Pulmonary Renal Syndrome in Childhood: A Report of Twenty-One Cases and a Review of the Literature

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Summary. In adults, the term specific pulmonary renal syndrome describes disorders with pulmonary and glomerular manifestations and includes Wegener’s granulomatosis, Goodpasture disease, and systemic lupus erythematosus. Nonspecific pulmonary renal syndrome refers either to pulmonary disease complicating glomerular disease, or glomerular diseases following pulmonary disease. Since little is known regarding pulmonary renal syndrome in childhood, we reviewed the charts of 21 pediatric patients with pulmonary renal syndromes treated by the Department of Pediatrics, University of Bern between 1991 and 1998; we also reviewed the pediatric literature that deals with specific pulmonary renal syndromes.

Specific pulmonary renal syndrome was noted in 3 children with systemic vasculitis (Wegener granulomatosis, N = 2; microscopic polyangiitis, N = 1) and 2 with systemic lupus erythematosus. Nonspecific pulmonary renal syndrome was observed in 12 patients with pulmonary edema (N = 9), pulmonary thromboembolism (N = 2), and pulmonary infection (N = 1) complicating the course of a glomerular disease, and in 4 children with a pulmonary disease followed by a glomerular disease. Review of the literature disclosed 52 cases of specific pulmonary renal syndrome other than systemic lupus erythematosus: Wegener granulomatosis (N = 28), Goodpasture disease (N = 13), and Henoch-Schönlein purpura (N = 11). In addition, hemolytic uremic syndrome complicated pneumococcal pneumonia in 32 cases.

We conclude that pulmonary renal syndromes need to be looked for in childhood. Apart from Wegener granulomatosis, Goodpasture disease, and systemic lupus erythematosus, Henoch-Schönlein purpura and hemolytic-uremic syndrome occasionally have both pulmonary and renal features. Pediatr Pulmonol. 2000; 29:382–388. © 2000 Wiley-Liss, Inc.

Key words: Goodpasture syndrome; hemolytic-uremic syndrome; kidney disease; pulmonary disease; Schönlein-Henoch purpura; vasculitis; Wegener granulomatosis.

INTRODUCTION

In adults, the term pulmonary renal syndrome is used to indicate the coexistence of severe pulmonary and renal disease in individuals without any concomitant destructive pulmonary disease. The term specific pulmonary renal syndrome describes disorders associating pulmonary (hemoptysis; lung hemorrhage; infiltrates or nodules) and glomerular manifestations and includes Wegener granulomatosis (or related systemic vasculitides such as microscopic polyangiitis and Churg-Strauss syndrome), Goodpasture disease, and systemic lupus erythematosus. The term nonspecific pulmonary renal syndrome refers either to pulmonary edema, pulmonary thromboembolism, or pulmonary infection complicating the course of glomerular disease, or to glomerular diseases following pulmonary disease, mostly an infection.1–10

Little is known regarding pulmonary renal syndrome in childhood. This might well be related to the fact that Wegener granulomatosis, microscopic polyangiitis, Churg-Strauss disease, Goodpasture disease, and systemic lupus erythematosus are rather rare in this age group. On the other hand, it is tempting to assume that some diseases primarily seen in children such as Henoch-Schönlein purpura or hemolytic-uremic syndrome might present with pulmonary and renal features.

We report on 21 pediatric patients with specific or nonspecific pulmonary renal syndromes, diagnosed and treated by the Department of Pediatrics, University of

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CASE REPORTS

Specific Pulmonary Renal Syndrome

Three children had a systemic vasculitis associated with circulating antineutrophil cytoplasmic autoantibodies (Table 1). The diagnosis of glomerulonephritis complicating peritonitis and Henoch-Schönlein purpura had been initially suspected in 2 patients. Based on typical histopathological findings, the final diagnosis was Wegener granulomatosis in 2 and microscopic polyangiitis in 1 patient. The patients were put on treatment with prednisone and cyclophosphamide. In addition, cotrimoxazol was given to the 2 patients with Wegener granulomatosis.

Two children presenting with a pulmonary renal syndrome were found to have systemic lupus erythematosus (Table 2). Both patients were treated with prednisone and azathioprin and are currently in remission.

Nonspecific Pulmonary Renal Syndrome

A nonspecific pulmonary renal syndrome was noted in 16 children. In 12 patients, pulmonary edema due to fluid overload (N = 9), pulmonary thromboembolism (N = 2), or pulmonary infections (N = 1) complicated the course of a glomerular disease, as shown in Table 3. In 4 children, a preexisting pulmonary disease was followed by a glomerular one, as listed in Table 4.

REVIEW OF THE LITERATURE ON PULMONARY RENAL SYNDROME IN CHILDHOOD

At least 28 pediatric patients with renal and pulmonary involvement and with a diagnosis of Wegener granulomatosis have been reported,11–31 as shown in Table 5. Apart from renal and pulmonary involvement, the great majority of these patients presented with either rhinosinusitis or otitis. In the reports no distinction was made between Wegener granulomatosis and microscopic polyangiitis.

The diagnosis of Goodpasture disease was seen in only 13 pediatric patients with a specific pulmonary renal syndrome,32–40 as shown in Table 6. In 2 of the 13 patients, no information on testing for circulating antibodies against glomerular basement membrane or renal biopsy findings was available.

The most common cause of specific pulmonary renal syndrome reported in the pediatric literature is systemic lupus erythematosus.41,42 The major extrarenal and extrapulmonary features in pediatric patients with renal and
pulmonary involvement in connection with systemic lupus erythematosus were recently reviewed by Nadorra and Landing. They include female predominance, cardiovascular involvement, hematological involvement, skin and joint involvement, and central nervous system involvement, as summarized in Table 7.

A recent review indicates that only 11 pediatric patients with Henoch-Schönlein purpura were reported with associated pulmonary and renal features, as shown in Table 8. The typical biopsy features of Henoch-Schönlein purpura, including either mesangial IgA deposition or a leukocytoclastic vasculitis accompanied by vascular IgA deposition, were not demonstrated in 5 patients.

Hemolytic uremic syndrome is a rare but recognized complication of systemic diseases caused by pneumococcal infection. The features of 32 pediatric patients with postpneumococcal hemolytic uremic syndrome are given in Table 9. The direct Coombs test was very often positive in this condition.

Churg-Strauss disease is rare in childhood. To our knowledge, no more than 4 pediatric cases of Churg-Strauss syndrome have been reported. No renal involvement was noted in the mentioned patients.

**DISCUSSION**

The term *pulmonary renal syndrome* is used to describe adult patients with serious and potentially threatening multisystem diseases dominated by a pulmonary and a renal component. Several reviews of this topic have appeared. Our study was performed to assess the features of pulmonary renal syndrome in pediatric patients. We observed that in childhood a diversity of specific and nonspecific conditions, which differ at least in part from those in adults, produce pulmonary renal syndrome, as summarized in Table 10.

Both in childhood and in adulthood, *nonspecific pulmonary renal syndrome* is more frequent than the *specific* one. This term refers either to pulmonary edema, pulmonary thromboembolism, or pulmonary infection (mostly caused by opportunistic organisms) complicating the course of glomerular disease, or to glomerular diseases following a pulmonary disease, mostly an infection caused by common organisms such as *Mycoplasma pneumoniae* or *Legionella pneumophila*. The tendency toward developing a *nonspecific pulmonary renal syndrome* is likely the same in children and adults with the exception of pneumococcal pneumonia, a well recognized cause of hemolytic uremic syndrome in childhood. The direct Coombs test is positive in this form of hemolytic uremic syndrome. The designation “secondary amyloidosis” refers to tissue deposition of fibrils composed of fragments of serum amyloid A protein. Secondary renal amyloidosis has been reported in cystic fibrosis with severe pulmonary involvement.

It has been assumed that the clinical presentation of acute glomerulonephritis with pulmonary hemorrhage (as manifested by hemoptysis or pulmonary infiltrates) is indicative of antiglomerular basement membrane antibodies, as seen in Goodpasture disease. These findings, however, are not diagnostic of antiglomerular basement...
membrane antibody disease, since they can be seen in systemic vasculitis and systemic lupus erythematosus. Vasculitides such as Wegener granulomatosis (more rarely microscopic polyangiitis or Churg-Strauss syndrome), Goodpasture disease, or systemic lupus erythematosus are the most common causes of specific pulmonary renal syndrome in adult patients. The present review of the pediatric literature suggests that, apart from the mentioned disorders, Henoch-Schönlein

### TABLE 4—Clinical and Laboratory Findings in Four Pediatric Patients With a Nonspecific Pulmonary Renal Syndrome

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (years)</th>
<th>Gender</th>
<th>Pulmonary disease</th>
<th>Glomerular disease</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>11</td>
<td>Male</td>
<td>Streptococcal pleuroneumonia (A-Streptococci recovered from pleural fluid)</td>
<td>Severe poststreptococcal glomerulonephritis with transient anuria and severe arterial hypertension</td>
<td>Blood C3-complement strongly reduced (transiently)</td>
</tr>
<tr>
<td>2</td>
<td>4</td>
<td>Male</td>
<td>Lobar pneumonia of unknown origin (pneumococcal?)</td>
<td>Mild glomerulonephritis</td>
<td>Blood C3- and C4-complement within normal range</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>Female</td>
<td>Lobar pneumonia of unknown origin (pneumococcal?)</td>
<td>Severe glomerulonephritis and renal failure not requiring dialysis (creatinine up to 365 μmol/L, urea up to 31.9 mmol/L)</td>
<td>Blood C3- and C4-complement within normal range</td>
</tr>
<tr>
<td>4</td>
<td>6</td>
<td>Female</td>
<td>Chronic lung edema and severe idiopathic dilated cardiomyopathy</td>
<td>Severe glomerulonephritis and systemic microscopic polyangiitis2</td>
<td>No clear-cut link between cardiomyopathy and microscopic polyangiitis</td>
</tr>
</tbody>
</table>

1Glomerular complication of an underlying pulmonary disease.
2Antineutrophil cytoplasmic autoantibodies (titer 1:160) against proteinase 3.

### TABLE 5—Features in 28 Pediatric Patients With Both Renal and Pulmonary (Lung Hemorrhage) Involvement Considered to Have Wegener Granulomatosis

<table>
<thead>
<tr>
<th>N</th>
<th>28</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female:male</td>
<td>20:8</td>
</tr>
<tr>
<td>Age, years1</td>
<td>12 (2–16)</td>
</tr>
<tr>
<td>Pulmonary involvement, N</td>
<td>28/28</td>
</tr>
<tr>
<td>Renal involvement, N</td>
<td>20/28</td>
</tr>
<tr>
<td>Rhinosinusitis, N</td>
<td>20/28</td>
</tr>
<tr>
<td>Otitis, N</td>
<td>5/28</td>
</tr>
<tr>
<td>Laryngotracheal involvement, N</td>
<td>3/28</td>
</tr>
</tbody>
</table>

1Median and range.

### TABLE 6—Features in 13 Pediatric Patients With Pulmonary Renal Syndromes Considered to Have Goodpasture Disease

<table>
<thead>
<tr>
<th>N</th>
<th>13</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female:male</td>
<td>10:3</td>
</tr>
<tr>
<td>Age, years1</td>
<td>14 (4.5–17)</td>
</tr>
<tr>
<td>Pulmonary involvement, N</td>
<td>13/13</td>
</tr>
<tr>
<td>Renal involvement, N</td>
<td>13/13</td>
</tr>
<tr>
<td>Circulating antibodies against GBM, N2</td>
<td>8/9</td>
</tr>
<tr>
<td>IgG deposits along GBM, N2</td>
<td>7/7</td>
</tr>
</tbody>
</table>

1Median and range.
2In 2 patients, no information on testing for circulating antibodies against glomerular basement membrane or renal biopsy findings was reported. GBM, glomerular basement membrane.

### TABLE 7—Major Extrarenal and Extrapulmonary Involvement1 in Pediatric Patients With Renal and Pulmonary Involvement in Systemic Lupus Erythematosus, as Reviewed by Nadorra and Landing

<table>
<thead>
<tr>
<th>N</th>
<th>11</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female:male</td>
<td>5:6</td>
</tr>
<tr>
<td>Age, years1</td>
<td>14 (4.5–17)</td>
</tr>
<tr>
<td>Renal involvement, N</td>
<td>11/11</td>
</tr>
<tr>
<td>Pulmonary involvement, N</td>
<td>11/11</td>
</tr>
<tr>
<td>Skin involvement, N</td>
<td>11/11</td>
</tr>
<tr>
<td>Joint involvement, N</td>
<td>11/11</td>
</tr>
<tr>
<td>Abdominal involvement, N</td>
<td>10/11</td>
</tr>
<tr>
<td>Cardiac involvement, N</td>
<td>3/11</td>
</tr>
</tbody>
</table>

1Median and range.

### TABLE 8—Features in 11 Pediatric Patients With Pulmonary Renal Syndromes Considered to Have Henoch-Schönlein Purpura

| Female:male | 5:6 |
| Age, months2 | 13 (5–31) |
| Direct Coombs test positive3 | 11/12 |
| Positive blood cultures | 26/32 |

1Information not available in 9 cases.
2Median and range.
3No information available in 20 cases.

### TABLE 9—Features in 32 Pediatric Patients With Hemolytic Uremic Syndrome Complicating Pneumococcal Pneumonia

<table>
<thead>
<tr>
<th>N</th>
<th>32</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female:male1</td>
<td>12:11</td>
</tr>
<tr>
<td>Age, months2</td>
<td>13 (5–31)</td>
</tr>
<tr>
<td>Direct Coombs test positive3</td>
<td>11/12</td>
</tr>
<tr>
<td>Positive blood cultures</td>
<td>26/32</td>
</tr>
</tbody>
</table>

1Information not available in 9 cases.
2Median and range.
3No information available in 20 cases.
purpura also causes a specific pulmonary renal syndrome in this age group. This fact is not surprising, considering that this disease is the most common systemic vasculitis that occurs in childhood. Interestingly, recent data suggest a subclinical pulmonary involvement in most children with Henoch-Schönlein purpura.

Churg-Strauss syndrome (or allergic angiitis and granulomatosis) is among the proposed etiologies of systemic diseases which share pulmonary and renal abnormalities. This multisystemic vasculitis is characterized by allergic rhinitis, asthma, and peripheral blood eosinophilia. The most common organs involved are the lung and the skin, followed by the cardiovascular, gastrointestinal, central nervous, and, more rarely, renal systems. Unlike other vasculitides, however, renal involvement has never been noted in children with this syndrome.

A large set of diagnostic markers can be used in patients with specific pulmonary renal syndromes. The presence of circulating antineutrophil cytoplasmic autoantibodies in pulmonary renal syndrome makes Wegener granulomatosis (or, more rarely, either microscopic polyangiitis or Churg-Strauss syndrome) the leading clinical possibility. Recognition of antilgomerular basement membrane antibodies is virtually diagnostic for Goodpasture disease. However, in some patients both positive antineutrophil cytoplasmic autoantibodies and antilgomerular basement membrane antibodies are present. Antinuclear autoantibodies, mostly antibodies directed against native deoxyribonucleic acid, are an essential component in systemic lupus erythematosus. Finally, decreased circulating levels of complement C3 occur both in systemic lupus erythematosus and poststreptococcal glomerulonephritis.

**CONCLUSIONS**

This article is the first to focus on pulmonary renal syndromes in pediatric practice. In childhood, pulmonary renal syndromes present as a rare but serious medical emergency. Since many causes may produce this syndrome and early diagnosis is crucial, the evaluation of a child presenting with pulmonary and renal symptoms includes, apart from a thorough history and physical examination, laboratory tests directed toward the possible causes of specific pulmonary renal syndrome. They include: 1) anti-glomerular basement membrane antibodies, which are essentially diagnostic of Goodpasture disease; 2) anti-neutrophil cytoplasmic antibodies, which are suggestive of Wegener granulomatosis or related diseases; 3) anti-nuclear antibodies in patients suspected of having lupus; 4) complement C3 levels, that are usually reduced in poststreptococcal glomerulonephritis and systemic lupus erythematosus; and 5) complete blood cell count and the direct Coombs test, that help to diagnose postpneumococcal hemolytic uremic syndrome. A skin biopsy is often indicated in adults with a pulmonary renal syndrome. However, since in Henoch-Schönlein purpura the rash is usually very distinctive, a skin biopsy is rarely indicated in young patients with the typical purpuric lesions.

**REFERENCES**


**TABLE 10—Specific and Nonspecific Conditions That Produce Pulmonary Renal Syndrome in Children**

<table>
<thead>
<tr>
<th>Specific pulmonary renal syndromes</th>
<th>Pulmonary disease complicating preexisting glomerular disease</th>
<th>Glomerular disease complicating pulmonary disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systemic lupus erythematosus</td>
<td>Pulmonary edema</td>
<td>Postinfectious glomerulonephritis</td>
</tr>
<tr>
<td>Wegener granulomatosis and</td>
<td>Pulmonary thromboembolism</td>
<td>Postpneumococcal hemolytic uremic syndrome</td>
</tr>
<tr>
<td>microscopic polyangiitis</td>
<td>Pulmonary infection¹</td>
<td></td>
</tr>
<tr>
<td>Henoch-Schönlein purpura</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Goodpasture disease</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

¹Mostly caused by opportunistic organisms.
Pulmonary Renal Syndrome


