Interesting aetiology in an adolescent male with pulmonary-renal manifestations: Granulomatosis with polyangiitis

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Sri Lanka Journal of Child Health, 2024; 53(1): 82-84
DOI: http://doi.org/10.4038/sljch.v53i1.10736

(Key words: Vasculitis, ANCA, Polyangiitis, Glomerulonephritis, Haematuria)

Introduction
Children with persistent respiratory manifestations and multisystemic involvement need careful evaluation for underlying connective tissue, rheumatological or immunodeficiency syndromes¹. We present an adolescent with persistent pneumonia and pleural effusion with pulmonary renal syndrome.

Case report
A 15-year-old male presented with fever for 4 days, cough and sore throat for 2 days, difficulty in breathing for 1 day and joint pain in knee and shoulder for 1 day. There was no history of bluish discolouration of limbs, rashes (Figure 1). Respiratory system examination revealed a central trachea, bilateral equal movements, bilateral equal air entry, bronchovesicular breath sounds and bilateral basal coarse crepitations in subscapular and infra-axillary areas. Other system examination was not significant.

On examination, child was febrile (102°F) with a pulse rate of 140 beats per minute, blood pressure of 88/56 mm Hg and tachypnoea (respiratory rate 52/minute). There was pallor, oedema of both feet, periorbital oedema and rash (Figure 1). Respiratory system examination revealed a central trachea, bilateral equal movements, bilateral equal air entry, bronchovesicular breath sounds and bilateral basal coarse crepitations in subscapular and infra-axillary areas. Other system examination was not significant.

Baseline investigations showed anaemia (haemoglobin 6.3 g/dL), leucocytosis (19,300 cells/cu mm, polymorphs 82%, lymphocytes 13%), platelet count 340,000/cu mm, mean corpuscular volume 75.6fL and mean corpuscular haemoglobin 23.7pg. Peripheral smear showed microcytic hypochromic anaemia without any haemolysis. Blood urea was 44 mg/dL, serum creatinine was 0.6 mg/dL, serum albumin was 2.3 g/dL and total cholesterol was 232 mg/dL. Coombs test (direct and indirect) and antinuclear antibody were negative. Urinary microscopy showed 30-40 red blood cells/high power field with dysmorphism, 2-3 pus cells/high power field and albuminuria (100mg/mmol). Urine culture was sterile. Chest x-ray showed diffuse bilateral opacities (Figure 2).

A provisional diagnosis of Henoch-Schonlein purpura was made in view of severe anaemia and rash and child was started on steroids, antibiotics and supportive treatment. Differential diagnoses of glomerulonephritis (acute or rapidly progressive) and connective tissue disorder were also considered. History was reviewed and revealed persistent nasal symptoms (epistaxis and discharge) in the past 4 months. Due to nasal, renal and pulmonary involvement, the possibility of vasculitis syndromes was considered. Bronchoscopy revealed no structural abnormality but lavage fluid showed numerous benign bronchial epithelial cells and a few haemosiderin laden alveolar macrophages with occasional lymphocytes and no eosinophils. Lung computed tomography (CT) showed large rounded peripheral area of consolidation in anterior segment of left upper lobe (3 x 3.3cm), multiple pulmonary nodules (6 x 6mm) in basal segments of both lower lobes and a few sub-centimetric non-necrotic pre/para tracheal, pre-vascular, sub-carinal lymph nodes (Figure 3).

Anti-neutrophil cytoplasmic antibody (ANCA) associated PR3 antigen was positive (40.04 U/ml). Ear nose and throat (ENT) evaluation showed no deviated nasal septum/polyps; hearing was normal. Ophthalmological evaluation had no evidence of uveitis. Renal biopsy showed segmental necrotizing glomerulonephritis involving 6 (42%) sampled glomeruli (Figure 4).

Based on clinical, radiological and histopathological findings a diagnosis of ANCA associated vasculitis like Granulomatosis with polyangiitis was made. Child was treated with cyclophosphamide pulse regime and prednisolone and discharged after 8 weeks with resolution of haematuria and respiratory distress. Child was lost to follow up after 4 months and was re-admitted after 2 months with severe renal failure and pulmonary haemorrhage but succumbed.

Discussion
Pulmonary renal syndromes are a group of diseases with distinctive clinical and radiological manifestations with different pathophysiological processes. Common diseases implicated are ANCA positive small vessel vasculitis and anti-glomerular basement membrane disease². Children with ANCA vasculitis with dual
positive disease like polyangitis and Goodpasture syndrome have been reported. Other diseases include ANCA negative vasculitis like IgA disease, drug induced vasculitis and autoimmune connective tissue diseases like systemic lupus erythematosus, polymyositis etc. We discuss here some atypical features in our case. In this case with the diagnosis of ANCA positive and Granulomatosis with Polyangitis (GPA), diffuse alveolar haemorrhage may lead to slow blood loss and anaemia without any clinical haemoptysis. A diagnosis of GPA was made on the basis of American College of Rheumatology (ACR) classification criteria (presence of 2/4 criteria have 88% sensitivity and 92% specificity) with presence of nasal inflammation, abnormal chest radiology with pulmonary nodules, abnormal urinary sediment with haematuria and renal biopsy showing inflammation. Another diagnostic criterion by ACR and European alliance for rheumatology based on scoring system on clinical and laboratory criteria was fulfilled in our child. We used indirect immunofluorescence assay for diagnosis of ANCA body in our case which has a higher specificity. Child was managed on standard management protocols for treatment of ANCA vasculitis and pulmonary renal syndromes.

In 1936, a German pathologist, Friedrich Wegener, described three cases of small-medium vessel vasculitis with granulomatous inflammation popularly called Wegener’s granulomatosis. In 2000, because of Wegener's Nazi ties, American College of Rheumatology, American Society of Nephrology, and European League Against Rheumatism recommended a change to disease-descriptive nomenclature.

We conclude that in children presenting with respiratory manifestations and multisystemic involvement especially pulmonary-renal syndromes may have uncommon underlying disorders like vasculitis or connective tissue disorders. Hence a careful evaluation will help in early diagnosis and appropriate management which may be helpful in reducing morbidity and mortality.

References


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**Figure 1:** Rash on both lower limbs, pinpoint petechial

**Figure 2:** Chest x-ray bilateral diffused infiltrates

**Figure 3:** A) Large rounded peripheral area of consolidation in anterior segment of left upper lobe measuring 3x 3.3 cm, no cavitations B) Multiple pulmonary nodules 6-8mm in basal segments of both lower lobes

**Figure 4:** Renal biopsy on silver stain showing A) crescentic glomerulonephritis B) 2 glomeruli with increased cellularity C) Glomerular proliferation and sclerosis