Clinical Problems

Analgesic Abuse, Ureteric Obstruction, and Retroperitoneal Fibrosis

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Summary

We report two cases of unusual ureteric obstruction in patients with an excessive consumption of analgesics. In a retrospective survey of seven cases of non-malignant retroperitoneal fibrosis seen in the last 15 years it was found that four had taken excessive amounts of analgesics. A careful drug history should be taken in all patients with retroperitoneal fibrosis and ureteric obstruction.

Introduction

Since the first description of idiopathic (non-malignant) retroperitoneal fibrosis by Ormond¹ cases have been recognized with increasing frequency,²⁻⁴ but we still know very little about its aetiology. Only in one relatively small group of cases has it been possible to identify its aetiological agent as methysergide, an ergot derivative administered for migraine. In no case seen at the London Hospital was there methysergide consumption, but it may be of more consequence that all patients in whom retroperitoneal fibrosis was ultimately diagnosed had suffered prolonged periods with pain in the back and over a half had taken analgesics in the hope of getting relief. The report of three cases of ureteric obstruction caused by a condition resembling retroperitoneal fibrosis in patients known to have taken large quantities of analgesics⁵ is therefore of particular interest. We report here two similar cases which prompted us to look again at the case histories of our patients with idiopathic retroperitoneal fibrosis to see if over-consumption of analgesics could have played a part in the aetiology of the disease.

Case 1

This patient was a 37-year-old housewife who was well until her third pregnancy, after which she developed severe puerperal depression and started consuming large amounts of analgesic tablets. She admitted taking more than 200 codeine compound tablets a week for three and a half years (total consumption: phenacetin 10 kg; aspirin 10 kg; codeine phosphate 300 g). She also took other drugs for depression and other analgesic tablets.

After two years she attended another hospital feeling "run down" and complaining of pain in the sacroiliac and lumbar regions. An excretion urogram showed diminished concentration of contrast medium on both sides, with dilatation of ureters and pelves. These changes subsequently became more severe and she became uraemic and anaemic.

On admission her blood urea was 25.9 mmol/l (156 mg/100 ml), haemoglobin 8.5 g/dl, sedimentation rate 60 mm in the first hour, and creatinine clearance 32 ml/min. Culture of her urine grew *Escherichia coli*.

Cystoscopy showed no abnormality, and there was no reflux in a micturating cystogram. Ureterography showed obstruction to each ureter over a 3-cm distance in the region of the brim of the pelvis (fig. 1).

FIG. 1—Case 1. Ureterogram showing each ureter obstructed over 3 cm in region of brim of pelvis.

Through a paramedian incision both ureters were explored. On each side they were blocked by a fusiform swelling surrounded by fibrous tissue (fig. 2). The appearance was unlike that found in previous cases of retroperitoneal fibrosis: there was no retroperitoneal plaque of fibrous tissue from which the ureters could be shelled out. The ureters themselves seemed to be converted into thickened swellings but were not drawn medially. On the left side a minute calculus (calcium oxalate) was found just proximal to the obstructing swelling. Having freed both ureters from their surroundings it proved impos-

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ible to cut away the overlying fibrous tissue on the ureter; indeed each lumen was completely obstructed. The affected zone of each ureter was removed and twin Boari flaps were constructed into which each ureter was anastomosed (fig. 3), and both flaps were then wrapped in omentum.⁶

FIG. 2—Case 1. Operation findings. Both ureters were ensheathed in fusiform lumps of oedematous fibro-fatty tissue.

FIG. 3—Diagram of bilateral Boari reconstruction of lower end of each ureter, which was performed using 12Ch Gibbon catheters as splints. Finished Boari anastomoses were then wrapped in omentum.

FIG. 4—Case 1. Transverse section of ureter showing oedema of lamina propria causing marked narrowing of the lumen and extension of fibrosis into surrounding connective tissue. (Haematoxylin and eosin. $\times 15$.)

The segments of the left and right ureters measured 2.2 cm and 3.2 cm respectively. Each had a very narrow lumen and was surrounded by firm white tissue. Microscopy of both showed oedema of the lamina propria, partial loss of lining epithelium, and oedematous fibrous

tissue extending through the muscle coat and surrounding the ureter (fig. 4). There was a moderate infiltration of acute and chronic inflammatory cells.

The catheter in the right ureter became obstructed after 48 hours, and a ring nephrostomy was inserted.⁷ A biopsy of the kidney was performed. The specimen contained cortex only and showed bands of interstitial fibrosis with a chronic inflammatory cell infiltration and marked tubular atrophy with pus present in many lumens. Some glomeruli were normal; others were shrunken with periglomerular fibrosis. Adjacent zones of parenchyma showed dilated proximal tubules and normal glomeruli. Though not diagnostic these features were consistent with the type of interstitial nephritis which is associated with analgesic damage and an ascending infection.

Case 2

This patient was a 69-year-old housewife who had started taking analgesic tablets when she was about 50 and admitted having taken at least eight Codis tablets daily since then—a total consumption of more than 30 kg of aspirin, 15 kg of phenacetin, and 300 g of codeine phosphate.

Five years later she had a right nephrectomy for calculus and chronic pyelonephritis at another hospital, after which she had recurrent urinary tract infections and subsequently developed hypertension and diabetes.

A month before admission, now aged 69 years, she began to have severe abdominal pain with tenderness in the left loin. She rapidly became oliguric and eventually anuric. On admission she was uraemic, in severe congestive cardiac failure, and was found to have a lump in the right breast. After dialysis her left kidney was explored and a nephrostomy performed for pyonephrosis, but she deteriorated and died.

Necropsy showed a carcinoma of the right breast with widespread metastases but none in the retroperitoneal space. The left kidney was contracted (169 g), had an irregular surface, and contained several abscesses. By then it was impossible to detect evidence of analgesic damage because of the effects of extensive infection and obstruction, but there was a localized stricture of the left ureter about 10 cm from the renal pelvis. Sections from this zone showed a similar histological appearance to those from the patient in case 1 (fig. 5) and confirmed the absence of carcinoma.

FIG. 5—Case 2. Transverse section of ureter showing oedema of lamina propria and fibrosis extending into surrounding connective tissue. (Haematoxylin and eosin. $\times 40$.)

Review of Cases of Retroperitoneal Fibrosis

The records of seven cases of "idiopathic" retroperitoneal fibrosis seen at the London Hospital in the last 15 years were studied and the patients interviewed. Granted that any retrospective study based upon a patient's recollections is apt to be difficult and inaccurate it was striking to discover that four of these seven patients admitted to overconsumption of analgesics.

The four patients were men with an average age of 50 years and all had a history of long-standing back pain. One patient had taken 600 tablets of codeine compound as well as 600 of paracetamol in the two months before he was admitted to hospital and had consumed analgesics in a lower dosage over the previous eight years.

Another admitted taking large doses of salicylate, phenacetin, and paracetamol for at least nine months. A third had been in the habit of taking codeine compound tablets for many years, and though he denied taking these in "large" doses, he had been admitted at one time with constipation induced by codeine. The fourth patient had been taking Codis and paracetamol for radiologically proved degenerative lumbar spine disease.

Discussion

Study of the necropsy records of the London Hospital raised the suspicion that a new disease appeared in the East End of London early in the 1950s. Before that time retroperitoneal fibrosis, or anything resembling it, is entirely absent from the necropsy records, which have been kept since 1907. It is true that once a new disease has been described it becomes more easy to recognize it, and cases might have gone undetected before Ormond's first case report in 1948.¹ Nevertheless, it may not be entirely coincidental that the first reports of analgesic nephropathy and retroperitoneal fibrosis appeared at about the same time.¹⁻⁸ Our review of the histories of patients known to have had retroperitoneal fibrosis supports such an association.

The impression has grown that non-malignant retroperitoneal fibrosis may not be a single disease entity but rather the end result of various pathological processes which may affect different parts of the ureter or retroperitoneal connective tissue. Most reports refer to a hard white plaque of fibrous tissue encasing the aorta and vena cava and their larger branches and drawing the ureters together towards the midline. This perivascular distribution of the fibrous tissue made Mitchison⁹ in his study of 40 cases suggest that damage to the aortic wall might be the essential aetiological factor both in cases without other obvious cause and in those related to methysergide consumption.

When other factors are found to be associated the distribution of the fibrous tissue seems to be different. Thus in the cases related to urinary tract infection described by Vest and Barellare¹⁰ and Behrens and Holland¹¹ the retroperitoneal fibrosis did not follow the usual pattern. It was principally periureteric

and Behrens and Holland gave it the name "periureteritis plastica" to distinguish it from the classical retroperitoneal plaque.

Phills *et al.*¹² described three siblings with the sickle-cell trait who developed retroperitoneal fibrosis and renal papillary necrosis. In one of these the fibrosis was a "periureteral hose-like sheath"—a description which would have fitted both our cases and those described by MacGregor *et al.*⁵ exactly. Since the sickle-cell trait and analgesic abuse may each be associated with lesions of the renal papilla and the ureter there may be similar pathogenetic factors involved, though the exact mechanisms remain unknown.

Discussions still continue over the relative importance of the various drugs which might be incriminated in analgesic nephropathy (*British Medical Journal*, 1974). All our patients had consumed phenacetin (in case 2 the patient consumed Codis at a time when phenacetin was a constituent), as had those described by MacGregor *et al.*⁵ Possibly, however, the damage is due to the combined effects of several drugs.

We suggest that one form of retroperitoneal fibrosis may result from the action of various analgesic drugs. Two recommendations follow: firstly, a very careful drug history should be taken from every patient who may have retroperitoneal fibrosis or any other unusual obstruction to the ureter. Secondly, attention should be paid to the histological changes in the kidneys of patients with retroperitoneal fibrosis, since the renal damage may in part be due to a coexisting and unsuspected analgesic nephropathy as well as obstruction.

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Medical Education

The Medical Student as Behavioural Psychotherapist

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Summary

A group of medical students were randomly selected from a larger group to carry out behaviour therapy under

supervision. Ten patients with phobic disorders and two with obsessive-compulsive neurosis were treated, and the results, assessed by ratings of proved reliability, compared favourably with other studies in which psychiatrists or nurses acted as therapists. A questionnaire survey showed that students involved in therapy had a more favourable opinion about this kind of treatment than those receiving only theoretical instruction. The results suggested not only that medical students make good behavioural psychotherapists but also that the subject is a worthwhile training experience which warrants inclusion in the curriculum.

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