IDIOPATHIC RETROPERITONEAL FIBROSIS ASSOCIATED WITH AN ARTERITIS

BY

E. A. JONES AND M. K. ALEXANDER

Warwick Hospital, Warwick

The first report in the world literature of the condition which is now generally known as idiopathic retroperitoneal fibrosis was that of Albarran (1905), but the first report in the English language did not appear until that of Ormond (1948). Since then many further case reports have been published, but the aetiology of the condition remains obscure.

The disease usually presents as a urological problem when the mass of retroperitoneal fibrous tissue causes deviation or obstruction of one or both ureters often resulting in hydronephrosis. It has become apparent, however, that the manifestations of the disease may not be limited to the pressure effects of the retroperitoneal lesion on neighbouring structures and that the disease may present as a systemic disturbance.

Case Report

A 64-year-old man awoke on January 1, 1965, with severe low back pain which persisted and was made worse by movement. For 3 days the pain was so severe that he was almost completely immobilized. There were occasional sharp shooting pains down the back of both legs and his back tended to "lock" after sitting. Following the onset of the pain he complained of general malaise, anorexia, and night sweats. There were no urinary symptoms. He was admitted to hospital on January 16.

During the previous 20 years he had had several attacks of low back pain, each of which had been much less severe than this attack.

Examination.—He was a stocky man. The body temperature was 99·5°F. There was no thyroid or lymph gland enlargement and no skin rash. No abnormal signs were found in the cardiovascular, respiratory, locomotor, and central nervous systems. The blood pressure was 110/70. The optic fundi appeared normal. There was an appendicectomy scar and the liver edge was just palpable at the right costal margin. No other abdominal viscera or masses were palpable and rectal examination was normal. The left testis was undescended.

Investigations.—Hb 14·1 g./100 ml.; W.B.C. 11,100/ c.mm.; polymorphs 80 per cent.; lymphocytes 16 per cent.; monocytes 4 per cent.; erythrocyte sedimentation rate 102 to 122 mm./hr (Westergren); serum urea 28 mg./100 ml.; serum sodium, potassium, and chloride within normal limits. Serum albumin 3·35 g./100 ml.; serum globulin 3·35 g./100 ml. Electrophoresis of the plasma proteins showed a slight increase in the alpha_2 globulin. Antinuclear factor not detected. No L.E.-cells seen in the peripheral blood (5 specimens). Rose-Waaler test negative; latex slide test positive; gastric parietal cell antibodies not detected;* thyroglobulin tanned cell agglutination titre 1 : 20;* colloid thyroid antibodies (immunofluorescent) negative;* cytoplasmic thyroid antibodies (immunofluorescent) positive;* cytoplasmic thyroid antibodies complement-fixation titre negative.* Bone marrow normal.

A mid-stream specimen of urine contained no albumen or sugar and was normal on microscopy and sterile culture.

Chest x ray showed a normal cardiac shadow and slightly increased markings at the right lung base.

Intravenous pyelogram showed partial obstruction and some hydronephrosis of the left kidney; the right kidney appeared normal. These findings were confirmed by retrograde pyelography.

Course.—The patient ran a continuous fever of 99·5 to 102°F. By February 10 the haemoglobin had fallen to 10·4 g./100 ml.

A laparotomy was performed on February 22, when the presence of a dilated left renal pelvis and retroperitoneal fibrosis was confirmed and a biopsy of the lesion taken. Post-operatively the patient was apyrexial.

On the third post-operative day he developed atrial fibrillation with a ventricular rate of 120 per min., which was confirmed electrocardiographically. He was given digitalis. The following day he developed severe pain in the left precordium which radiated down the left arm. The pain lasted for 4 hours and was associated with a soft apical systolic murmur and a few rales at both lung bases. A further electrocardiogram showed that the rhythm had reverted to sinus, but there were supraventricular and ventricular ectopic beats and ST depression most marked in lead V4. The following morning the serum SGOT was 79 units.

Termination.—Later that morning (February 27) the patient collapsed suddenly. The peripheral pulses were not palpable and the electrocardiogram showed ventricular fibrillation. Resuscitative measures which included direct current defibrillation resulted in only temporary restoration of a regular cardiac rhythm which was complicated by right bundle branch block. He died in 3 hours after the collapse.

*Estimated by Dr. D. Doniach, Middlesex Hospital Medical School, London.
Post mortem Examination.—The body was that of a rather poorly-nourished middle-aged man with a healing laparotomy scar. Apart from the signs of congestive cardiac failure, visible abnormalities were confined to the retroperitoneal tissues, urinary tract, and cardiovascular system.

There was an ill-defined area of fibrous thickening in the retroperitoneal tissues overlying the lower part of the abdominal aorta below the origin of the renal arteries and extending to the left to encircle the ureter. There was no fibrosis above the level of the renal arteries or below the rim of the pelvis or in the region of the right ureter. The inferior mesenteric and median sacral arteries which ran through the fibrous mass were occluded by greyish-brown thrombus.

There was a minor degree of hydronephrosis of the left kidney.

The heart was of normal size. The main coronary arteries appeared widely patent and showed only a mild degree of atheroma. There was a small area of fibrosis in the epicardial tissues adjacent to and partly surrounding the origin of the circumflex branch of the left coronary artery but there was no stenosis of that artery. Fresh thrombus was found in a branch of the anterior descending artery.

Histology

RETROPERITONEAL TISSUE.—This consisted of fibrous tissue variably infiltrated by plasma cells, lymphocytes, and eosinophils, which had largely replaced the normal fat. The tissue contained numerous lymphoid foci without germinal centres. Two branches of the inferior mesenteric artery showed inflammation of the walls without evidence of tissue destruction and one branch was thrombosed.

CORONARY ARTERY (a branch of the anterior descending artery—Figure).—There was a panarteritis with a mixed cellular infiltrate, including lymphocytes, eosinophils, macrophages, and plasma cells. This extended into the surrounding fatty connective tissue. The infiltrate was not accompanied by any evidence of destruction of the arterial wall, but the intima was thickened by cellular fibrous tissue and fresh ante mortem thrombus completely occluding the lumen.

HEART (left ventricle).—There were multiple, mainly subendocardial, foci of swelling, refractility, and granularity of muscle fibres, together with loss of striations of muscle fibres. There were several minute perivascular foci of mixed chronic inflammatory cells.

KIDNEY.—The lumina of several large branches of the renal artery were concentrically narrowed by cellular fibrous tissue. There was a mild chronic inflammatory infiltrate in the walls of these vessels without evidence of tissue destruction but with much adventitial fibrosis. The renal parenchyma showed no abnormality.
LIVER.—There was moderate fatty infiltration. The smaller portal tracts appeared normal, but two arteries in a large tract showed endarteritis obliterans with some adventitial infiltration by lymphocytes, plasma cells, and eosinophils.

SUPERIOR MESENTERIC ARTERY.—There was a little patchy cellular infiltration of the adventitia, together with some fibrosis and intimal thickening.

THYROID.—The greater part of the parenchyma appeared normal, but there were several small foci of glandular atrophy with fibrosis and patchy lymphoid infiltration.

PITUITARY.—There were several small collections of lymphocytes and plasma cells in the capsule of the pars posterior.

The voluntary muscle, spleen, and bone marrow were normal.

Discussion

The features in this case, which are suggestive of a connective tissue disorder, are the constitutional disturbance, fever, the development of a mild anaemia, an elevated erythrocyte sedimentation rate, and a positive latex slide test. Constitutional disturbance, fever, mild anaemia, and elevation of the erythrocyte sedimentation rate have been reported in other cases of idiopathic retroperitoneal fibrosis (Hawk and Hazard, 1959; Dineen, Asch, and Pearce, 1960; Margoles and McQueeney, 1960; Hoffman and Trippel, 1961; Haché, Utz, and Woolner, 1962; Ormond, 1962; Kay, 1963; Que and Mandema, 1964; Reidbord and Hawk, 1965). Other features suggestive of a connective tissue disorder which have been described in association with idiopathic retroperitoneal fibrosis are pleural effusion (Hawk and Hazard, 1959; Kay, 1963), pericarditis (Kay, 1963; Reidbord and Hawk, 1965), changing radiological markings in the lungs (Hoffman and Trippel, 1961), arthropathy (Kay, 1963), pulmonary fibrosis, Raynaud's syndrome (Que and Mandema, 1964), muscle tenderness (Reidbord and Hawk, 1965), and purpura (Haché, Utz, and Woolner, 1962; Reidbord and Hawk, 1965). Plasma protein changes with reversal of the albumin/globulin ratio (de Gennes, Bricaire, Tourneur, and Cournot, 1960; Kay, 1963; Que and Mandema, 1964) and positive serological tests (i.e. the demonstration of antinuclear factors and a positive Schultz-Dale reaction and a positive Coombs consumption test) have also been reported in this condition (Que and Mandema, 1964).

The findings in this case support the suggestion of Hoffman and Trippel (1961) that idiopathic retroperitoneal fibrosis may be associated with a generalized vasculitis. It would seem that the vasculitis may affect primarily either the small muscular arteries, as in the cases of Hoffman and Trippel (1961) and Reidbord and Hawk (1965), or larger arteries as in the present case. In the former instances there are features in common with polyarteritis nodosa. Indeed one case of polyarteritis nodosa in association with idiopathic retroperitoneal fibrosis has been observed (quoted by Ormond, 1962), and one of the cases of Hoffman and Trippel (1961) had renal vasculitis and perivascularitis with an eosinophilic infiltrate which were considered highly suggestive of polyarteritis nodosa. Reidbord and Hawk (1965) have also described renal involvement, the histology of the kidneys in their case showing a proliferative glomerulonephritis. In the present case the inflammatory cell infiltrate was limited to larger arteries and there was fibrosis around the origin of the circumflex branch of the left coronary artery. These features are more like the lesions described in Takayasu's disease, which is characterized by an arteritis of the aorta and its major branches and stenosis or occlusion of its major branches by fibrous tissue (Schrire and Asherson, 1964). However, fragmentation and necrosis of elastic tissue of large arteries, which appear to be features of Takayasu's disease (Schrire and Asherson, 1964), do not seem to have been described in association with idiopathic retroperitoneal fibrosis and were not features of the present case. Involvement of the coronary arteries occurs in Takayasu's disease, but is rare. Cases presenting as angina pectoris and myocardial infarction have been described (Schrire and Asherson, 1964). Coronary arteritis has also been described in several conditions which are classified as disorders of connective tissue, e.g. polyarteritis nodosa (Rose and Spencer, 1957), Wegener's granulomatosis (Allen and Moen, 1965), giant cell arteritis (Pauluy and Hughes, 1960), and rheumatic fever (Zeek, 1952). The fibrosis around the origin of the coronary artery in the present case is similar to the lesions described in a case of idiopathic retroperitoneal fibrosis by Reed and Stinely (1959), in which there was extensive perivascular fibrosis of the coronary arteries. It is possible that such fibrosis may have been the end result of a coronary arteritis.

The histological picture of the retroperitoneal tissue in idiopathic retroperitoneal fibrosis may be regarded as being at one end of the spectrum of tissue changes which can occur in connective tissue disorders, i.e. mucoid degeneration, fibrinoid necrosis, and collagenous hyalinization (Robbins, 1957). The presence of a lymphocyte and plasma cell infiltrate in the lesion and the association of positive serological tests are consistent with a disturbance of immune mechanisms. The lesion...
has been discussed in the light of experimental work on hypersensitivity phenomena by Hoffman and Trippel (1961).

There appears to be a relationship between idiopathic retroperitoneal fibrosis and the thyroid gland. This is suggested by finding focal thyroiditis and two different thyroid antibodies in low titre in the present case. Thyroid antibodies have been found in the serum of several cases of idiopathic retroperitoneal fibrosis, mostly in men (Doniach, 1965). It is interesting to note that there is a considerable overlap of positive serological tests between Hashimoto’s disease, systemic lupus erythematosus, and rheumatoid arthritis (Hijmans, Doniach, Roitt, and Holborow, 1961).

Idiopathic retroperitoneal fibrosis has been observed in association with Riedel’s struma (Haché, 1961; Doniach, 1965). It has also occurred with idiopathic mediastinal fibrosis (Tubbs, 1946; Partington, 1961), a lesion which usually causes partial obstruction of the superior vena cava, and with sclerosing cholangitis (Bartholomew, Cain, Woolner, Utz, and Ferris, 1963), a condition which almost invariably presents as obstructive jaundice. With regard to the latter association, it is of interest that Raper (1956) described a case of idiopathic retroperitoneal fibrosis with obstructive jaundice due to compression of the lower end of the common bile duct by the retroperitoneal lesion. Furthermore, Riedel’s struma and sclerosing cholangitis have been described in the same patient (Bartholomew and others, 1963). The histology of the lesions in idiopathic retroperitoneal fibrosis, Riedel’s struma, idiopathic mediastinal fibrosis, and sclerosing cholangitis is similar (Barrett, 1958; Hawk and Hazard, 1959; Haché and others, 1962; Haché, Woolner, and Bernatz, 1962; Bartholomew and others, 1963), and these four conditions may represent manifestations of a similar pathological process in different parts of the body. Another condition with a similar histological picture is pseudotumour of the orbit. This does not appear to have been described with idiopathic retroperitoneal fibrosis, but has been reported in association with thyroiditis (Andersen, Seedorff, and Halberg, 1963) and with Riedel’s struma (Arnott and Greaves, 1965).

**Summary**

A case of idiopathic retroperitoneal fibrosis associated with a generalized arteritis, which was most marked in the coronary arteries, is described. The possible relationship of idiopathic retroperitoneal fibrosis to the connective tissue disorders, to autoimmune disease of the thyroid gland, and to Riedel’s struma, idiopathic mediastinal fibrosis, and sclerosing cholangitis is discussed.

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**REFERENCES**


La fibrose rétropéritonéale idiopathique associée à l'artérite

RÉSUMÉ
On décrit un cas de fibrose rétropéritonéale idiopathique associée à une artérite généralisée, particulièrement intense aux artères coronaires. On discute la possibilité d'un rapport entre la fibrose rétropéritonéale idiopathique et les désordres du tissu conjonctif, la maladie auto-immune de la glande thyroïde, la strume de Riedel, la fibrose médiastinale idiopathique et la cholangite sclérosante.

Fibrosis retroperitoneal idiopática asociada con arteritis

SUMARIO
Se describe un caso de fibrosis retroperitoneal idiopática asociada con una arteritis generalizada, particularmente acusada en las arterias coronarias. Se discute la posible relación entre la fibrosis retroperitoneal idiopática y los disturbios del tejido conectivo, la enfermedad autoinmune de la glándula tiroide, el bocio de Riedel, la fibrosis mediastinal idiopática y la colangitis esclerosante.