection may simulate signs of vasculitic syndromes, leading to a misdiagnosis of PAN [9]. However, typical microaneurysms and histopathological findings of the nephrectomized kidney confirmed the diagnosis of PAN. Although coincidence can not be completely excluded, HIV positivity may be accepted as the possible cause of PAN in this patient.

Despite various reports about the association of HIV infection with systemic vasculitis, for unknown reasons, this association remains rare, compared with other viral agents [2, 3]. Gherardi et al. [3] performed muscle, nerve, and skin biopsies in 148 symptomatic HIV-infected individuals and documented inflammatory vascular disease in 34 patients (23%). Among these 34 patients, only four were classified as having PAN according to the ACR criteria [8]. In this study, HIV antigens and genome were detected in perivascular cells of two patients having necrotizing vasculitis, and HIV-like particles were seen by electron microscopy in another patient with necrotizing vasculitis [3].

Different mechanisms have been described for HIV-associated vasculitis [2]. Viruses can infect endothelial cells and alter their function and biology, including induction of receptors for the Fc portion of IgG, induction of receptor for C3b, and promotion of leukocyte adherence. Infected endothelial cells express class II antigens and are capable of producing interleukin-1 (IL-1). The vascular deposition of HIV antigens may suggest the role of immune complexes as in HBV-induced PAN. An excess of CD8+ lymphocytes, defects in immune regulation, and opportunistic infections in the late stages of HIV infection may also contribute to endothelial cell inflammation [2, 3, 9].

When viral infection is diagnosed and considered to be responsible for vasculitis, a specific therapeutic approach should be prescribed. Treatment is based on the combination of antiviral agents and symptomatic or immunomodulating therapies [10]. Antiviral therapy facilitates virus clearance and seroconversion to specific antibodies. Plasma exchange is a powerful treatment that clears circulating immune complexes. On the other hand, steroids and cytotoxic agents stimulate virus replication and favor disease chronicity and deleterious effects due to the presence of virus. Hepatitis B virus-related PAN can be cured with the combination of antiviral agents (mainly interferon alpha) and plasma exchanges. Hepatitis C virus-related cryoglobulinemia may respond to interferon alpha and sometimes to plasma exchanges [10]. In HIV-related vasculitis, it is most appropriate to treat the HIV infection by highly active antiretroviral treatment (HAART). The combination of HAART with plasma exchanges can cure the vasculitis. Medium-dose steroids are generally reserved for the treatment of life-threatening conditions for short periods of time. Though harmful effects of cytotoxic therapies in HIV infection are feared, it should not be forgotten that malignant lymphomas occurring in HIV-infected patients have been successfully treated with cytotoxic agents [2, 9, 10]. The failure of treatment in our patient was most probably due to irregular drug treatment and the lack of follow-up.

In conclusion, the association of HIV with systemic vasculitis may be considered rare, compared with other viral agents. However, cases of HIV-associated PAN are reported increasingly often in the literature. The presence of bilateral renal hematomas due to the rupture of microaneurysms may be an ordinary finding in PAN. However, bilateral renal hematomas during the course of HIV-associated PAN are quite rare, and to our knowledge this would be the second case reported in the literature [11]. Human immunodeficiency virus infection should always be kept in mind while evaluating patients with PAN, since finding a viral etiology would modify the treatment of the PAN.

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