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Polyarteritis nodosa in a patient on hemodialysis; a case report

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Abstract

We represent a 40-year-old woman with end-stage renal disease (ESRD) of unknown etiology referred to the emergency department with episodes of chills and fever during hemodialysis. Further assessments revealed vasculitic skin rashes, as well as abdominal tenderness and later on, bloody diarrhea. Abdominal pain worsened during the course of admission, and as a result, the patient underwent cholecystectomy and appendectomy. Necrotizing vasculitis was diagnosed based on biopsy specimens taken from gall bladder and skin rashes. The diagnosis of poly arteritis nodosa (PAN) was established based on pathologic report and rheumatologic tests. Methylprednisolone pulses were administrated for 3 days followed by oral prednisolone and cyclophosphamide. After treatment, the signs and symptoms subsided. The present case report highlights the importance of timely diagnosis of PAN to prevent potentially irreversible consequences.

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Introduction

Poly arteritis nodosa (PAN) is a multi-system necrotizing vasculitis of small and medium sized muscular arteries with characteristic involvement of the renal and visceral arteries (1,2). Renal disease symptoms can vary from chronic hypertension due to narrowing of the renal arteries and thus activation of the renin-angiotensin system (3) to ESRD. Although pulmonary vasculature is not inflicted in this disease, bronchial arteries may be involved. Granulomas, significant eosinophilia and allergic diathesis are generally absent, and unlike other vasculitides, PAN is not associated with anti-neutrophil cytoplasmic antibodies (ANCA) (4).

Key point

Vascular lesions in poly arteritis nodosa (PAN) are characterized by transmural necrotizing inflammation of small and medium-sized muscular arteries. Necrosis of the arterial wall results in a homogenous, eosinophilic appearance referred as fibrinoid necrosis. Renal failure is one of the most common manifestations of PAN and is seen in almost 60% of the cases.

Case Presentation

A 40-year-old woman was referred to the emergency department with history of fever and chills during hemodialysis. She was a known case of end-stage renal disease (ESRD) and has been under hemodialysis by internal jugular permcath as the dialysis route access thrice weekly for the past 8 months. The episodes of fever and chills during dialysis had first started about one month prior to the current admission. The patient also mentioned periodic abdominal pain which was a generalized pain with no radiation or specific position and was not related to feeding. One month before current admission upper endoscopy showed no pathology. The severity of pain was intensified during the course of the disease. Furthermore, the patient gradually showed nausea and vomiting, and diarrhea (loose stool without apparent blood). Since a few days before admission, palpable purpuric lesions on the distal parts of upper and lower extremities were noted. She had recently been admitted to a local hospital and

received antibiotic therapy, however no improvement had been achieved. Other than hypertension for the past seven years, she had no remarkable points in her past medical history. Amlodipine and losartan were administrated to control hypertension.

Prior ultrasound study had revealed small size echogenic kidneys (no further study was conducted to clarify accurate diagnosis for the underlying pathology of ESRD).

Physical examination

The patient was conscious at admission. The vital signs were as blood pressure; 150/94 mm Hg, pulse rate; 74 beats per minute (bpm), respiratory rate; 16 per minute, and oral temperature was 39°C. Other findings in physical examination included pale conjunctiva and dry oral mucosa. No signs of infection at the exit site of the indwelling catheter nor tenderness on subcutaneous tunnel were observed. The heart and lung examinations were unremarkable. Positive shifting dullness as well as generalized tenderness without rebound tenderness and guarding were found in abdominal physical examination. Widespread purpuric non-blenching lesions were seen on the distal parts of all four limbs.

Differential diagnosis

The most common differential diagnoses of fever and chills in ESRD patients were considered. These included catheter infection, sepsis due to meningococcemia, subacute bacterial endocarditis and finally vasculitis. The patient underwent plain abdominal X-ray, chest X-ray and abdominopelvic ultrasound. No significant ultrasound findings were noticed except for moderate amount of ascites. Laboratory findings of the patients are illustrated in Table 1.

Treatment

The patient was admitted to the nephrology ward for further evaluations. Serial Blood cultures as well as urine culture revealed no microbial growth. Empiric antibiotic therapy was initiated after obtaining serial blood cultures and urine culture samples.

Punch biopsies of skin lesions were obtained, and the samples were sent for microscopic studies. Rheumatologic tests revealed negative P-ANCA (0.6 u/mL), C-ANCA (0.2 u/mL), and anti-ds DNA (0.5 IU/mL), along with borderline ANA (0.8 titer).

Serum IgA level was 257 mg/dL (reference range;70-400 mg/dL). The results of serum complement proteins were as C3; 95 mg/dL (reference range; 90-180 mg/dL), C4; 21 mg/dL (reference range; 10-40 mg/dL), and CH50: 94 u/mL (reference range; 70-150 u/mL).

During the course of admission, rebound tenderness was developed and patient's abdominal pain aggravated. She also mentioned blood in her stool. The patient underwent abdominal-pelvic CT scan with intravenous and oral contrast that revealed moderate ascites and increased intestinal wall thickness in the right lower quadrant. The gall bladder also showed increased thickness and few small stones.

Liver function tests and pancreatic enzymes were AST; 21 U/L, ALT; 21U/L, ALP; 366 U/L, total bilirubin; 0.66 mg/dL, direct bilirubin; 0.21 mg/dL, and serum amylase and lipase were 41 U/L and 22 IU/L respectively.

Urgent surgery counseling was requested in order to assess surgical emergencies such as ischemic colitis. The surgeon suggested explorative laparotomy which revealed massive intra-abdominal fluid and thickening and stones in the gall bladder. Cholecystectomy and appendectomy were done while fluid and tissue samples were sent for pathologic studies.

Pathologic assessments on the gall bladder sample revealed segmental necrotizing vasculitis involving the cystic artery (Figures 1 and 2). The biopsies of skin lesions also showed fibrinoid necrosis of dermal arteries (Figure 3).

The patient was administrated with intravenous methyl prednisolone (500 mg) for three consecutive days to manage vasculitis. After that, oral corticosteroid (1 mg/kg prednisolone per day) and cyclophosphamide (endoxan 50 mg daily) were initiated. Following these therapeutic regimens, the signs and symptoms gradually improved (Figure 4). Finally, the patient was discharged with a stable clinical condition.

Discussion

In the present report, the most probable diagnosis is PAN.

Table 1. Laboratory data of the patient

CBC/**diff**	WBC: 5400/µL P: 73.1% L: 18.2%	Hb:8.1 g/dL MCV:87.7 fl	Plt : 171000/µL	
Venous blood gas analysis	pH: 7.47	PCo2:31.1	HCo3:21 meq/L	
	Urea: 44 mg/dL Creatinine: 4.83 mg/dL	Na: 136 meq/L K:4.4 meq/L	Calcium: 7.7 mg/dL Phosphorus: 5.6 mg/dL	Albumin: 2.9 g/dL
	Iron: 24 mcg/L TIBC: 451 mcg/ml Ferritin: 926 ng/ml	Intact PTH:88 pg/ml Vitamin D3:16 ng/ml		
Ascites analysis	Serum-ascites albumin gradient (SAAG): 1	Fluid albumin: 1.9 g/dL Serum Alb:2.9 g/dL	Fluid protein: 3.1g/dL Total protein: 5.1g/dL	WBC: 2600/µL Neutrophil: 80%

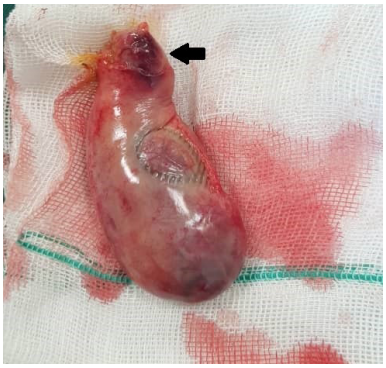

Figure 1. Macroscopic evaluation of gall bladder. Necrotizing areas can be seen specially on the cervical zone.

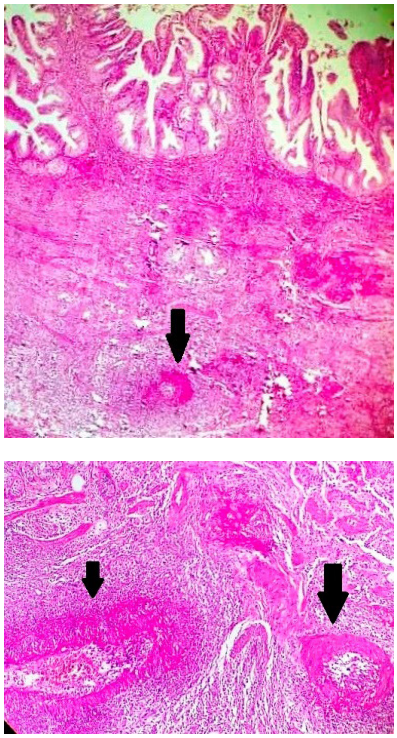

Figure 2. Gall bladder biopsy examination showing necrotizing vasculitis (black arrows).

Abdominopelvic CT scan did not reveal any aneurysm although CT angiography is the modality of choice. However, there is at least three important issues regarding this diagnosis. First; severe fibrinoid necrosis is hallmark of PAN that was seen in our patient. Second; cystic artery involvement which is a medium sized artery and third one, was the presence of necrotizing cholecystitis.

This was the first report of PAN in a patient with ESRD, on hemodialysis. The patient had history of hypertension for the past seven years and was recently diagnosed with ESRD of unknown etiology. The presence of PAN might be suspected by the clinical and radiologic findings however; the diagnosis should definitely be confirmed by biopsy of

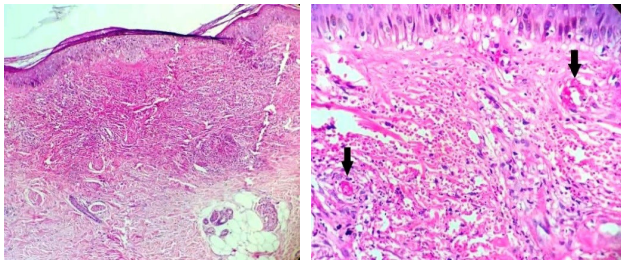

Figure 3. Skin lesions biopsy examination revealed fibrinoid necrosis (black arrows).

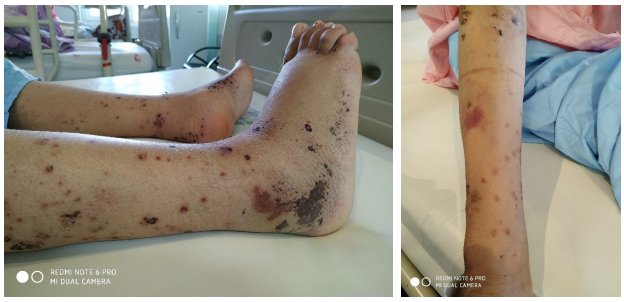

Figure 4. Skin rashes improved after treatment of vasculitis with intravenous and oral corticosteroids.

clinically affected organs (5).

In fact, tissue biopsy examination is the cornerstone of the diagnostic process in PAN. Vascular lesions in PAN are characterized with transmural necrotizing inflammation (2) of small and medium-sized muscular arteries. Characteristically, veins are not involved in PAN. The lesions are segmental and tend to involve bifurcation and branches of the arteries (6). The cellular infiltrates constitute polymorphonuclear leukocytes and mononuclear cells. Necrosis of the arterial wall results in a homogenous, eosinophilic appearance referred as fibrinoid necrosis (6). This feature was apparent in tissue biopsies obtained from our patient.

Clinically, histories of episodic fever and abdominal pain were observed in our patient. Actually, patients with PAN usually represent with vague symptoms such as weakness, malaise, headache, abdominal pain, fever and arthralgias; however, these symptoms can rapidly progress to a fulminant illness. The clinical picture can be complicated with signs and manifestations related to organs involvement. These include skin lesions, hypertension, renal insufficiency, neurologic dysfunction and abdominal pain. Nonetheless, patients might not have all the signs and symptoms at once. Accordingly, we found signs related to skin lesions, as well as renal and gastrointestinal involvements in our patient.

There are currently no diagnostic serologic tests for PAN, and the diagnosis is mainly based on the characteristic findings of vasculitis in biopsy specimens of the involved organs, as well as features in renal angiogram (2,6).

The prognosis of untreated PAN is extremely poor with a reported 5-year survival rate of 10% to 20% (an average rate of 13%) (1,7). Renal failure, as well as mesenteric, cardiac or cerebral infarctions are the major causes of death (5). With the introduction of effective treatments, the survival rate has currently increased reaching a 5-year survival rate of approximately 80% (8). In the present case, a favorable outcome was obtained following treatment with steroids and cyclophosphamide. It has been reported that the combination of prednisolone and cyclophosphamide (and glucocorticoids alone in milder forms of PAN) can result in durable disease remission.

Conclusion

Renal failure is one of the most common manifestations of PAN and is seen in almost 60 % of the cases. If underdiagnosed, renal failure can lead to death in patients with PAN. In general, any delay in the diagnosis of PAN or underestimation of its renal manifestations can lead to disease progression and clinical deterioration as seen in our patient.

Authors' contribution

AHA, BK, BS, AA and RD participated in the conception of the case report, data collection and drafted the manuscript. AHA, BK, BS, AA and RD contributed to drafting, critical reviewing, and finalization of the manuscript. All authors contributed to development of the manuscript and approved the final manuscript

Conflicts of interest

The author declared no competing interests.

Ethical considerations

Ethical issues including plagiarism, double publication, and redundancy have been completely observed by the author. The patient gave her consent to be published as a case report.

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