Acute interstitial nephritis due to 5-aminosalicylic acid

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Thought to be the main active component of sulfasalazine, 5-aminosalicylic acid (5-ASA) has been available as adjunctive therapy for ulcerative colitis for the past few years. Side effects were expected to be less severe with 5-ASA used alone than with sulfasalazine because of the absence of the sulfa moiety. Since the introduction of 5-ASA there have been two reports of interstitial nephritis due to this agent.[1,2]

I describe a case in which 5-ASA induced acute interstitial nephritis similar histologically to that associated with nonsteroidal anti-inflammatory drugs (NSAIDs).[1] The case is unique because the acute interstitial damage was accompanied by polyuria and polydipsia.

Case report

A 29-year-old man with ulcerative colitis, initially diagnosed in 1983, was referred for renal assessment in November 1989. Over the past 6 years his previous physician had prescribed intermittent courses of oral prednisone and sulfasalazine therapy. In May 1989 the patient's current gastroenterologist had changed the therapy from sulfasalazine, 4 g/d, to enteric-coated 5-ASA, 2.4 g/d in divided doses, because of a flare-up of ulcerative colitis. The oral therapy with prednisone, 20 mg/d, had gradually been tapered over 3 weeks. In August 1989 the patient started using enemas with betamethasone, 5 mg at bed time. One month later he had requested oral sulfasalazine therapy instead of 5-ASA therapy, but by the beginning of October the betamethasone enemas and the sulfasalazine therapy had been stopped and the 5-ASA therapy resumed.

At presentation 1 month later the patient reported the abrupt onset of polyuria and polydipsia. The blood urea level had increased from within normal limits to 13.9 mmol/L. The serum creatinine level was 210 μmol/L and the serum uric acid level 599 μmol/L. The serum levels of glucose, calcium, sodium and potassium in random blood samples were 5.6, 2.39, 139 and 4.4 mmol/L respectively. The specific gravity of the urine was less than 1.005, and microscopy revealed 50 to 60 leukocytes per high-power field. Culture of midstream urine showed no growth. In a 24-hour urine collection (6252 ml) the total protein level was 0.70 g/d and the creatinine clearance 38 (normally 80 to 120) ml·min/1.73 m^2. The blood hemoglobin level decreased from 159 g/L in August to 114 g/L in November, and the leukocyte count was 10.4×10^9/L (52% young neutrophils, 14% mature neutrophils, 18% lymphocytes, 14% monocytes and 1% eosinophils).

The patient appeared adequately hydrated and was afebrile. Apart from slight pallor there were no significant physical findings.

Sonography revealed the kidneys to be of normal size but slightly echogenic. A renal cyst and a nonobstructing calculus were noted in the upper pole of the left kidney. Light microscopy of a renal biopsy specimen showed seven glomeruli; one was obsolescent, and the others were normal. However, there was marked interstitial edema and inflammation composed mainly of small lymphocytes, with a few neutrophils. No oxalate or uric acid crystals were found. Immunofluorescent study did not reveal immune deposits in the glomeruli but did show focal deposits of fibrin in the interstitial tissue and granular C3 deposits in the walls of the interstitial vessels.

The 5-ASA therapy was stopped, and the option of total colectomy was discussed with the patient in

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case the colitis flared up. One week later the serum creatinine level decreased to 140 μmol/L; since the colitis had not flared up no additional therapy was prescribed.

The polyuria and the polydipsia resolved within 1 week after the 5-ASA therapy was stopped, and the renal function progressively returned to normal over the next 2 months (Fig. 1). The specific gravity of the urine by the beginning of March 1990 was up to 1.020, and microscopy yielded negative results.

Comments

Drug-induced acute interstitial nephritis commonly occurs with the use of certain antibiotics, diuretics and other, miscellaneous drugs.[3] In the case I have reported, 5-ASA, a relatively new drug, induced acute interstitial nephritis, which resolved after the drug's withdrawal, without the use of the normally recommended steroid therapy.[3]

Some drugs can induce polyuric renal failure. These include lithium carbonate, amphotericin B and demeclocycline. In those cases, and presumably in the one I have presented, the polyuria is thought to be related to impairment of the kidney's concentrating ability because of inhibition of the action of antidiuretic hormone on the distal tubule.[4] In contrast, patients receiving NSAIDs who have acute interstitial nephritis present with fluid retention and oliguric renal failure.[5]

If polyuria and polydipsia commonly occur early in 5-ASA-induced interstitial nephritis they could be useful markers to alert clinicians to the potential nephrotoxic effects of continued use of 5-ASA in susceptible patients.

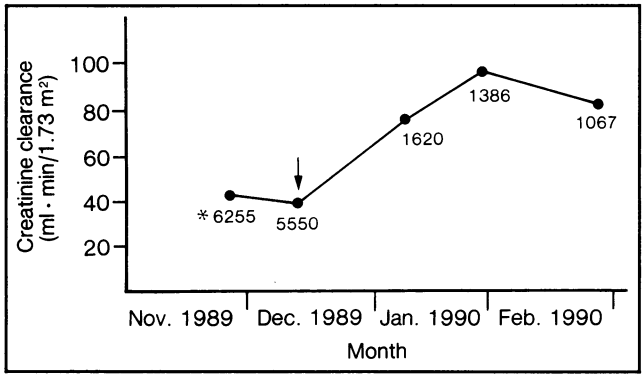

Fig. 1: Creatinine clearance in patient with acute interstitial nephritis due to 5-aminosalicylic acid (5-ASA) therapy. Numbers under each point represent volume (in millilitres) of 24-hour urine collection; arrow indicates point at which renal biopsy was done and 5-ASA therapy stopped.

References

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A hanging matter

Someone may be perfectly rational, yet commit manslaughter, adultery, theft: he will easily find a physician who testifies that the action must be credited to temporary insanity. In the past, proof of insanity during a crime required proof of irrational behaviour before the act was committed; now, the opposite seems to be true. Some time ago . . . a lawyer who defended a thief claimed that the exaggerated "thieving area" of the defendant's skull suggested an irresistible urge to steal; and that he could thus not be held responsible for the theft. "One more reason to hang him," replied the judge, "since it is obvious that he will steal again, sooner or later."

— Christoph Wilhelm Hufeland (1762-1836)