

Retroperitoneal fibrosis¹

Although Ormond is usually credited with the first description of retroperitoneal fibrosis (RPF) (Ormond 1948), in fact Albarran (1905) recognized it many years before and gave details of two cases. Kolischer (1922) may also have been describing the same condition when he pointed out that the upper ureter can become tethered in nonspecific perinephritis. Perard & Orsini (1935) reported a case of a woman with obstructive anuria occurring two months after an allergic illness, which was probably RPF. If so, it supports the hypothesis that it may arise from an immunological disorder.

Ormond (1948) described two cases. In the first, the process was not understood, no operation was done and the patient died. In the second, ureterolysis was performed and the ureter placed in the peritoneum to good effect. He could find no similar case in the literature.

Raper (1955), at a meeting at the Royal Society of Medicine, first drew our attention to RPF in this country, and showed how successful surgery could be (Raper 1956). He subsequently followed one case for over eleven years (Raper 1960).

We probably know little more about the condition now than we did twenty years ago. The early symptoms are so nonspecific that the correct diagnosis is often delayed until renal failure occurs. Patients commonly complain of backache, severe enough to need referral to a rheumatologist or orthopaedic surgeon, while others have abdominal pain suggesting dyspepsia, cholecystitis, diverticulitis and so on. Exploratory laparotomy may be unhelpful unless the condition is in the surgeon's mind. Sometimes it is missed altogether, and at others it is assumed to be malignant infiltration of the retroperitoneal tissues.

About three-quarters of patients present with some manifestation of renal failure and about one-third as emergencies with anuria or gross oliguria. Haematuria or renal colic are exceptional.

Hypertension occurs in about half of the cases and is reversible in about half of these, depending on the history and the success of ureterolysis. Some manifestation of this, such as heart failure, catastrophic nose bleed or hypertensive encephalopathy, may be the first evidence of disease. The mechanism of hypertension is obscure. Experimentally, ureteric obstruction can cause an increase in renal vein renin, possibly from abnormal sodium loss following transitory tubular damage. The same mechanism may operate in man. Volume-dependent hypertension, if both ureters are obstructed, can undoubtedly occur without change in renal vein renin.

Obstruction of the inferior vena cava or iliac veins is not usual on presentation, although varicose veins are common. More important, however, is the risk of thromboembolism, either before the diagnosis is made, after ureterolysis, or later. It occurs in about one-quarter of the patients. With this incidence, preoperative subcutaneous heparin has a place, with long-term anticoagulant therapy in selected cases.

Urgent drainage by ureteric catheterization or percutaneous nephrostomy may be life-saving in the initial management. Rarely dialysis is necessary. The percutaneous technique needs expertise which is not always available, but has the added advantage of allowing antegrade urography and pressure flow studies.

Once the idea of RPF is entertained, the provisional diagnosis is made on pyelography. High-dose nephrotomography is most valuable, showing hydronephrosis and a dilated, kinked upper ureter. In severely obstructed kidneys a negative pyelogram is sure evidence of obstruction as the cause of acute renal failure. In patients with anuria, this is frequently the most useful investigation as it leads on to early surgical relief of the obstruction.

When tomography is inadequate, an ascending urogram shows medial deviation of the ureter at the site of the stricture and marked kinking of the proximal ureter above it. The plaque is usually at the level of the fourth lumbar vertebra but may spread down to the pelvis or up to the renal hilum. It occasionally involves other tissues such as the porta hepatis or mediastinum. Both ureters may not be affected simultaneously or at the same level. Medial displacement of normal ureters is not uncommon and in itself is an unimportant finding (Saxton *et al.* 1969).

The ESR in 80–90% of patients is raised, often to high levels, but the cause is not understood. In most cases it falls after ureterolysis, even though the plaque is not removed. There is little evidence that the high ESR is caused by pyelonephritis or by an immunological disorder. Autoantibodies have not been found, except occasionally to smooth muscle, and this may reflect secondary involvement of smooth muscle in the plaque.

Histological examination is not as helpful as one would expect. The plaques consist mainly of fibrous tissue with a varying amount of cellular infiltration with lymphocytes and plasma cells, while some areas show almost pure collagen. Fat cells, nerve cells and smooth muscle are seen and are presumably trapped by the proliferative nature of the fibrous tissue.

An identical histological picture can be found in malignant retroperitoneal fibrosis. Webb & Dawson-Edwards (1967), among other authors, described two cases secondary to a carcinoma of the breast and the stomach. More commonly,

¹ Based on Mr C H Kinder's Presidential Address to Section of Urology, 26 October 1978

however, malignant RPF is secondary to a lymphoma or lymphosarcoma. Malignant RPF may be microscopically and macroscopically indistinguishable from idiopathic RPF, and ureterolysis is both possible and therapeutic. Only the subsequent course of the disease makes the true diagnosis clear. For this reason, the final diagnosis may only be made in retrospect.

Ormond (1974) stressed that fibrosis confined to the pelvis was usually malignant. If neurological changes occur, this too makes malignant RPF almost certain.

It is not often appreciated that an abdominal aneurysm may present with uraemia, secondary to ureteric involvement with a perivascular fibrosis. Surprisingly, medial deviation of the ureters is more likely to occur than lateral displacement (Allibone & Saxton 1979). Ureteric obstruction from surgical trauma, radiotherapy or metastatic lymphadenopathy is less confusing.

There is some difference of opinion in the use of steroids in the treatment of RPF. First described by Ross & Tinckler (1958), steroids have been used with great success by some (Mitchinson *et al.* 1971). The latter authors described three cases in two of whom withdrawal of steroids caused relapse on several occasions. Morandi & Grob (1971) and Hawk & Hazard (1959) had similar experiences. Some would treat the condition empirically with steroids alone, while others perform ureterolysis on one side and, after obtaining a biopsy, treat the other with steroids.

Where acute renal failure is present, it would seem logical to perform early ureterolysis and reserve steroids for the spread of the disease to other structures, such as the inferior vena cava, porta hepatics or mediastinum.

Ureterolysis is best performed through a midline incision, mobilizing the ascending and descending colon. In this way the full extent of the plaque is apparent and both ureters can be freed at the same time. This exposure is easier than through the loin.

If the ureter is mobilized above and below the plaque, a longitudinal incision can be made in the line of the ureter on the anterior aspect of the plaque. Gentle blunt dissection will then free the ureter. Further layers of fibrous tissue can be stripped from the ureter, but if this is too extensive devascularization can lead to urinary leakage. Once freed, the ureter is best placed laterally and kept there by stitching the peritoneum to the psoas. In the pelvis this is not possible and the ureters should be placed within the peritoneum. If the viability of the ureter is in doubt, an omental wrap has much to offer.

If the ureter is torn it is best repaired over a splint and the kidney drained, but a stricture is common. Ileal replacement of the ureter is always possible. In about a quarter of the cases, one

kidney is so badly damaged that ureterolysis has nothing to offer. A preoperative radioisotope renal scan can be very helpful in coming to this decision (DMSA).

Rarely, pyonephrosis is the presenting pathology and only nephrectomy is practical. Late nephrectomy for uncontrolled hypertension may occasionally give dramatic results where the kidney has been badly damaged. Recurrence after ureterolysis is probably the result of inadequate mobilization and should not occur.

In studying the natural history of idiopathic RPF, it is apparent that if the kidney has not been severely damaged, and if ureterolysis is adequate, the patient is usually cured. Rarely does the disease spread to other structures causing such problems as portal hypertension. More often death is due to gross renal damage. We have followed six patients for more than 10 years and four for 16, 18, 19 and 21 years; the first three are still alive. Fourteen patients have been followed for more than 5 years.

The aetiology is still unknown, although there is no doubt that drugs can be incriminated: methysergide is the most common but dihydroergotamine, ergotamine, hydrallazine and methyl dopa can also be causative agents. Analgesic abuse may also be responsible.

It is commonly believed that this is an immunological response to some agent, but so far there is little evidence that this is so. Recently, Palmer *et al.* (1978) described a case associated with other fibrotic manifestations where there was a deficiency of alpha-1-trypsin. Three of our cases have been examined for this with negative results.

Retroperitoneal fibrosis is an intriguing condition and we still have much to learn about it.

C H Kinder

*Surgeon, Department of Urology
Guy's Hospital, London SE1 9RT*

References

- Albarran J
(1905) *Association Française d'Urologie* 9, 511
- Allibone G W & Saxton H M
(1979) (in press)
- Hawk W A & Hazard J B
(1959) *American Journal of Clinical Pathology* 32, 321
- Kolischer G
(1922) *Journal of Urology* 8, 149
- Mitchinson M J, Withycombe J F R & Arden Jones R
(1971) *British Journal of Urology* 43, 444
- Morandi L P & Grob P J
(1971) *Archives of Internal Medicine* 128, 295
- Ormond J K
(1948) *Journal of Urology* 59, 1072
- (1974) *Transactions of the American Association of Genito-Urinary Surgeons* 62, 12
- Palmer P E, Wolfe H J & Kostas C I
(1978) *Lancet* i, 221
- Perard J & Orsini
(1935) *Congres Français d'Urologie* 37, 629
- Raper F P
(1955) *Proceedings of the Royal Society of Medicine* 48, 736
- (1956) *British Journal of Urology* 28, 436
- (1960) *Proceedings of the Royal Society of Medicine* 53, 690

Ross J C & Tinckler L F

(1958) *British Journal of Surgery* 46, 58

Saxton H M, Kilpatrick F R, Kinder C H, Lessof M H,

McHardy Young S & Wardle D F H

(1969) *Quarterly Journal of Medicine* 38, 159

Webb A J & Dawson-Edwards P

(1967) *British Journal of Surgery* 54, 508

Multiple sclerosis: treatment and prophylaxis¹

The finding by Millar *et al.* (1973) that linoleic acid (LA) (in the form of sunflower seed oil) appeared, in a double-blind two-year trial, to exert some moderate influence in reducing the number, severity and duration of acute episodes of multiple sclerosis (MS) in young ambulant patients with recurring bouts of illness, was interpreted initially (Field & Shenton 1975) to depend upon a nontoxic immunosuppressive activity of LA. However, this view has now been shown to be untenable, since after 6 months the immunosuppressive effect of LA (as demonstrated by Mertin in acute tail graft experiments and experimental allergic encephalomyelitis in guinea pigs) passes off (Meyer-Rienecker *et al.* 1976, Field & Joyce 1978), not only in MS but also in kidney transplantation (McHugh *et al.* 1977).

It is now recognized that the effect of LA and γ -linolenate is to restore the anomalous inherited constitution of cell surfaces in MS to normal (Field & Joyce 1978). MS is 5–20 times more common in near relatives of an MS propositus than in the general population, though our own figures suggest that 40 times is nearer the mark. Children born with 'Thompson's anomaly' (i.e. reduced electrophoretic mobility of the red blood cell with both LA and arachidonic acid (AA) (Field *et al.* 1977), if it extends to the oligodendrocyte surface, will lay down abnormal myelin, and there is indeed evidence that the whole brain is affected in MS in regions apart from gross plaques. Such abnormal myelin, once laid down, may be liable to spontaneous (perivenous) breakdown (abiotrophy) or to disintegration from nearby antigen-antibody reaction (Wisniewski & Bloom 1975) or other similar disturbance.

Myelination takes place very actively from mid-fetal life until 5 years of age, and thereafter with diminishing intensity to the age of 16 but (from animal experiments) appears to continue throughout life. Clearly, if the oligodendrocyte surface could be transformed as early as possible after birth, then non-MS susceptible myelin might be laid down. It would seem that the defective myelin

of MS is poorly 'zipped up' in that slippage along the intraperiod line (the original oligodendrocyte surface) is an early change in degeneration in MS. Serious consideration should be given to scanning all children born into MS families, and therefore at small but special risk to develop the disease, with a view to picking out 'candidates' who might then be treated prophylactically with γ -linolenate. This is likely to be the major field of effectiveness of this material. The position is in some ways analogous to phenylketonuria, which if recognized at birth is amenable to prevention, but if missed and established is highly refractory to treatment. There is no evidence that polyunsaturated fatty acids (PUFAs) are themselves oncogenic, though when given to animals already inoculated with appropriate tumours they have been shown to increase the 'take percentage' – something quite different from the suggestion that PUFAs themselves produce tumours. Indeed, workers in this field have themselves been at pains to point this out (Hopkins *et al.* 1976). Exhibition of γ -linolenate to seemingly normal children may be criticized on psychological grounds but certainly not, on present evidence, on the grounds of oncogenicity.

The geographic distribution of MS with its preponderance in 40°–60° north and south latitudes is a long-established 'fact' in MS, though its simplicity may be deceptive (Kurtzke 1977). Many correlates with the distribution of MS have been established, some difficult to accord biological significance. However, amongst the putative geographical predisposing factors (GPF) has been the consumption of milk (Agranoff & Goldberg 1974) and this immediately links with the LA and AA considerations outlined above. Twomey (1974) dismisses a correlation with milk consumption on the grounds that 'MS is extraordinarily rare among Africans living on their own continent, though milk is an important food in many parts of Africa'. Dean (1977), like Twomey (1974), fails to appreciate the critical importance of adequate linoleic acid intake by the child at the critical time when myelination is most intense, i.e. up to about 5 years of age and thereafter more slowly to 16 years of age and even beyond (Yakovlev & Lecours 1967). It is immaterial that the 'Afrikanders of South Africa . . . eat . . . a diet . . . which has a quite unusually high level of saturated fat – mutton 3 times a day . . . and yet they don't get or very seldom get multiple sclerosis' (Dean 1977). Breast milk is especially rich in fatty acids of long C chains (which are 'essential'). Thus Bentivoglio (1961) shows that linoleic acid (which he considers 'really indispensable') makes up 8.3% (6.8–10.4%) of human milk fat against 1.6% (0.5–2.8%) cow's milk fat. Linoleic acid is also richer in human milk. In a fuller discussion of the essential fatty acid (EFA) content of human milk, Insul & Ahrens (1959) conclude that it is approximately

¹ Based on paper read to Section of Neurology, 2 March 1978.