

Inflammatory Tumour of the Retroperitoneum – A Case Report

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Abstract

Introduction: Neoplastic growths of myofibroblasts occurring on a background of plasma cell and lymphocytic proliferation have been designated as inflammatory myofibroblastic tumours (IMTs). These unusual tumours were first described in pulmonary location in adults. Though extrapulmonary masses have been reported in children; retroperitoneal growths are exceedingly rare. We report a case of retroperitoneal IMT that presented with constitutional symptoms without any palpable abdominal mass. **Clinical Picture:** A previously well 12-year-old boy presented with fever, right-sided flank pain and weight loss of 1-month duration. There were no foci of infection. The erythrocyte sedimentation rate (ESR) was raised; the white cell count was normal. An abdominal computed tomography (CT) scan revealed a right suprarenal tumour measuring 3.5 cm without any calcification. The urinary catecholamines and vanilmandelic acid were normal. **Treatment:** A laparotomy with complete excision of the tumour was performed. Final histology revealed an inflammatory myofibroblastic tumour without any correlates of aggressive behaviour. **Outcome:** Postoperatively, the constitutional symptoms of fever, weight loss and raised ESR normalised. Follow-up CT was normal and further treatment was not necessary. **Conclusion:** Although rare, IMTs should be considered in any abdominal solid tumour with associated constitutional and laboratory features of an inflammatory response. Complete surgical excision is effective treatment for biologically benign tumours.

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Introduction

First diagnosed as pulmonary tumours in the adult population, inflammatory myofibroblastic tumours (IMTs) are true neoplasms that are also known to occur in children in various extrapulmonary locations.¹ Although abdominal IMTs have been reported, retroperitoneal tumours are exceedingly rare.¹ Since needle biopsy and frozen section in these tumours are unreliable, a preoperative suspicion obviates the need for radical treatment whilst awaiting confirmation on final histology of the completely excised mass.^{2,3}

Case Report

A previously well 12-year-old Chinese boy was seen for a low-grade fever, dull ache in the right flank and weight loss of 4 kg for 1 month. Dietary history was normal.

Physical examination did not reveal any focus of infection. The abdomen was unremarkable. The leukocyte count was 12.83 with a normal differential; haemoglobin (Hb) 10.6 g/dL, haematocrit 33.7%; mean corpuscular volume 71.5 fL; mean corpuscular Hb 22.5; mean corpuscular Hb concentration 31.5 g/dL and platelet count 586,000/mm³. The erythrocyte sedimentation rate (ESR) was 113 mm/h (normal, 1 to 7). Initial ultrasound raised the suspicion of a mass between the liver and the kidney. Computed tomography (CT) scan of the abdomen (Fig. 1) revealed a 3.5-cm diameter, right-sided homogenous suprarenal mass without any calcification or contrast enhancement. The margins were well defined and there was a clear plane between the adjacent kidney, liver, crura of the diaphragm and inferior vena cava. Urinary dopamine (173 nmol/L) and vanilmandelic acid (<5 umol/L) were within normal

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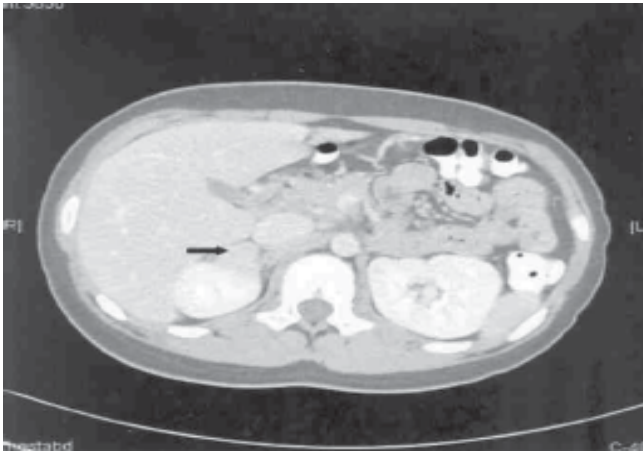


Fig. 1. Computed tomography scan of abdomen showing retroperitoneal tumour.

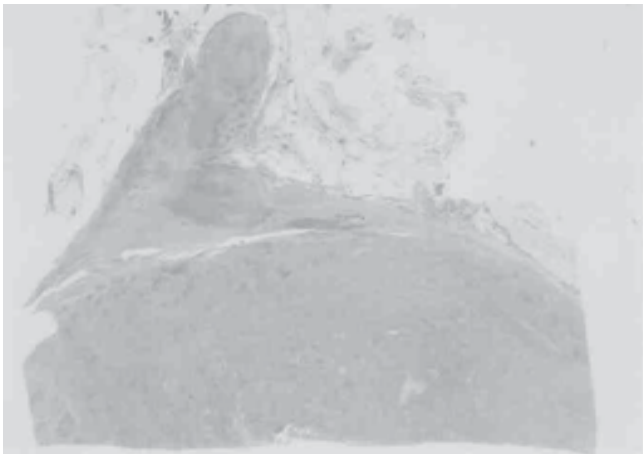


Fig. 2a. Proliferating spindle cells on a background of mixed inflammatory infiltrate (x2).

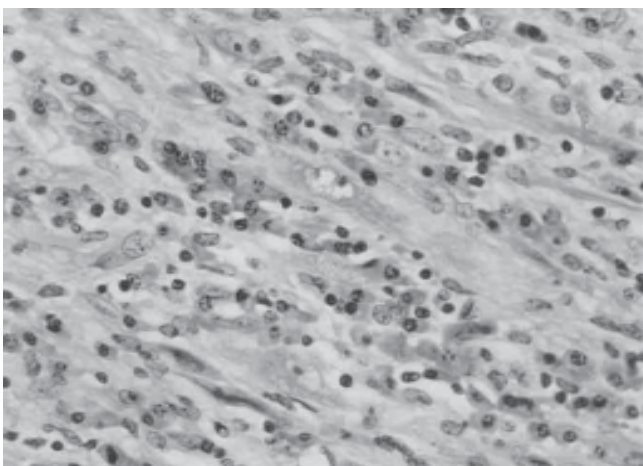


Fig. 2b. Proliferating spindle cells on a background of mixed inflammatory infiltrate (x600).

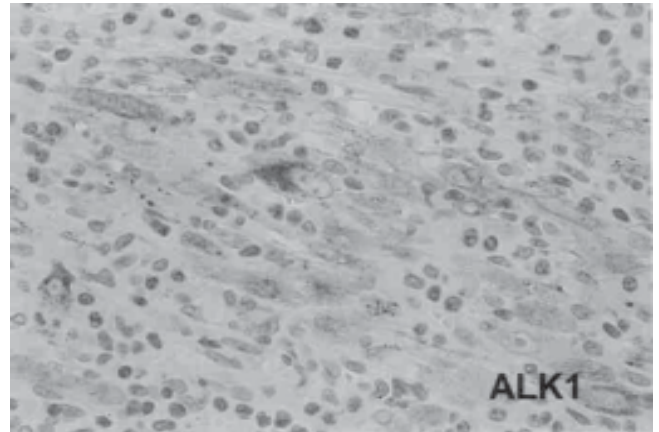


Fig. 3. ALK 1 immunostaining (x600).

limits. The literature was reviewed and a laparotomy was performed, aiming for complete surgical excision. This revealed a solid retroperitoneal tumour in close proximity to, but separate from the adrenal gland. The adrenal gland and right kidney were normal. The tumour was adherent to the surface of the adrenal and the inferior surface of the right lobe of the liver. The tumour was separated from the liver but a thin margin of the adrenal gland was excised along with the tumour to achieve complete removal. No other masses were found within the abdomen.

Histopathology (Figs. 2 and 3)

Grossly, the tumour was encapsulated with a solid, homogenous, whitish cut surface measuring 4.2 x 3.6 x 3.4 cm and a closely apposed thin sliver of adrenal gland. The capsular surface of the tumour was relatively smooth and showed adherent peri-adrenal fat.

Histology showed a tumour composed of interwoven fascicles of plump spindle cells, sometimes dispersed in a “herring-bone” (but not a storiform) configuration. The tumour cells possessed abundant, eosinophilic-to-amphophilic cytoplasm that lacked cross-striations. Their nuclei were variably enlarged, rounded-to-elongated and vesicular, with dispersed chromatin and variably conspicuous nucleoli. The nuclear constrictions or “waisting” of epithelioid histiocytes (as in a mycobacterial spindle cell pseudotumour) were not discerned, and special stains for acid-fast bacilli (including *Mycobacterium avium intracellulare*) were negative. Tumour emboli, mitoses and foci of tumour cell necrosis were not identified. Round cell transformation (which has been associated with aggressive behaviour) was not identified.⁴⁻⁶ The tumour was enclosed by a fibrohyaline pseudocapsule which was fairly well-defined. The bone marrow showed reactive trilineage haematopoiesis without any malignant infiltration.

Immunohistochemically, the tumour cells showed patchy expression of actin and scattered, focal positivity for desmin, but not for the more smooth muscle-specific marker h-caldesmon, nor was there any nuclear expression of the striated muscle transcription factor myogenin, in keeping with myofibroblasts. In addition, there was variable, patchy coexpression of anaplastic lymphoma kinase (ALK) protein in a cytoplasm-restricted pattern consistent with variant *ALK* gene translocations that are known to occur in inflammatory myofibroblastic tumours, particularly in childhood.^{4,6} The tumour cells did not express follicular dendritic cell markers (CD21 and CD35), thereby excluding a follicular dendritic sarcoma. There was prominent admixture with reactive, mature, often aggregated plasma cells, polytypic by kappa and lambda light chain immunostaining in an approximate 2:1 ratio, as well as fewer small, round lymphocytes and occasional lymphoid follicles with their reactive germinal centres. No staining for CD10 suggestive of entrapped renal elements was discerned. Furthermore, lesional elements were completely negative for synaptophysin and S100; there was, therefore, no evidence to support a ganglioneuroblastic tumour or paraganglioma. Immunostaining for broad-spectrum (MNFI16) and low-molecular weight (Cam5.2) cytokeratin highlighted only a subset of the entrapped adrenal cortical elements, leaving the tumour cells negative, and the possibility of a (biphasic) synovial sarcoma was further negated by lack of CD34, CD99 and bcl-2 expression. Negativity for these latter two markers and for CD 34 also weighed against a solitary fibrous tumour (which may express a myofibroblastic phenotype). Negative staining for CD34 and CD117/c-kit excluded a stromal tumour of “gastrointestinal” phenotype (GIST).

The final histological diagnosis was an IMT of the retroperitoneum invading the adrenal with clear resection margins.

Postoperatively, the fever subsided within 1 day. Within a month, the patient regained weight and the laboratory abnormalities normalised. About 6 months later, the patient has no clinical and CT evidence of tumour recurrence and has a normal full blood count and ESR.

Discussion

Neoplastic proliferation of myofibroblasts admixed with inflammatory cells has been previously known under various synonyms such as inflammatory pseudotumour, plasma cell granuloma, inflammatory myofibrohistiocytic proliferation, pseudosarcomatous myofibroblastic proliferation and xanthomatous pseudotumour.⁷ This confusion in nomenclature arose due to the ambiguity in determining whether the origin is a post-inflammatory reactive process or whether it is a true neoplasm. Proponents

of the post-inflammatory theory argued that it can occur after surgery, trauma, ventriculo-peritoneal shunts, radiotherapy and steroids and in association with infectious agents such as *Mycobacterium avium intracellulare*, *Corynebacterium equi*, *Campylobacter jejuni*, *Bacillus sphaericus*, *Coxiella burnetti*, Epstein Barr virus and *Escherichia coli*.^{3,8,9} On the other hand, IMTs have the propensity for local recurrence and distant metastases.⁷ More definitive evidence of its neoplastic origin rests on its frequent clonal alterations in chromosome 2p23.^{4-6,10-12}

However, while showing clonal evidence of being a true neoplasm, it is usually not a clear-cut malignant tumour, hence not being referred to as a “sarcoma” from the outset. It is mainly seen in children and young adults and the lungs are the most commonly affected site.¹ Paediatric extrapulmonary tumours have been reported within the mesentery, liver and retroperitoneum, bladder, head and neck, extremities, appendix and kidneys.^{1,7}

The clinical presentation varies depending on the anatomical site. Intraabdominal tumours usually present with an abdominal mass with features of inflammation; such as fever and weight loss.¹

Haematologically, there is hypochromic microcytic anaemia and raised ESR.¹³ The leukocyte counts are normal. These abnormalities may be indicative of tumour recurrence following complete excision.⁷

Radiologically, the findings are non-specific and only reveal a solid well-defined mass.^{14,15} Calcification has been described.

The pathological diagnosis rests on the appearance of myofibroblasts with an inflammatory infiltrate consisting of plasma cells, lymphocytes and occasionally histiocytes.^{4,6,16} The discovery of a characteristic set of cytogenetic and molecular genetic aberrations involving the *ALK* gene, while incorporating IMTs into the growing list of soft tissue neoplasia that are each characterised by their own distinctive molecular genetic pathology, enables IMTs to be distinguished from these other entities by their different chromosomal translocations involving the corresponding oncogene loci. However, *ALK* expression is not entirely specific to IMTs as it may be seen in some of its other mesenchymal mimics, notably rhabdomyosarcoma.⁴ Furthermore, *ALK* abnormalities are not restricted to mesenchymal tumours, since, after all, it was first discovered in the corresponding lymphoma. Certain features such as cellular atypia, ganglion-like cells, necrosis, nucleolar prominence and mitotic activity, including atypical mitotic figures expression of p53 and aneuploidy are predictive of aggressive behaviour.^{5,17} The histopathologic differential diagnosis includes spindle cell tumours of other lineages, as well as pseudoneoplastic spindle cell proliferations. The

other types of spindle cell pseudotumour were eliminated in the detailed immunophenotypic analysis, while the presence of ALK protein expression essentially serves as a surrogate marker for the translocation involving the *ALK* locus at chromosome 2p23,^{4,6} hence excluding a reactive myofibroblastic proliferation.^{4,6}

One report justifies surgical excision as the only treatment in children based on their favourable prognosis in this age group.¹⁶ Nevertheless, this remains the only proven mode of cure and is proposed as the first line of treatment in all cases. Recurrence occurs in about 15% to 37% cases of abdominal tumours especially within a year of surgery.^{9,16} Apart from local recurrence, distant metastases and malignant sarcomatous transformation have been reported.^{9,16} Neither chemotherapy nor radiotherapy or even immunomodulation has been consistently effective against such aggressive tumours.¹ A recent report of successful treatment of a malignant tumour with sequential excisional surgery and combination chemotherapy suggests that the treatment for each case of aggressive IMT has to be individualised.⁷

In conclusion, inflammatory myofibroblastic tumours are true neoplasms of proliferating myofibroblasts with an associated inflammatory component. They have a variable biologic behaviour that ranges from the frequently benign lesions to more aggressive variants. Final diagnosis is based on histomorphological features and immunoperoxidase phenotyping. Due to their rarity, there are no well-defined protocols for treatment especially in cases of malignant behaviour. Complete surgical excision should be the aim of curative treatment. Long-term clinical, radiological and laboratory follow-up is indicated because of the potential for local recurrence even after many years.

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