CASE REPORT

Polyarteritis nodosa with a chronic relapsing course

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Abstract

Polyarteritis nodosa is a medium artery vasculitis that can cause fatal complications. It commonly follows an acute monophasic course that may remit after treatment or cause serious morbidity or death. A 24-year-old patient described here had many vasculitic episodes in the past 16 years causing infarction of different organs. The last episode was most serious which caused mononeuritis multiplex, digital gangrene, bowel gangrene and subsequent perforations. There was strong clinical suspicion of this disease right from the beginning. However, diagnosis could not be proved objectively with multiple angiographies and biopsies till the end when CT angiography of abdomen revealed aneurysms in mesenteric vessels. He survived serious complications of disease and even surgery for bowel perforations but died of cerebellar abscess resulting from immunosuppressive therapy. Unfortunately he did not tolerate intravenous cyclophosphamide. Corticosteroid pulses and intravenous immunoglobulin also could not prevent the progression of digital gangrene and bowel infarction.

INTRODUCTION

Polyarteritis nodosa (PAN) is a medium artery vasculitis, which presents clinically as a multisystem disorder with serious complications. It is not associated with anti-neutrophil cytoplasmic autoantibodies [1]. Chapel Hill International Consensus Conference (CHCC) has defined PAN as distinct from microscopic polyangiitis which primarily affects small vessels [2, 3]. Diagnosis of PAN is difficult primarily because of lack of a serological marker and frequent unavailability of suitable tissue for histological confirmation of diagnosis.

Classical PAN follows a monophasic course in the majority of cases. However, about 21% patients with PAN have a chronic relapsing course [4]. Recently, we encountered a young 24-year-old male with features of this disease evolving indolently over 15 years. This is clearly a very unusual type of presentation and hence this case-report.

CASE REPORT

A 24-year-old male presented with persistent, severe abdominal pain and gangrene of his toes for 6 months. His history dated back to 1999 when he was 8-year old and he had tender macular lesions over legs, abdominal pain, weight loss, testicular pain, persistent fever and right ulnar palsy. There was no past history of any comorbid illness. Serum inflammatory markers were raised and HIV and hepatitis B surface antigen (HbsAg) were negative. Orchidopexy was performed for suspected torsion of right testis which failed to relieve the pain. PAN was suspected on clinical grounds by a pediatrician and conventional angiography of abdominal vessels and CT scan of abdomen were normal. After treatment with prednisolone and oral cyclophosphamide, his symptoms subsided and after four months he stopped the treatment. He had a long remission until February 2003, when abdominal pain recurred. This was managed conservatively and disease went into remission after a few days.

In February 2007, disease relapsed with left testicular pain. Orchidopexy was done on the left side and testicular biopsy showed left testicular atrophy and acute orchitis without arteritis. It was managed conservatively and symptoms remitted after a few weeks. Diagnosis of PAN was not suspected due to lack of objective findings and spontaneous resolution of symptoms.
In November 2014, 6 months before presenting to us, he had fourth relapse with abdominal pain and pain in toes of both feet. This time the abdominal pain was very severe with marked anorexia and progressive loss of weight. Video colonoscopy, jejunal biopsy and CT angiography of abdomen was normal and capsule endoscopy revealed jejunal and ileal ulcers. PAN was reconsidered and treatment with prednisolone and azathioprine was started. Symptoms showed no response and abdominal pain continued unabated. Thereafter dry gangrene of toes of both feet developed. Anti-nuclear antibody (ANA), Anti-neutrophil Cytoplasmic antibody (ANCA), anti-ENA and HbsAg were repeatedly negative. Serum lead and cryoglobulin levels were normal. Intravenous cyclophosphamide pulse was given but he did not tolerate it so it was discontinued. He was treated with various pain management measures including NSAIDs, tramadol, pregabalin, amitryptiline and buprenorphine patches but to no avail.

He presented to our center with a body weight of 24 kg. Toes of his both legs and fingers were gangrenous (Fig. 1). Because of his earlier history of intolerance to intravenous cyclophosphamide (CYC) infusions, oral CYC 50 mg/d was started along with prednisolone. Since intensity of abdominal pain was not consistent with repeatedly normal colonoscopy and angiographic findings, a major functional component was considered as an explanation. Psychotherapy and antidepressants proved futile. However, after a month he developed acute peritonitis because of gangrene and perforation in multiple segments of ileum and colon. Right hemicolecotomy, small bowel resection and ileocolostomy were performed. CT angiography of the abdomen showed multiple splenic infarcts, bilateral renal cortical infarcts and microaneurysms of terminal branches of abdominal aorta (Fig. 2). For the first time angiographic evidence of the disease was seen. Ironically, the histopathology did not reveal evidence of vasculitis in the resected specimen. Postoperatively, intravenous immunoglobulin (IVIG), 0.4 mg/kg/d was given for 5 days. In spite of surgery and IVIG, pain in his abdomen, fingers and toes continued. After 15 days, he developed cerebellar abscess and large hydrocephalus (Fig. 3). Urgent suboccipital craniotomy with abscess drainage and extraventricular drainage was done. However, he did not recovery and succumbed to his illness.
DISCUSSION

Classical PAN is known to present with emergencies such as abdominal catastrophes like bowel perforation and massive hemorrhage. Prolonged fever, severe hypertension and neurological manifestations such as mononeuritis multiplex and cerebrovascular accidents are common symptoms [5]. The present case illustrates the difficulty in establishing the diagnosis of PAN despite strong clinical suspicion from the beginning. First, the diagnosis of PAN is mainly clinical. Diagnostic criteria are weak and when applied may not always be applicable as shown by French study group [6]. The diagnostic yield of biopsy of a symptomatic nerve or muscle is 70% whereas that of an asymptomatic site is less than 30%. Angiographic findings reveal aneurysms or stenosis in about 66% cases [4]. This patient had classical clinical presentation but histological and radiological evidence of PAN eluded us until terminally when microaneurysms could be found on angiography.

Second, classical PAN is believed to be monophasic self-limited disease that tends not to recur once remission is induced. In a series of 348 patients, the one and five-year relapse rate for patients with non-HBV-associated PAN were 9.2 and 24%, respectively [4]. However, a study conducted in India showed that there was no relapse in any of the 15 patients who achieved remission [7]. This patient had multiple relapses in the course of the disease which kept on damaging one new organ in each relapse. The last relapse was the most serious, persisting and resistant to treatment. Such a chronic protracted case is rarely reported in the literature [8].

The common causes of mortality in this illness are renal failure and mesenteric, cardiac or cerebral infarction. Untreated, this disease has 5-year survival rate of 13% and with treatment survival rate improving to about 80% [5]. This patient survived various complications of the disease but died of immunosuppression-related complication, namely cerebellar abscess.

Conventional treatment consists of glucocorticoids and intravenous cyclophosphamide pulses for inducing remission [9]. Rituximab may be used in resistant cases [10]. We could not administer rituximab to this patient as he had received cyclophosphamide in recent past and also undergone a major abdominal surgery. His disease was refractory to cyclophosphamide and IVIG.

Diagnosis of PAN in this patient was difficult due to lack of radiological and histological evidence. His disease was chronic, relapsing and refractory to standard treatment.

CONFLICT OF INTEREST STATEMENT

All the authors hereby declare that no conflict of interest exists and there are no financial or personal relationships or affiliations that could influence (or bias) the author’s decisions, work or manuscript.

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ETHICAL APPROVAL

Ethical approval from institutional ethical committee has been taken before submitting this article.

CONSENT

Consent from the parents of the deceased patient has been taken for this case report.

GUARANTOR

Ashok Kumar as corresponding author agrees to be guarantor for the accuracy of final manuscript and submission of this article.

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