HLA-B27 (antigen) in retroperitoneal fibrosis in a family

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Abstract

Idiopathic retroperitoneal fibrosis is a rare disease of undetermined aetiology. It is important to distinguish this entity from retroperitoneal fibrosis secondary to malignancy or specific inflammatory disease. There have been no prior means of excluding this condition without surgical exploration and histopathologic study of the excised tissue. A genetic predisposition is suggested for the development of idiopathic primary retroperitoneal fibrosis in patients who are HLA-B27 antigen positive. In this study we present three cases of idiopathic retroperitoneal fibrosis in a family (2 brothers and their grandfather). The presence of HLA-B27 antigen positivity was identified in two of them.

Key words: retroperitoneal fibrosis, HLA-B27, familial retroperitoneal fibrosis.

Case report

Case one. An 8-year-old boy presented with lower extremity oedema, which was not generalized oedema. Urine analysis and renal function tests were normal. Cardiac echography was normal. Other laboratory studies containing serum albumin were in the normal range. Ultrasonography study showed: severe hydronephrosis of the left kidney and moderate hydronephrosis on the right side. Delayed films of intravenous urography (12 hours after injection of contrast) and tortuous ureters with medial deviation were visualized (Figures 1, 2, 3). A CT scan of pelvis and abdomen after contrast injection showed several masses that compressed the iliac vein and the left ureter, causing left hydronephrosis. Laparascopic biopsy of these masses showed inflamed fibro-connective tissue. HLA-B27 antigen positivity was identified in this case.

Case two. The brother of the first case was a 13-year-old boy who referred with right flank pain and microscopic haematuria. Renal function tests were normal. Ultrasonography of abdomen and pelvis showed that the right kidney had mild to moderate hydronephrosis without any stone. Proximal and mid ureter were dilated with medial deviation. There were multiple hypoechoic foci suggesting lymphadenopathy or fibrosis in the retroperitoneal space. Retrograde pyelography findings were similar to those of intravenous urography (Figures 4, 5). CT scan of abdomen and pelvis with contrast injection had several intra-abdominal masses. Excised biopsy had reactive lymphatic tissue. HLA-B27 antigen positivity was identified in this case too.

Case three. The grandfather of our two mentioned cases was a 70-year-old man who was admitted for acute massive scrotal haemorrhage.

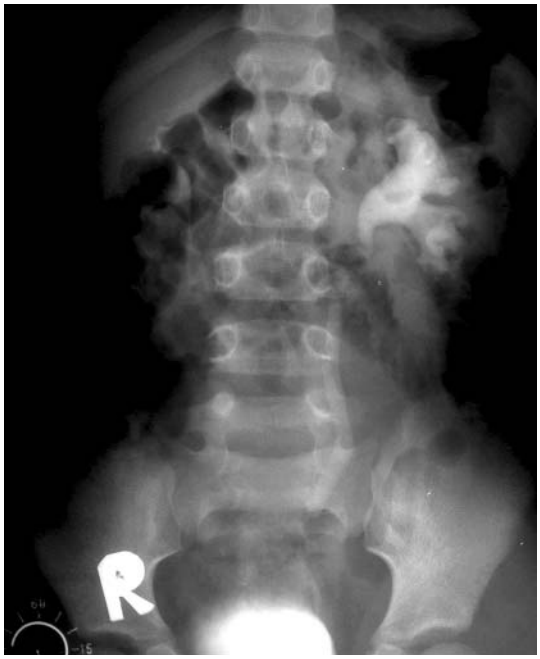

Figure 1. IVU (30')

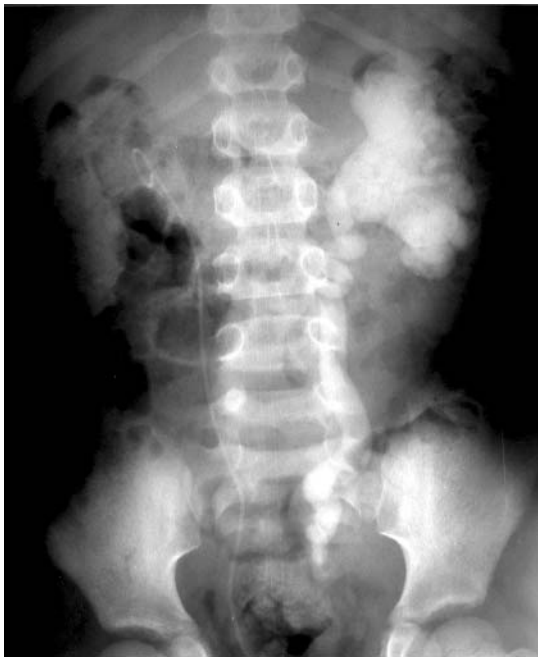

Figure 2. IVU (After 12 hous)

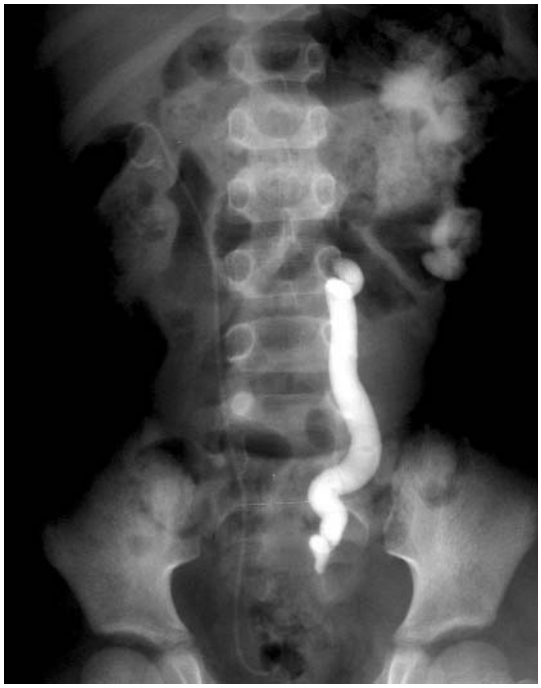

Figure 3. Retrograde pyelography

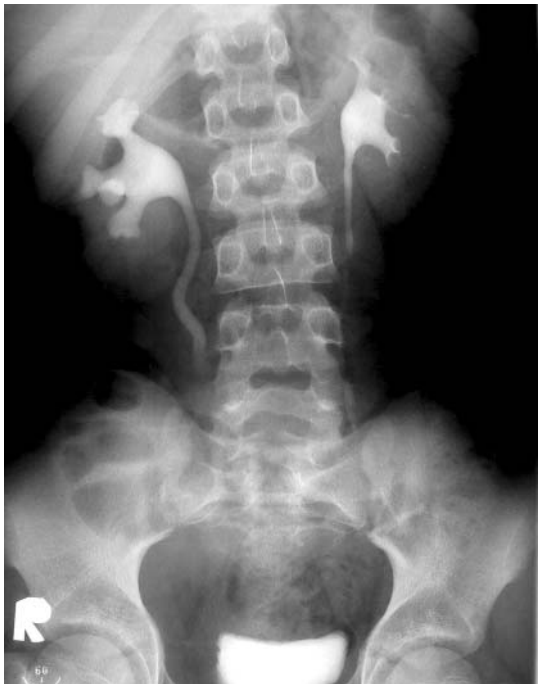

Figure 4. IVU (30')

Abdominopelvic ultrasound and CT scan showed moderate right hydronephrosis. Dilated scrotal veins were evident on physical examination. Intravenous urography showed lateral deviation of both ureters with mild bilateral hydronephrosis. CT scan of pelvis and abdomen with contrast injection showed deviation of the aorta and partial obstruction of inferior vena cava. Venography showed obstruction in the deep veins of the pelvis and abdomen; the superficial veins were normal. Excisional biopsy and retroperitoneal lymph node dissection showed retroperitoneal fibrosis.

Discussion

The aetiology of idiopathic retroperitoneal fibrosis remains unclear [1-3]. Its association with polyarteritis nodosa, systemic lupus erythematosus, Raynaud's phenomenon and drugs such as alpha-methyldopa

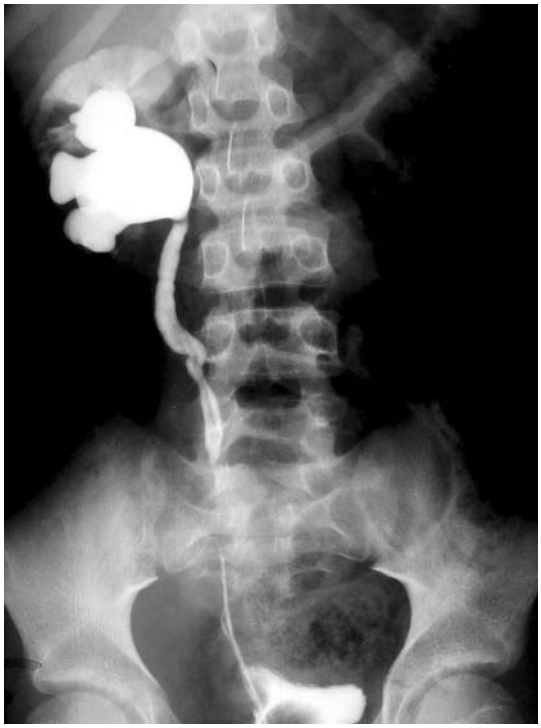

Figure 5. Retrograde pyelography

and hydralazine suggests that in some cases idiopathic primary retroperitoneal fibrosis may be a manifestation of a widespread connective tissue disorder [2].

Although initial medical management of primary retroperitoneal fibrosis has been advocated by several authors, the accepted treatment remains surgical exploration [4-7]. Mistaken diagnoses or failure to obtain adequate tissue specimens has resulted in delay of therapy in patients with retroperitoneal lymphomas, sclerosing Hodgkin's diseases, metstatic carcinoma to the retroperitoneal spaces and specific inflammatory conditions [4].

A genetic predisposition to idiopathic primary retroperitoneal fibrosis may exist. During the last decade human histocompatibility antigens have been associated with an increasing number of illnesses. The HLA-B27 tissue antigens are similar chemically to the membrane antigens of micro-organisms, thereby providing the opportunity for immunologic cross-reactivity between the organisms and the host's own tissue [4]. Alternatively, individual HLA antigen on host's cells may provide a receptor site for an invading organism. A possibility is that the HLA system is not responsible for susceptibility to disease but is linked to immune response genes [4].

The conjunction of histocompatibility antigen HLA-B27 with idiopathic primary retroperitoneal fibrosis was first suggested by Olsson [2]. This link is quite plausible when it is considered that: 1) HLA-B27 antigen is present in the majority of patients with ankylosing spondylitis and Reiter's syndrome, two connective tissue diseases in which aortitis may be the prominent feature, and 2) Aortitis is found consistently perhaps as an antecedent event, in pathologic studies of idiopathic primary retroperitoneal fibrosis. Furthermore, the HLA-B27 antigen may be a predisposing factor for the development of fibrotic changes, e.g. the striking upper lope pulmonary fibrosis seen in ankylosing spondylitis and the increased incidence of pneumoconiosis in HLA-B27 positive asbestos workers [2].

Conclusions

The 3 reported cases, including our patients, of HLA-B27 positive retroperitoneal fibrosis have been in young men. Its presence in these 2 cases may suggest an association between retroperitoneal fibrosis and the HLA-B27 antigen.

A systematic study should be undertaken to determine the incidence of the HLA-B27 antigen in patients with retroperitoneal fibrosis. Should the association of HLA-B27 antigen with retroperitoneal fibrosis be of diagnostic significance, as in ankylosing spondylitis, its presence would allow differentiation of primary retroperitoneal fibrosis from other diseases that present with a similar clinical picture. In addition to the diagnostic value of tissue typing, an attempt at medical management with steroids would appear to be reasonable in HLA-B27 positive individuals. As the number of patients with retroperitoneal fibrosis may not be adequate at any one institution, we suggest that other patients with this disease undergo tissue typing to further substantiate their possible association.

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