KIDNEY BIOPSY TEACHING CASE

Acute-Onset Hearing Loss With Renal Failure: Differential Diagnosis

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HEARING LOSS IS NOT associated commonly with most renal diseases. Alport syndrome is considered the classic example of a disorder that features both renal failure and hearing loss. In this condition, the hearing loss can be evolving slowly and is sensorineural in origin. Acute sudden hearing loss is a rare accompaniment of renal disease or renal failure. However, there are a variety of systemic disorders that can be associated with these 2 conditions. The systemic vasculitides (both primary and secondary) represent a heterogeneous group of diseases. In some of these conditions, auditory involvement is 1 of the systemic manifestations, thus expanding the differential diagnosis in these patients.

We present a case of an 11-year-old boy with upper- and lower-respiratory symptoms, acute sudden hearing loss, and acute onset of renal failure. The kidney biopsy showed crescentic glomerulonephritis.

CASE REPORT

An 11-year-old boy of African descent who previously was in good health developed an upper-respiratory tract infection with nasal congestion, nonproductive cough, occasional epistaxis, subjective fever, and fatigue. The primary care physician began therapy initially with antihistamines and nasal decongestants and later with an oral third-generation cephalosporin because of persistent symptoms. During the next 6 weeks, the patient developed anorexia and weight loss, followed by macroscopic hematuria, oliguria, and facial swelling with intermittent episodes of nonbilious emesis. Most prominently, he also developed a marked acute decrease in hearing that required his parents to speak loudly at home and was even noted by his schoolteacher. There was no history of foreign body or barotrauma to the ears and no ear discharge or masses around the pinna. There was no history of skin rashes, joint pain or swelling, hemoptysis, or chest pain. The past medical history was significant for sickle cell trait, also present in his parents. Both paternal and maternal grandmothers developed end-stage renal disease as a result of diabetes, but there was no family history of autoimmune diseases.

Physical examination showed bilateral periorbital and lip swelling, without tenderness in the face or sinuses. Anterior rhinoscopy showed dried blood without obvious septal excoriations or purulent discharge. External ear examination results were normal. Tympanic membranes were nonmobile to insufflation and had mucoid effusions bilaterally. He had mild to moderate bilateral pitting edema in the lower extremities. The remainder of the physical examination was unrevealing.

Initial laboratory data included a chemistry panel with the following values: sodium, 124 mEq/L (124 mmol/L); potassium, 5.7 mEq/L (5.7 mmol/L); chloride, 92 mEq/L (92 mmol/L); bicarbonate, 31 mEq/L (31 mmol/L); blood urea nitrogen, 61 mg/dL (21.8 mmol/L); creatinine, 8.8 mg/dL (778 μmol/L); calcium, 8 mg/dL (2 mmol/L); phosphorous, 3.8 mg/dL (1.23 mmol/L); and albumin, 2.2 g/dL (22 g/L). Hemoglobin level was 8.9 g/dL (89 g/L), and hematocrit was 26%. High-sensitivity C-reactive protein level was 141 mg/L (normal, <5 mg/L), and erythrocyte sedimentation rate was 109 mm/h. Urinalysis showed a specific gravity of 1.011, pH of 5.5, protein concentration of 100 mg/dL, and 330 red blood cells/high-power field.

Renal ultrasound showed normal-size echogenic kidneys with poor corticomedullary differentiation. A computed tomographic scan showed diffuse mucoperiosteal thickening within the paranasal sinuses, mastoid air cells, and middle-ear cavities bilaterally, with a normal nasal septum. Chest computed tomographic scan showed nodular opacities in the upper lobes of both lungs, as well as on the right lower lobe. There were bilateral pleural effusions and cardiomegaly.

Serological studies, including antinuclear antibody and C3 and C4 complement levels, yielded normal or negative results. Immunofluorescence staining for antineutrophil cytoplasmic antibodies (ANCAs) showed a cytoplasmic granular fluorescence pattern (cytoplasmic ANCA positive) without perinuclear fluorescence (perinuclear ANCA negative). The direct enzyme-linked immunosorbent assay for ANCA against proteinase 3 was strongly positive at 158 units.

A renal biopsy was performed.

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Renal Biopsy

The biopsy specimen consisted of renal cortex with up to 13 glomeruli per section. Virtually every glomerulus was involved with cellular crescents (Fig 1). Crescents were circumferential and associated with capillary wall destruction and even focal rupture through Bowman capsule into the interstitium. There was accompanying neutrophil infiltration, karyorrhectic nuclear debris, and fibrin deposition. Some relatively intact capillary loops compressed by crescents did not show prominent hypercellularity. No specific glomerular basement membrane abnormality was observed on silver stains. There was focal irregular tubular dilatation accompanied by epithelial attenuation and focal epithelial mitotic figures. Scattered interstitial infiltrates consisted of lymphocytes and plasma cells with associated tubulitis and tubule destruction (Fig 2). Blood vessels were thin walled, and no vasculitis was identified.

Immunofluorescence Microscopy

Nineteen glomeruli were present for immunofluorescence evaluation. Focal mesangial granular staining was noted for immunoglobulin G (IgG; trace), IgM (trace to 1^+), C3 (1 to 2^+), C1q (trace), and κ and λ light chain (trace). Focal capillary wall deposition of C3 (1^+) also was observed. However, there was no distinct capillary wall granular staining for IgG, IgM, IgA, or C1q. Focal tubular albumin deposition (2^+) was present. Small arteries and arterioles had focal C3 deposition (2^+).

Electron Microscopy

Ultrastructural analysis supported the light microscopic observation. Some glomerular capillary loops that were intact showed regular glomerular basement membranes and intact foot processes. There was focal endothelial and podocyte swelling. Some glomerular intracapillary leukocytes, including neutrophils, were noted. No electron-dense deposits were identified.

Pathological Diagnosis

Biopsy findings were consistent with a pauci-immune crescentic glomerulonephritis. Based on clinical, serological, and biopsy findings, a diagnosis of Wegener granulomatosis (WG) was made.

Clinical Follow-Up

The patient became anuric and required initiation of renal replacement therapy in the form of hemodialysis. He later was transitioned to peritoneal dialysis therapy. Pulse methylprednisolone (at a dose of 30 mg/kg/d) was administered for 3 consecutive days, followed by intravenous cyclophosphamide and a tapering dose of prednisone. Enalapril therapy was initiated for hypertension, and subcutaneous recombinant human erythropoietin was administered for anemia. After 3 months of therapy, inflammatory marker levels had decreased, with a C-reactive protein level of 0.2 mg/L (normal) and erythrocyte sedimentation rate of 20 mm/h. Anti–proteinase 3 level had decreased to 46 units and subsequently became negative. Repeated computed tomographic scans showed improved aeration of the paranasal sinuses, decrease in size of the right upper-lobe nodular opacity, and clearance of the left upper-lobe and right lower-lobe lung changes. The hearing deficit also improved. However, renal function has not improved, and he continues to be dialysis dependent.

DISCUSSION

Pediatric conditions associated with renal vasculitis usually are part of a systemic multiorgan disease and rarely are renal limited. WG, originally described in 1931, is an idiopathic necrotizing granulomatous small-vessel vasculitis that predominantly affects the respiratory and renal systems.[1]

Mucosal inflammation and ulceration leading to epistaxis, sinusitis, and hearing loss are common upper-airway symptoms in WG for which patients seek medical attention.[2] However, both conductive and sensorineural hearing loss are common. Granuloma formation within the middle ear and Eustachian tube can result in conductive hearing loss, whereas sensorineural hearing loss suggests a neurodegenerative process of unclear cause that is believed to be irreversible.[3] Renal involvement, estimated to occur in up to 80% of patients during the entire course of the disease, may progress to end-stage renal failure and represents one of the most serious disease manifestations.[1] However, renal disease can be asymptomatic, and because children frequently have respiratory symptoms secondary to infection or allergy, making an early diagnosis can be challenging.

The clinical association of hearing loss in the context of acute renal injury can be seen in a number of other conditions, which include vasculitides and autoimmune disorders. Hearing loss has been reported in patients with polyarteritis nodosa,[4] but it is not as well substantiated as in those with WG. Moreover, a clear distinction between classic polyarteritis nodosa and microscopic polyangiitis has not always been made in some studies. Hearing loss has been observed in patients with myeloperoxidase-ANCA–positive microscopic polyangiitis.[5] Both classic polyarteritis nodosa and microscopic polyangiitis have been described in childhood.[6] In classic polyarteritis nodosa, vasculitis involves medium-size renal arteries, especially the interlobar and arcuate arteries, leading to aneurysmal lesions and associated renal infarcts. Glomeruli usually are spared.