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Original article

A syndrome of acute interstitial nephritis and anterior uveitis

Timothy E. Bunchman[1] **and Jeffrey N. Bloom**[2]

[1] Division of Pediatric Nephrology, University of Michigan, Ann Arbor, Michigan, USA
[2] Department of Ophthalmology, St. Louis University School of Medicine and the Cardinal Glennon Children's Hospital, St. Louis, Missouri, USA

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Abstract. A syndrome of acute interstitial nephritis (AIN) and anterior uveitis is described in two children and the literature is reviewed. These disorders appear to improve, in uncontrolled studies, with systemic and topical ophthalmic corticosteroid treatment. Although the renal and ocular prognoses appear good, it is important to recognize that patients with AIN are at risk for uveitis and if present, consultation with an ophthalmologist is recommended.

Key words: Acute interstitial nephritis – Anterior uveitis – Iritis

Introduction

Acute interstitial nephritis (AIN) is an uncommon cause of renal insufficiency in childhood [1]. The etiology of AIN in children may be multifactorial, ranging from drug induced to idiopathic [2]. The finding of urinary eosinophils or the presence of eosinophilic infiltrate in the renal interstitium may be associated with drug-induced AIN.

Anterior uveitis (AU) or iritis is an uncommon ophthalmic disorder of childhood [3]. There are multiple systemic and non-systemic etiologies for this inflammation of the anterior portion of the globe. Erythema of the eye, photophobia and decreased vision are frequent manifestations of AU, although it may present without signs or symptoms in children [3].

An association between idiopathic AIN and AU has been described as a consequence of immune-modulated AIN [4, 5], associated with systemic vasculitis [3] as well as idiopathic [6, 7]. We report here two pediatric patients with this combination of findings.

Case reports

Case 1

This 15-year-old white male presented with a 3-week history of non-specific malaise associated with intermittent abdominal pain and low-grade fever. Laboratory investigation revealed an elevated serum creatinine of 5.0 mg/dl. Upon referral to the pediatric nephrology department, he was found to be normotensive with no obvious rashes or edema. Urinalyses revealed 1+ blood with 1+ protein and a specific gravity of 1.010. Microscopic inspection of the urine was unremarkable. Laboratory investigation confirmed the finding of an elevated serum creatinine. In addition, C3, C4 and CH_{50} levels were normal and anti-nuclear antibody (ANA) and hepatitis B surface antigen were not detected. Marginally elevated levels of anti-streptococcal antibody were detected. A complete blood count (CBC) revealed a hematocrit (Hct) of 33% and a white blood cell count (WBC) of 9,500/mm^3 without eosinophils. Urinary Wright stain revealed the presence of urinary eosinophils. A renal biopsy showed normal glomeruli, although severe AIN with eosinophils was present. Immunofluoresence did not show any glomerular or tubular basement membrane immunoglobulin deposition. Intravenous Solumedrol (10 mg/kg per day for 3 days) was begun, followed by oral prednisone (2 mg/kg per day). Improvement of renal function occurred within 48 h of initiation of steroid therapy, with normalization approximately 6 weeks later. The prednisone was tapered and discontinued over 4 weeks. Eosinophiluria was present for 2 weeks.

Approximately 3 months after normalization of the renal function, the patient complained of new-onset ocular erythema and discomfort. Slit lamp biomicroscopy revealed inflammatory cells and protein in the aqueous humor of the anterior segment of the eye, indicative of AU. He was treated with topical ocular steroids with resolution of this AU over the next 6 months. At the 3-year follow-up, his serum creatinine is 1.0 mg/dl, he has no hematuria, pyuria or proteinuria, his blood pressure is normal and his ocular examination is normal. The etiology of the AIN was never well defined.

Case 2

This 13-year-old white female had a 4-week history of malaise associated with intermittent abdominal pain and fevers to 103° F with signs and

Correspondence to: T. E. Bunchman, University of Michigan – C. S. Mott Children's Hospital, Box 0297, Women's L2602, 1521 Simpson Road East, Ann Arbor, MI 48109, USA

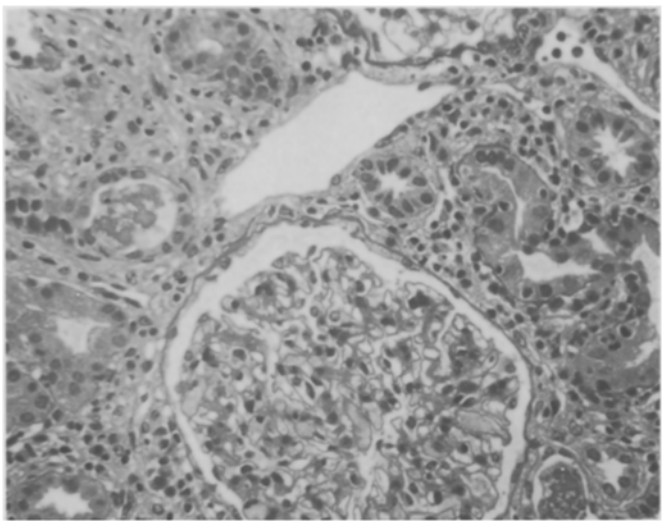

Fig. 1. Renal biopsy of patient no. 2 (trichrome stain, ×40). Normal glomerulus is shown with a prominent interstitial infiltrate of which 10% of the cells are composed of eosinophils

symptoms of sinusitis. She was placed on 5 days of amoxicillin therapy. Because of no improvement of symptoms, laboratory investigations were carried out which showed an elevated creatinine of 11 mg/dl. Upon referral to the pediatric nephrology department, she was found to be normotensive with no evidence of vascular rashes, weight change or peripheral edema. Laboratory investigation revealed an elevated serum creatinine of 15 mg/dl, blood urea nitrogen of 95 mg/dl, sodium 134 mEq/l, potassium 4.2 mEq/l, carbon dioxide 14 mEq/l, calcium 9.3 mg/dl and phosphorus 5.4 mg/dl. C3, C4 and CH_{50} levels were normal; ANA, anti-neutrophil cyotoplasmic antibody and hepatitis B surface antigen were not detected. A CBC revealed a Hct of 39% and a WBC of 7,300/mm^3 without eosinophils. The urinalysis revealed trace protein and 1+ blood. Microscopic examination of the urine was negative. Urine Wright stain revealed evidence of urine eosinophils. The child underwent a percutaneous renal biopsy which demonstrated normal glomeruli with severe AIN, including the presence of eosinophils (Fig. 1). Immunofluoresence did not show any glomerular or tubular basement membrane immunoglobulin deposition. Intravenous Solumedrol therapy followed by oral prednisone (2 mg/kg per day) was begun. Resolution of her AIN occurred over the next 6 weeks without the need for dialysis. The prednisone was tapered and discontinued over 8 weeks. The eosinophiluria resolved over 3 weeks. Two months after discontinuation of her oral steroid therapy, she complained of ocular discomfort as well as conjunctival erythema. Ophthalmic examination revealed evidence of AU. She was treated with topical ocular steroids with immediate improvement of her symptoms and complete clinical resolution within 6 weeks of therapy. At the 1-year follow-up, her blood pressure is normal, her urinalysis showed no evidence of proteinuria, hematuria, pyuria, her creatinine is 1.2 mg/dl and her ocular examination is normal.

Discussion

Eosinophilic AIN may be associated with a drug-induced form of AIN. The penicillin group of antibiotics have been known to cause AIN with usual resolution of AIN after discontinuation of medication. One patient mentioned here had been previously treated with a brief course of amoxicillin which was started after the onset of symptoms. The other patient had no previous treatment with penicillin. The current treatment of choice for AIN is the withdrawal of the offending agent, as well as supportive treatment of renal insufficiency [1, 2, 8]. The role of corticosteroids is controversial. Resolution of AIN usually occurs within 4–6 weeks of initial identification. Residual mild renal insufficiency may be a long-term sequela [2].

An association between AIN and AU has been reported, with the iritis usually bilateral, which may precede, follow or occur concomitantly with the AIN [4–14]. The two children mentioned, whose range of recovery of AIN to onset of AU was 2–3 months, are consistent with the other reported cases. It could be postulated that the AU may have flared earlier in the course of the patients' illness, but due to early administration of steroid therapy the finding of AU was delayed. Too few patients with this combination of symptoms exist to address this clinically. The mechanism of this association is not defined. The suggested treatment for the AIN and AU has been systemic as well as ocular corticosteroids. No controlled trials have evaluated corticosteroid treatment versus non-treatment, in order to determine if spontaneous resolution of this syndrome occurs.

The etiology of this ocular-renal disorder is uncertain. The lack of positive ANA serology, hypocomplementemia, anti-neutrophil cytoplasmic antibodies or hepatitis surface antigenemia suggests that this syndrome is unlikely to be associated with collagen, vascular or hepatitic diseases. The good prognosis and rapid resolution with corticosteroids, without recurrence after their discontinuation, further indicates that systemic vasculitides are unlikely etiologies of this syndrome. The possibility of drug-induced AIN, with the incidental findings of AU, should be considered in the presence of eosinophiluria, yet this finding has not been noted in the AIN and AU literature [4, 6–11].

In vitro testing for sensitivity to amoxicillin was not performed in patient no. 2. Without this evidence, an association between the AIN and amoxicillin can not be excluded. Clinical symptoms predated the antibiotic administration by 3 weeks, making the amoxicillin as the causitive agent of her AIN unlikely.

A syndrome of AIN and AU, as well as bone marrow or lymph node granulomas, is discussed in the literature [15, 16]. Both the children, as deemed by lack of palpable lymph nodes on physical examination as well as normal chest X-rays, lack the additional findings of granulomas that have been associated previously.

We report an association between AIN and AU, previously reported in the adult population and more recently in the pediatric literature. Resolution of the AIN and the AU in this pediatric population occurred after treatment with corticosteroid therapy. No control studies to date confirm whether corticosteroid therapy is necessary in the treatment. We suggest that when one identifies a patient with AIN, observation for AU is important. If ocular symptoms do occur, then prompt examination and treatment by an ophthalmologist is recommended.

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Literature abstracts

J Nucl Med (1992) 33: 2094–2098

Volume expanded diuretic renography in the postnatal assessment of suspected uretero-pelvic junction obstruction

Kevin K. L. Choong, Simon M. Gruenewald, Elisabeth M. Hodson, Vincent F. Antico, David C. Farlow, and Ralph C. Cohen

Controversy surrounds the role of ^{99m}Tc-diethylenetriamine pentaacetic acid renography in suspected uretero-pelvic junction obstruction in early life. Accordingly, we retrospectively reviewed 18 patients (28 hydronephrotic kidneys) with a mean age of 2 mo (range: 1 wk-6 mo) who underwent a total of 36 scans using intravenous volume expansion (10 ml/kg) and furosemide diuresis (1 mg/kg). Initial scans were classified as obstructed, not obstructed or indeterminate using differential renal function, furosemide washout $T_{1/2}$ and visual assessment of tracer clearance. Those initially classified as obstructed ($n = 8$) have been surgically confirmed. In the indeterminate ($n = 6$) and nonobstructed ($n = 14$) groups, three and two kidneys, respectively, developed obstruction on progress scans. Mean follow-up in the nonsurgical patients was approximately 9 mo (range: 4–17 mo). A total of 13 kidneys had developed obstruction by renographic criteria, and to date 12 have surgical confirmation. Our data indicate that: (1) scans classified as obstructed correlate well with surgery; (2) an initial classification of indeterminate or nonobstructed does not excluder later development of obstruction; and (3) serial scans corectly stratify children with possible uretero-pelvic junction obstruction.

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The "well tempered" diuretic renogram: a standard method to examine the asymptomatic neonate with hydronephrosis or hydroureteronephrosis

A report from combined meetings of The Society for Fetal Urology and members of The Pediatric Nuclear Medicine Council – The Society of Nuclear Medicine

Perinatal hydronephrosis (HN) and hydroureteronephrosis (HUN) are recognized more frequently as the routine use of prenatal ultrasonography increases. The decision-making process for those instances of urinary tract dilatation that require surgical correction and those that do not is based in part on the findings of diuresis renography. The methodology for performing this test has differed among nuclear medicine practitioners and the surgical findings are occasionally discrepant from the diuretic renogram interpretation. Consequently, the Society of Fetal Urology (SFU) and the Pediatric Nuclear Medicine Council (PNMC) of the Society of Nuclear Medicine met to develop by consensus a more uniform methodology. A standard method has been agreed upon for the following facets of diuretic renography: patient preparation (hydration and bladder catheterization), diuresis renography technique (radiopharmaceutical used, patient position during examination, data acquisition parameters, diuretic pharmaceutical and dosage; time of injection and regions of interest to monitor diuretic effect), and data analysis (percent differential renal function, curve pattern analysis and methods of measuring diuretic response). Pooled diuresis renogram data are being collected for analysis for correlation with surgical results and clinical outcomes to determine the most appropriate information to be derived from the diuretic renogram in neonates with HN and HUN.