Acute renal failure associated with diflunisal

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Summary

The case of a 44-year-old man with acute oliguric renal failure due to tubulo-interstitial nephritis after 3 months' diflunisal is reported. The possible mechanisms are discussed.

Introduction

Diflunisal has been reported as causing acute allergic interstitial nephritis (Chan *et al.*, 1980) resulting in acute oliguric renal failure. A case of acute renal failure due to tubulo-interstitial nephritis after 3 months of diflunisal is reported here. Recently, phenylakalonic acids with analgesic and anti-inflammatory properties such as fenoprofen and naproxen have been reported as causing tubulo-interstitial nephritis manifested by acute renal failure and often accompanied by nephrotic syndrome but without signs of hypersensitivity such as fever, rash, and eosinophilia (Wendland, Wagoner and Holley, 1980). Diflunisal is not a phenylakalonic acid but is the difluorophenyl derivative of salicylic acid; it has analgesic and anti-inflammatory properties but with fewer side effects than salicylic acid.

Case report

A 44-year-old man was admitted with acute oliguric renal failure. He had been treated for the previous 3 months with diflunisal (250 mg twice/day) for low backache due to lumbar spine osteoarthritis. The only other analgesic treatment was occasional paracetamol and dextropropoxyphene (Distalgesc). Over 3 months he had lost 35 kg which was associated with anorexia and nausea. One week before admission he was noted to be oliguric, hypertensive (200/115 mmHg) and was subsequently admitted with symptoms and signs of fluid overload due to oliguria. Investigations at this time showed: haemoglobin 11.7 g/dl; white cell count $11.0 \times 10^9/l$;

eosinophils $224 \times 10^6/l$; ESR 30 mm/hr; urea 30.5 mmol/l; creatinine 1651 $\mu\text{mol/l}$; potassium 6.43 mmol/l; serum amylase 88 Somogyi units; urine contained no casts; no red cells but 10 neutrophils, no eosinophils and no growth. Antistreptolysin O titre 50 i.u./ml; IgG 16.5 g/l; IgA 3.8 g/l; IgM 1.1 g/l; antinuclear factor negative; C_3 122 mg/dl, C_4 54 mg/dl; hepatitis B surface antigen negative; chest radiograph, cardiomegaly plus congestion; intravenous urogram with tomograms, no obstruction, poor nephrogram. A renal biopsy showed tubulo-interstitial nephritis with no eosinophil infiltration. Diflunisal had been stopped 2 days before admission to this renal unit. Within 24 hr of starting peritoneal dialysis a diuretic phase had resulted in a 4-litre urine output in 24 hr. Dialysis was therefore discontinued and intravenous saline was needed to keep pace with urine losses. Recovery was uneventful and the patient was discharged with a serum creatinine 290 $\mu\text{mol/l}$; clearance 44 ml/min. Three months following acute renal failure a further renal biopsy was performed which showed tubular necrosis and interstitial fibrosis with a striking lack of interstitial cellular infiltration similar to the previous biopsy. At this time the patient was hypertensive with a creatinine of 350 $\mu\text{mol/l}$ and clearance of 35 ml/min.

Comment

Clinically and histologically there has been an incomplete recovery from tubulo-interstitial nephritis due to diflunisal. There was nothing to suggest a hypersensitivity reaction (Chan *et al.*, 1980) and therefore corticosteroids were not used. Diflunisal has similar anti-inflammatory analgesic properties to acetylsalicylic acid and there is a cross-over in allergic sensitivity reactions between aspirin and diflunisal (Tempero, Cirillo and Steelman, 1977). Aspirin, indomethacin, fenoprofen (Wendland *et al.*, 1980) and diflunisal (Steelman *et al.*, 1976) all

decrease renal synthesis and excretion of prostaglandin E_1 . It has therefore been postulated that renal vasoconstriction from inhibition of PGE_1 synthesis might reduce renal blood flow and result in tubular necrosis (Johnson, 1980). This may explain the rapid recovery from acute oliguric renal failure but does not account for interstitial fibrosis seen in this case.

References

- CHAN, L.K., WINEARLS, C.G., OLIVER, D.O. & DUNNILL, M.S. (1980) Acute interstitial nephritis and erythroderma associated with diflunisal. *British Medical Journal*, **280**, 84.
- JOHNSON, W.J. (1980) Nephrotoxicity of non-steroidal anti-inflammatory drugs. *Proceedings. Mayo Clinic*, **55**, 120.
- STEELMAN, S.L., SMIT-SIBINGA, C.T.H., SCHULZ, P., VANDEN HEUVEL, W.J.A. & TEMPERO, K.F. (1976) The effect of diflunisal on urinary prostaglandin excretion, bleeding time and platelet aggregation in normal human subjects. (Abst.) *XIIIth International Congress of Internal Medicine*, Forssa, Finland.
- TEMPERO, K.F., CIRILLO, V.J. & STEELMAN, S.L. (1977) Diflunisal: a review of pharmacokinetic and pharmacodynamic properties, drug interaction and special tolerability studies in humans. *British Journal of Clinical Pharmacology*, **4**, 31.
- WENDLAND, M.L., WAGONER, R.D. & HOLLEY, L.F. (1980) Renal failure associated with fenopron. *Proceedings. Mayo Clinic*, **55**, 103.