CASE REPORT

Tubulointerstitial nephritis and uveitis: a rare cause of renal failure

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Abstract
We report two cases of tubulointerstitial nephritis and uveitis syndrome occurring in adults. Both patients had the characteristic marked constitutional symptoms, uveitis, and renal failure. After treatment with systemic corticosteroids, renal function improved. This is contrary to previous reports that have indicated a poor prognosis in adults.

Key words: Acute disease, Hypergammaglobulinemia, Nephritis/interstitial, Nephrotic syndrome, Uveitis/complications

CASE REPORT

Case 1
A 40-year-old woman presented with a 6-week history of sore throat, malaise, and profound nausea and vomiting. Her medications were roxithromycin 300 mg daily for the previous 5 days. Clinical examination was normal. Urine examination revealed mild proteinuria and pyuria but neither hematuria nor casts. Full blood count revealed a normal white cell (including normal eosinophil count) and platelet count but a marginally low hemoglobin concentration of 114 (115-165) g/L. Liver function tests and electrolytes were normal, but serum urea was 25.6 (2.1-9) mmol/L and creatinine was 0.42 (0.06-0.13) mmol/L. Erythrocyte sedimentation rate was 102 (3-12) mm/hour. Antinuclear antibody was positive with a titer of 1:2560 (nucleolar pattern). However, antibodies to deoxyribonucleic acid and extractable nuclear antigen were negative. Antineutrophil cytoplasmic antibodies were negative. Angiotensin converting enzyme level was normal. Serum protein electrophoresis revealed a polyclonal hypergammaglobulinemia. Serology for the Epstein-Barr virus, cytomegalovirus, human immunodeficiency virus, toxoplasma, brucella, Lyme disease, and arbovirus was normal. Chest x-ray was normal. A renal biopsy revealed acute interstitial nephritis (predominantly lymphocytes with some plasma cells, eosinophils, and a reasonable number of neutrophils).

The patient responded quickly to prednisone (1 mg/kg/day for 2 weeks then tapered over 6 weeks). Her symptoms, hemoglobin, urea, creatinine, and hypergammaglobulinemia normalized over the next month. Three months later, she experienced bilateral anterior uveitis, which resolved promptly with topical corticosteroid treatment. The patient remained well, without recurrence of disease 4 years later.

Case 2
A 34-year-old woman presented with a 3-week history of anorexia, nausea, vomiting, and weight loss. Four months previously she had bilateral anterior uveitis, which resolved quickly with topical corticosteroid treatment. She was taking no medications. Clinical and urine examinations were normal. A full blood count...
revealed a normal white cell (including normal eosinophil count) and platelet count but a low hemoglobin concentration of 80 g/L. Liver function tests and electrolytes were normal, but urea was 23.7 mmol/L and creatinine was 0.57 mmol/L. Erythrocyte sedimentation rate was 105 mm/hour. A polyclonal hypergammaglobulinemia was present. Antinuclear antibody, extractable nuclear antigen, and antineutrophil cytoplasmic antibodies were negative. Angiotensin-converting enzyme level and chest x-ray were normal. Serology for the Epstein-Barr virus, cytomegalovirus, and human immunodeficiency virus were normal. A renal biopsy revealed interstitial fibrosis, tubular atrophy, and interstitial nephritis (predominantly lymphocytes with occasional plasma cells, epithelioid histiocytes, eosinophils, and one focal granuloma).

The patient responded quickly to prednisone (1 mg/kg/day for 3 weeks then tapered over 10 weeks). The patient’s symptoms, hemoglobin, and hypergammaglobulinemia normalized in 4 weeks. Serum creatinine also improved quickly with eventual normalization (0.12 mmol/L) 16 months later. The patient remained well without recurrence of disease 4 years later.

DISCUSSION
Both patients were diagnosed with the tubulointerstitial nephritis and uveitis syndrome (TINU). This is a distinct ocularrenal syndrome that remains a diagnosis by exclusion (1). First described in 1975 (1), it occurs predominantly in adolescent girls (2). It is characterized by uveitis, tubulointerstitial nephritis, and marked constitutional symptoms (3). The uveitis is typically anterior, bilateral, nongranulomatous, and controlled with topical corticosteroids. It often relapses, but long-term ocular sequelae are rare (3,4). It may precede, follow, or occur simultaneously with tubulointerstitial nephritis (3). The tubulointerstitial infiltrate generally consists of T lymphocytes, plasma cells, neutrophils, variable eosinophils, and occasional granuloma (5). It responds well to systemic corticosteroids with some cases resolving spontaneously (6). Complete resolution is typical. Relapse of the nephritis is rare (4).

Tubulointerstitial nephritis and uveitis syndrome in adults is less well described, but persistent renal impairment is said to be common and occurs in 50% of cases (2,7). However, a review of the English literature revealed that only three of the 25 adult cases reported had a persistently increased serum creatinine (2-4,6-18). Of the six patients not treated with systemic corticosteroids, three patients had a persistently increased serum creatinine. In contrast, none of the 19 treated patients had a persistently increased serum creatinine. These data (and the two patients in this report) suggest that TINU in adults may not be as unfavorable as previously thought, especially when treated with systemic corticosteroids.

The pathogenesis is unknown, but likely involves an autoimmune reaction against constituents common to the renal tubulointerstitium and uveal tract (6). T cell-mediated immune mechanisms have been suggested (6). HLA-DR6 is frequently associated with this syndrome (8). Similarities with sarcoidosis have been noted. Both have a predominance of T-helper cells often with granuloma formation in their tubulointerstitial infiltrate (5). Although sarcoidosis limited to the eye and kidney is rare, the only difference in these cases seems to be a normal serum angiotensin-converting enzyme level in the patients with TINU (19). Whether TINU is part of the sarcoidosis spectrum remains to be seen.

In conclusion, TINU is a readily treatable disease that carries a favorable outcome, especially in young girls. Although TINU in adults was previously thought to have a poor prognosis, treatment with systemic corticosteroids seems to lead to an improved outcome.

REFERENCES