Atypical Clinical Course of Antineutrophil Cytoplasmic Autoantibodies-Associated Vasculitis

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We report a 16-year-old previously healthy boy who was admitted to hospital with fever, constitutional symptoms, purpura, additive arthritis, dysentery, rapid progressive renal failure, resembling Henoch- Schuenlein purpura, accompanied with retropharyngeal abscess. Kidney biopsy revealed rapid progressive glomerulonephritis with crescent formation, without immune deposition in immune fluorescent study. Serologic study revealed positive proteinase antineutrophil cytoplasmic antibody (ANCA). Intravenous methyl prednisolone plus and cyclophosphamide pulse were administered with a diagnosis of ANCA-associated vasculitis. Serum creatinine level reduced during the treatment and the patients was discharged with good clinical condition. This was the first case in which the ANCA-associated vasculitis was presented with retropharyngeal abscess. Other unusual findings were bloody diarrhea, raised purpura, and additive arthritis in an adolescence, which are more characteristic for Henoch-Schuenlein purpura.

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Case Report

INTRODUCTION

The antineutrophil cytoplasmic antibody (ANCA)-associated vasculitides are characterized by the occurrence of systemic necrotizing vasculitis (potentially leading to damage in various organs), together with the presence of ANCA in serum, which is highly specific for the diagnosis of vasculitis (98.6%).[1,2] The ANCA-associated systemic vasculitides include Wegener granulomatosis (WG), microscopic polyangiitis, Churg-Strauss syndrome, and necrotizing crescentic glomerulonephritis.

Two distinct ANCAs have been noted. Cytoplasmic ANCAs are highly associated with WG, while perinuclear ANCAs are associated with microscopic polyangiitis and Churg-Strauss syndrome.[3] Wegener Granulomatosis usually presents as a triad of airway necrotizing granulomas, systemic vasculitis and focal necrotising glomerulonephritis. The diagnosis of WG is based on clinical findings and positive ANCA against proteinase 3 serology. Proteinase ANCA pattern has specificity for WG of up to 98% in the acute phase, and it seems that its titer is related with disease activity. A biopsy is rarely histologically diagnostic.[3-5] The clinical presentation can vary, and it may affect several organs. The most common symptoms are related to the upper and lower airways, especially recurring bloody rhinorrhea, rhinosinusitis, and cavitary and nodular lesions in the lungs.[5]

Here we describe an unusual presentation of cytoplasmic ANCA-associated vasculitis with raised purpura, polyarthritis, dysentery, and rapid progressive renal failure, similar to Henoch-Schuenlein purpura (HSP), accompanied with fever and retropharyngeal abscess in an adolescent.

CASE REPORT

A 16-year-old boy was admitted to our teaching hospital because of malaise and weakness since last

4 weeks. He had generalized pain that followed by additive swelling and redness of joints, which was started by knee joints then progressed to elbow and both ankles. Two weeks before admission, nausea and vomiting were added to patient`s symptoms followed by anorexia, nocturia, and small red raised lesions in the lower limbs. Three days before admission, a darkly urine plus dysentery, abdominal pain, and lower limbs edema were also added to his symptoms. He had no history of pervious diseases like asthma or the use of any drugs or special substances, and there was no family history of diseases.

On the admission day, he had vertigo, nausea, vomiting, anorexia, sore throat, frequency, darkening of urine, dysentery, limbs pain, and edema. Vital signs on admission were as follows: blood pressure, 130/85 mm Hg; pulse rate, 100/min; respiratory rate, 20/min; body temperature, 38.5°C; and body weight, 50 kg. Physical examinations revealed raised purpura on the lower limbs, mild abdominal tenderness, and pitting edema. Laboratory findings during admission were as follows: urea, 170 mg/dL; creatinine, 7 mg/dL; sodium, 134 mEq/L; potassium, 4.8 mEq/L; leukocyte count, 9.1 × 10^9/L, with 74% neutrophil cells and 2% eosinophil cells; and hemoglobin, 6.5 g/dL. Urinary sediment revealed 2 to 3 leukocytes per high-power field and many erythrocytes per high-power field, more than 30% of which were dysmorphic.

The suspected diagnosis on admission was acute glomerulonephritis associated with HSP. Secondary workup was started. Due to patient's pyrexia on the first day, empiric treatment with vancomycin and ceftriaxone was started after diagnostic evaluation. On the third day after admission, the patient had unilateral oropharyngeal swelling. Otolaryngology consult was performed because of paratonsilar swelling and uvula edema. A cervical and basal skull computed tomography scan was ordered by otolaryngologist and patient antibiotics were changed to intravenous penicillin, 3 million U once, and then 1.5 million U every 6 hours, and metronidazole, 500 mg, 3 times per day.

Computed tomography revealed swelling and blunting of left parapharynx and retropharyngeal space accompanied with left tonsil swelling strongly suggestive of abscess formation (Figure 1). In the next visit by otolaryngologist, the patient

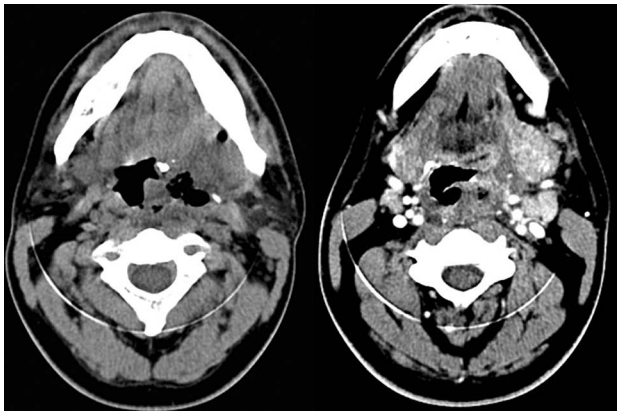

Figure 1. Cervical computed tomography scan of the patient revealed abscess formation in the parapharynx and retropharyngeal spaces.

was candidate for surgery and abscess drainage. Due to spontaneous drainage, surgical operation was canceled. Subsequently patient's body temperature gradually decreased and antibiotic therapy with penicillin and metronidazole was continued. Other paraclinical findings on the first days were as follows: normal chest radiography, edematous kidneys with increased size, and enhanced renal parenchymal echogenicity with increased corticomedullay differentiation in ultrasonography. Echocardiography showed no vegetation, and the ejection fraction was 65%. Other laboratory findings were as below: uric acid, 9 mg/dL; aspartate and alanine aminotransferase, within reference ranges; complements C3, C4, and CH50, within reference ranges; antinuclear antibodies, negative; anti-double-stranded DNA, negative; and serology tests for hepatitis B virus, hepatitis C virus, and human immunodeficiency virus, negative. The antistreptolysin O titer was 100 and antiphospholipid antibody was weekly positive. Lupus anticoagulant test was negative. Perinuclear ANCA was negative and cytoplasmic ANCA was positive (2.1 u/mL; reference, < 0.5 u/mL; enzyme-linked immunosorbant assay). The 24-hour urine parameters were as follows: volume, 1000 mL; creatinine, 900 mg; protein, 843 mg.

A decision was made to perform a kidney biopsy and methyl prednisolone pulse, 500 mg, was started and continued for 3 consecutive days with a probable diagnosis of rapid progressive glomerulonephritis. Immunofloroscent microscopic study of the kidney tissue revealed no precipitation of immunoglobulin and complement in glomeruli

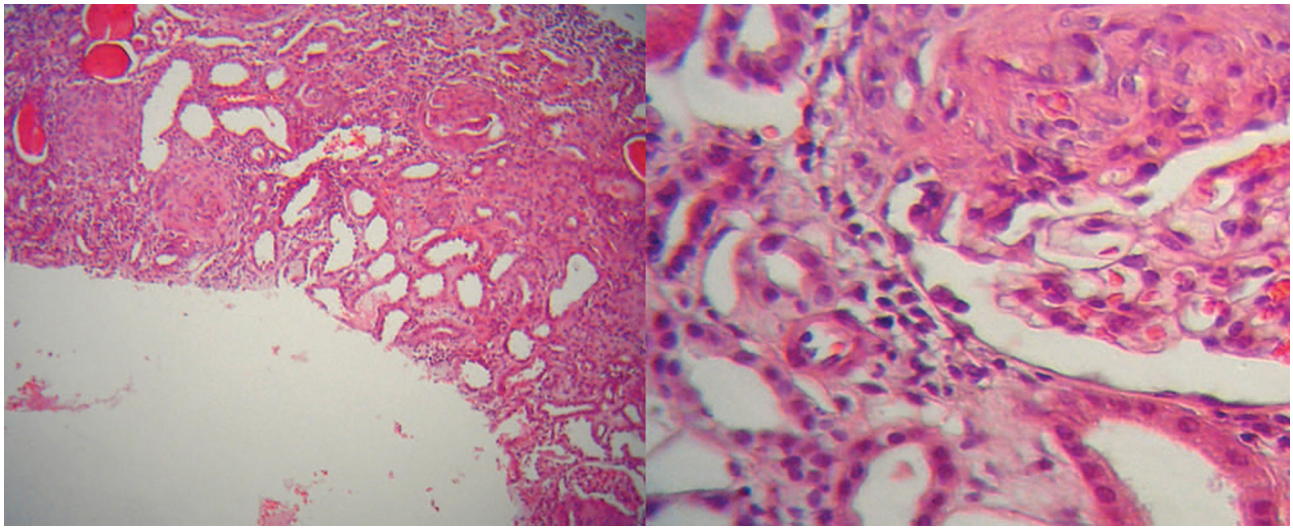

Figure 2. Light microscopic study of the renal tissue showed cellular and fibrocellular crescent in glomeruli. There was moderate to severe mixed inflammatory cells infiltration with moderate fibrosis in interstitium (Alcian blue).

and also intristitium highly suggestive of pouci-immune glomerular disease. Light microscopic study showed 9 glomeruli 5 of which had cellular crescent and 1 was sclerotic. There was moderate to severe mixed inflammatory cells infiltration with moderate fibrosis (Figure 2). Due to the serologic findings accompanied with light microscopic and immunoflurosent microscopic finding that showed pouci-immune crescentic glomerulonephritis, the diagnosis of ANCA-associated vasculitis, mostly WG, was made.

The specimen could not be sent for electron microscopic study. Then, intravenous cyclophosphamide pulse, 500 mg/m^3, was administered. Blood culture and also abscess drainage culture were negative for microorganisms may be due to previous antibiotic administration. Serum creatinine level decreased within 2 weeks and the patient was discharged with a serum creatinine level of 2.5mg/dL, on 30 mg prednisolone daily and good general condition . The patient was advised to refer for follow-up. Despite continuing treatment with oral cyclophosphamide and prednisolone, kidney function tests were gradually deteriorated during the next months and after 1-year follow-up, the patient was a candidate for hemodialysis. After 6 months of dialysis he received a kidney transplant from a living unrelated donor. He was doing well with functioning allograft on his last follow-up visit.

DISCUSSION

Understanding the pathogenesis of ANCA-associated vasculitis is important for the development of novel therapeutic agents, and important advances have been made in recent years.[2,6,7] Constitutional symptoms, such as fever, myalgia, anorexia, weight loss, malaise, and night sweats, are common in vasculitis, like our case.[6] This case presented with anorexia, weight loss, malaise, and systemic pain 1 month before admission. This presentation is not distinguishable between patients with small-vessel vasculitis (SVV) such as HSP and ACNCA-associated vasculitis. In WG, there is a predilection for the upper and lower respiratory tracts and the kidneys to be involved. Upper respiratory tract symptoms include rhinorrhea, epistaxis, sinusitis, otitis media, collapse of the nasal bridge, and tracheal stenosis. In contrast to typical presentation of ANCA-associated vasculitis, our case did not have lower respiratory tract symptoms, and the only upper respiratory tract symptom was sore throat and then retropharyngeal tender mass with fever on examination that was presented within the first days of admission.

Cervical computerized scan revealed retropharyngeal abscess. He had generalized pain followed by an additive swelling and redness of joints which was started by knee joints then progressed to the elbow and both ankles. The dermal and joint manifestation of this case were raised purpura in the lower limbs, additive arthritis that more compatible with HSP, which is typically presented with palpable purpura affecting the lower extremities, arthritis, nephritis and colicky

abdominal pain like dysentery.[8] Colicky abdominal pain with dysentery was also one of the symptoms of our patients that mimic the patients with HSP. Common gastrointestinal manifestation of ANCA-associated vasculitis is ischemia and hemorrhage, in contrast to this case that presented with dysentery and bloody diarrhea.[5] Renal manifestations are common in the form of hematuria, proteinuria, and red cell casts, and they can result to the rapid deterioration of renal function.

The most frequent renal lesion caused by ANCA-associated vasculitis is glomerulonephritis. Although there are different frequencies of proteinase 3 ANCA and myeloperoxidase-specific ANCA among different types of SVV, neither ANCA subtype provides a diagnostic test that allows for the diagnostic differentiation among different phenotypes of ANCA-SVV. However, in a patient with signs and symptoms of SVV, like our case, ANCA positivity does confirm the presence of some form of ANCA-associated SVV, which is often useful for directing management even if the specific type of ANCA- associated SVV has not yet been determined. Common dermal vasculitic findings in ANCA- associated SVV are palpable purpura (usually in the lower extremities), petechia, ulcers, nodules, ecchymoses, and bullae. The resolution of the differential diagnosis in patients with renal-dermal vasculitic syndromes is very important because the prognosis and appropriate treatments are quiet different among the diagnostic possibilities.[6,7] The clinical syndrome of palpable purpura, nephritis, and ANCA is nearly diagnostic for ANCA- associated SVV, although tissue confirmation of vasculitis is comforting before the institution of toxic immunosuppression treatments.[9] Based on clinical and laboratory findings and tissue confirmation of crescentic glomerulonephritic without glomerular deposition of immunoglobulin and/or complement, the diagnosis of WG was made. Unfortunately, we could not send the kidney tissue for electron microscopic study.

In conclusion, this case presented with skin lesion (raised purpura), fever, additive polyarthritis, and colicky abdominal pain, that is clinically more common in HSP than ANCA-associated vasculitis. The other atypical finding in our case was retropharyngeal abscess, and this is a first reported case of WG presented with retropharyngeal abscess.

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CONFLICT OF INTEREST

None declared.

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