

CASE REPORT

Renal inflammatory myofibroblastic tumor – a new case report

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Abstract

Renal inflammatory pseudotumor is uncommon, benign tumor that has been classified into separate group but there is a risk that this lesion could be misdiagnosed. The aim of this work is to report a new case of 57-years-old man presented in our hospital with hematuria, minimal grade fever and right flank pain. Magnetic resonance imaging (MRI) and sonography revealed a tumor of the right mediorenal parenchyma, 2.5 cm in diameter. The patient underwent right nephroureterectomy under the diagnosis of renal cell carcinoma. Macroscopically examination carried out on the removed kidney showed a 2/2/1.5 cm yellowish, gelatinous, well circumscribed, mediorenal and pericaliceal mass. Fragments of the tumor were fixed in 10% formaldehyde, included in paraffin, and the sections were stained with HE, VG and immunohistochemically with vimentin (VIM), MNF116, SyN, smooth muscle actin (ACT), desmin, CD68, S100, HMB45, and CD117. The histological examination revealed a compact spindle cell proliferation, a hypocellular fibrous area in an edematous myxoid background infiltrated by small lymphocytes, histiocytes, some plasma cells and small bone area. The spindle cells were diffuse positive for VIM, ACT, CD68 and negative for desmin, MNF116, SyN, S100, HMB45, and CD117. The pathologic diagnosis was renal inflammatory pseudotumor, raising the problem of differential diagnosis, as the clinical and imagistic aspects are similar to those of a renal carcinoma and the problem in establishing a preoperative correct diagnosis.

Keywords: inflammatory pseudotumor, kidney, immunohistochemistry.

Introduction

Inflammatory myofibroblastic tumors (IMT) are uncommon tumors characterised by unpredictable clinical behavior [1]. They may develop at several anatomical sites, e.g., the airways and gastrointestinal tissues, soft tissues, the orbit, the spleen, or the lymph nodes [2], in virtually any anatomic location and at any age. It was described for the first time in the lung and called plasma cell granuloma [3]. Over 200 cases of this tumor of the lung have been described in literature [1].

Inflammatory myofibroblastic tumor of the genitourinary tract is rare and has been classified into separate groups based on their anatomical site and postulated etiology [4].

A large number of benign and malignant soft tissue lesions can contain cells with myofibroblastic features. Inflammatory myofibroblastic tumor is a distinctive entity, also known as inflammatory pseudotumor. It is a „tumor composed of differentiated myofibroblastic spindle cells and usually with numerous plasma cells and/or lymphocytes” [5]. In the genitourinary system, it most commonly occurs in the bladder. It really originates in the kidney, renal pelvis and ureter [6].

The pathogenesis is not very well known and there are questions whether it represents an exaggerated reactive process or a true neoplasm [7].

The frequent clinical findings are fever, night sweats, fatigue, weight loss, lymphadenopathy and laboratory characteristics are polyclonal hypergammaglobulinemia and elevation in erythrocyte sedimentation. All this may suggest an infection of autoimmune cause [8].

Matsubara O *et al.* (1998) have identified infectious agents in IMT, including bacterial, rickettsial, fungal or viral agents, but only in isolated cases [9].

The presence of human herpesvirus-8 DNA sequences, as well as an overexpression of human interleukin-6 and human cyclin D1 in myofibroblastic cells of inflammatory myofibroblastic tumor (inflammatory pseudotumor), has recently been reported [7].

These cytokines probably have a paracrine action and many sustain myofibroblastic growth. Inflammatory etiology may not be applicable to all tumors since some recent research have demonstrated the presence of chromosomal abnormalities (2p23) and occasional documented cases showing aggressive local

behavior and metastasis of the tumor supporting the theory that at least some of these tumors are true neoplasms [6, 10–12].

Macroscopically, they are usually circumscribed, white to tan masses that may be nodular, with occasionally infiltrating margins. Other features can be myxoid appearance, scar-like areas [13].

There are three main histological patterns: nodular fasciitis-like, fibrous histiocytoma-like and desmoid or scar tissue-type [14].

The aim of this work is to report a new case and review of the literature of a renal IMT.

A 57-years-old man presented in our hospital with hematuria, minimal grade fever and right flank pain. Abdominal computer tomography (CT) and magnetic resonance imaging (MRI) revealed a tumor of the right kidney. Under the diagnosis of right renal cell carcinoma, he underwent right nephrectomy and ureterectomy. We indented to contribute with our experience in diagnose and to define prognosis and outcome of patients presenting with renal inflammatory myofibroblastic tumor.

☐ Material and methods

Macroscopically examination carried out on the removed kidney showed a 2/2/1.5 cm yellowish, gelatinous, well circumscribed, mediorenal and pericaliceal mass.

Many tissue samples of the radical nephrectomy were fixed in formalin and paraffin sections were stained with Haematoxylin–Eosin and Van Gieson. Immunohistochemistry was performed on 3 µm thick sections from 10% formalin fixed, paraffin-embedded specimens, according to the streptavidin–biotin method [15], modified by Bussolatti G and Gugliotta P [16], Miller K [17] and Ardeleanu Carmen *et al.* [21].

The primary antibodies were as follows: vimentine (Dako, Denmark 1:50), MNF116 (Dako, Denmark 1:50), SyN (Dako, Denmark 1:50), ACT (Sigma, USA 1:4000), desmine (Dako, Denmark 1:50), CD68 (Dako, Denmark 1:50), S100 (Dako, Denmark 1: 600).

The endogeneous biotin was blocked by adding an excess of avidin followed by washing and addition of free biotin. All specimens were counterstained with Mayer's Hematoxylin, examined and photographed on a Nikon Eclipse 600 microscope.

☐ Results

Microscopic examination showed a proliferation of spindle cells in a fascicular pattern (Figure 1) separated by a myxoid and edematous stroma containing numerous blood vessels (Figure 2).

A diffuse infiltrate of lymphocytes (Figure 3), histiocytes and some plasma cells was scattered throughout the lesion (Figure 4).

The spindle cells had a long and eosinophilic cytoplasm without cross-striations. Nuclei were round or oval with minimal pleomorphism and sometimes contained a small nucleolus. No lipoblasts or atypical mitosis were seen. Focal area of hemorrhage was observed (Figure 5).

Within inflammatory infiltrate, we have found numerous round laminated bodies known as “liesegang rings” which can be confused with cysts or ova of parasites (Figure 6).

The urothelial lining was ulcerated. Diffuse immunopositivity for vimentin (Figure 7) and CD68 (Figure 8), focal positivity for smooth muscle actin were present. Because VIM and ACT are smooth muscle markers and CD68 is an inflammatory marker, they are strongly suggesting a diagnosis of IMT.

The remaining immunostaining including desmin, MNF116, synaptophysin, S100, HMB45, CD117 was negative.

☐ Discussions

Inflammatory myofibroblastic tumor is a relatively rare neoplasm. It is more common in children without sex predilection, though extrapulmonary forms are more common in adult females [14].

The patients often present with fever of unknown origin and other nonspecific symptoms. Usually it has a benign course and in most of the cases it is a slow growing, locally confined tumor with less metastatic potential [14].

The tumor commonly occurs in lung. Extrapulmonary IMT are rare. The main cellular component in IMT is the spindle myofibroblastic cell. Three histologic patterns were identified in the tumors, including a myxoid vascular pattern, a compact spindle cell pattern, and a hypocellular fibrous pattern (nodular fasciitis-like, fibrous histiocytoma-like and desmoid or scar tissue-type). The first pattern, nodular fasciitis-like, consists in elongate myofibroblasts with variably abundant eosinophilic cytoplasm and large vesicular nuclei set within a loose or myxoid stroma. Predominant cells are neutrophils, lymphocytes and eosinophils, with only a small number of plasma cells. The second pattern is more cellular, with spindle fibroblasts and myofibroblasts set in a compact stroma. Predominant cells tend to be plasma cells. The third pattern features a stroma with dense hyalinization and paucicellular, only a few plasma cells and lymphocytes. In some tumors, large “histiocyte-like” or “ganglion cell-like” cells are present, with large vesicular nuclei and prominent nucleoli. These cells may be more prominent in recurrences, but their presence does not seem to affect patient outcome [13].

We initially approached our case as renal cell carcinoma due to the patient symptoms: hematuria, right flank pain and fever along with CT and MRI findings. Weight loss was not observed in our case. Microscopic examination revealed a predominantly fascicular spindle cell proliferation in an edematous myxoid background admixed with variable amounts of extracellular collagen, lymphocytes, plasma cells and some histiocyte-like cells with large vesicular nuclei and prominent nucleoli.

Immunohistochemical and electron microscopic studies supported a myofibroblastic proliferation. The cells are smooth muscle actin, muscle-specific actin and vimentin positive [13].

Figure 1 – Spindle cell component
(HE staining, ob. ×10)

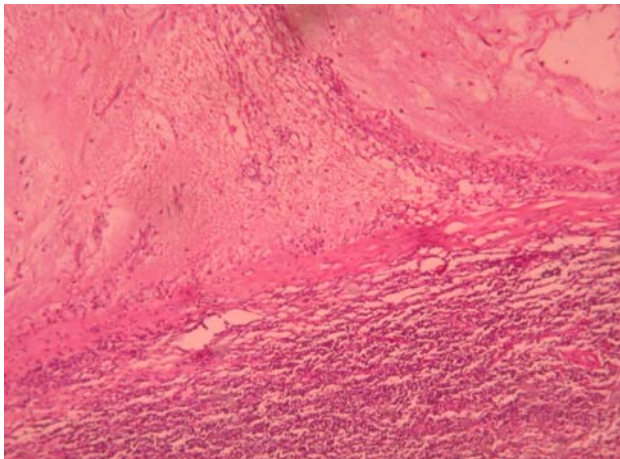
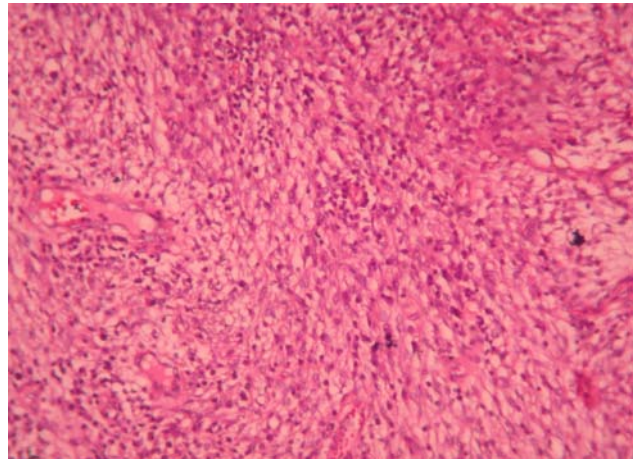


Figure 2 – Myxoid and oedematous stroma
containing numerous blood vessels
(HE staining, ob. ×10)

Figure 3 – Diffuse infiltrate of lymphocytes
(HE staining, ob. ×10)

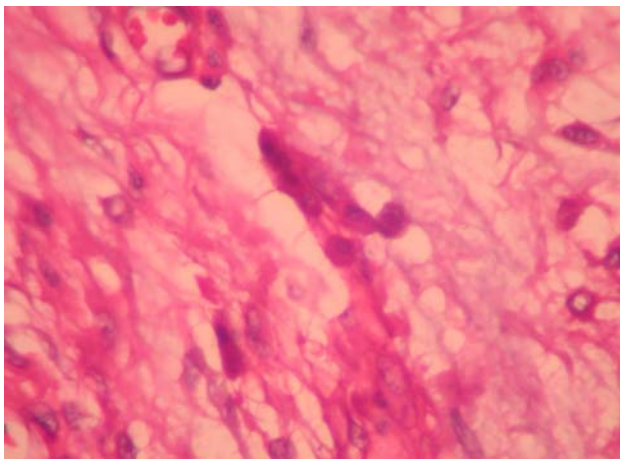
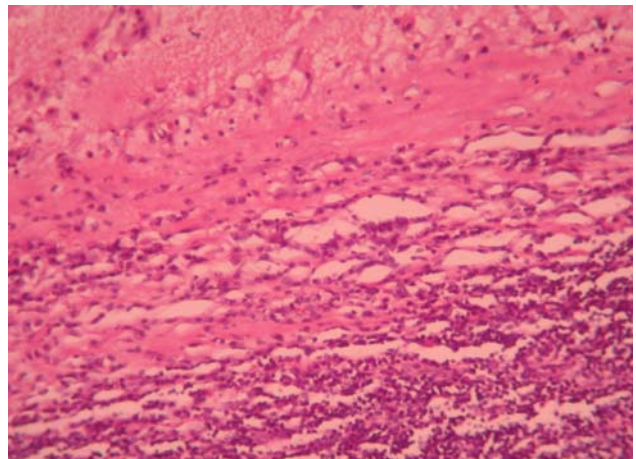


Figure 4 – Histiocytes and some plasma cells
(HE staining, ob. ×40)

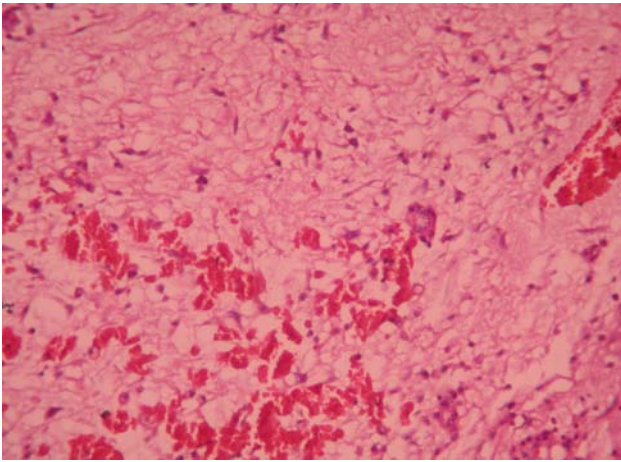


Figure 5 – Focal area of hemorrhage
(HE staining, ob. ×10)

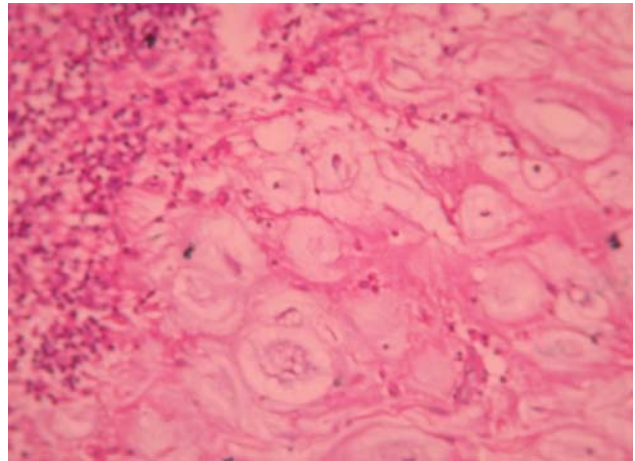


Figure 6 – Liesegang rings
(HE staining, ob. ×40)

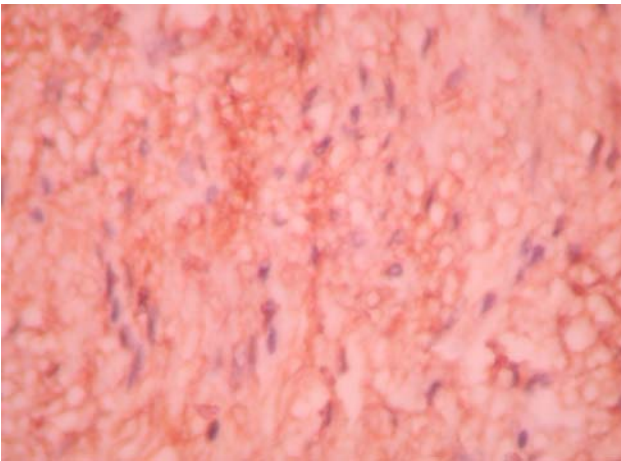


Figure 7 – Diffuse positivity for VIM
(HE staining, ob. ×40)

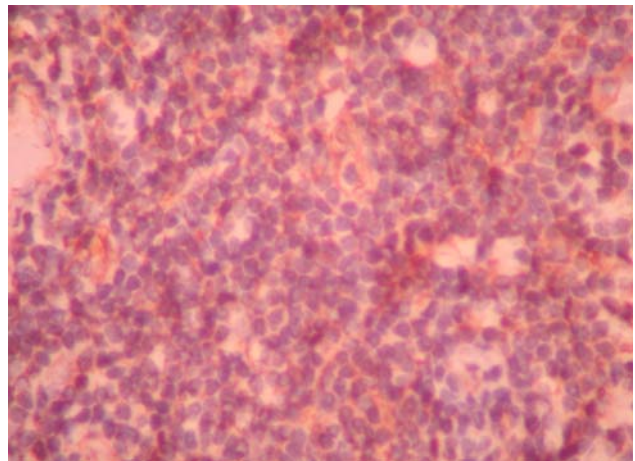


Figure 8 – Diffuse positivity for CD68
(HE staining, ob. ×40)

Some studies reported positivity for desmin [10] while others reported cells negative for desmin [22]. ALK and p80 are consistently expressed at the immunohistochemical level.

Immunohistochemistry for vimentin (VIM), MNF116, SyN, smooth muscle actin (ACT), desmin, CD68, and S100 were performed.

ALK, which results from a rearrangement in chromosome 2p23, is more commonly seen in pediatric than in adult cases, suggesting a different molecular pathogenetic mechanism between the two groups. P53 mutation and MDM2 amplification are rare [23]. Abnormalities of ALK and p80 and evidence of chromosomal rearrangements of 2p23 occur in a significant proportion of IMTs and are associated with a higher frequency of recurrence. These findings confirm the neoplastic nature of a subset IMT with ALK abnormalities [24].

One study revealed IMFT positivity for smooth muscle actin, desmin and cytokeratin in 78–89% cases, resulting in potential confusion with sarcomatoid carcinoma or leiomyosarcoma. In contrast, cytoplasmic anaplastic lymphoma kinase (ALK1) staining was present in IMFT (89%), but was not seen in any other lesion examined [11].

We must also exclude angiomyolipoma (which is HMB45 positive), myxoid fibrosarcoma and malignant fibrous histiocytoma.

Inflammatory myofibroblastic tumor can recur and occasionally the recurrence can be uncontrolled [18]. There were many discussions about the metastatic potential of this tumor. Recent studies reveal that it should be considered intermediate tumor with the potential to recur but with rare metastatic potential rather than sarcomas [18]. However, there are some predictors for aggressive behavior and metastatic potential of IMT, which include presence of ganglion like cells, cellular atypia, aneuploidy and p53 overexpression [19].

Concerning differential diagnosis diffuse sclerosing lesions such as sclerosing mesenteritis and retroperitonitis (retroperitoneal fibrosis), sclerosing mediastinitis and sclerosing cholangitis are all fibroblastic and myofibroblastic proliferative disorders associated and can be mistaken with inflammatory myofibroblastic tumor because the presence of variable degrees of inflammation. They are processes that are more diffuse and are rare in children [18].

Nodular fasciitis is another differential diagnosis because the pattern fasciitis-like, but IMT are larger than nodular fasciitis and tend to occur primarily in a younger age group [18]. IMT can mimic fibrous histiocytoma, a smooth muscle tumor, fibromatosis and other spindle cell proliferations [18].

Immunohistochemistry allows us to distinguish all these tumors. Calcifying fibrous pseudotumor (CFP), a recently described lesion, is characterized by a predominantly lymphoplasmacytic infiltrate with abundant hyalinized collagen and psammomatous or dystrophic calcifications. It has been postulated that CFP may represent a sclerosing end stage of inflammatory myofibroblastic tumor (IMT) [25].

Follicular dendritic cell (FDC) tumors can mimic inflammatory pseudotumor [26] and lymphomas [18].

Little data is available in the management of IMT. Most patients with IMT are cured by excision. There have been no documented benefits from radiation or chemotherapy [18].

In our case, the tumor was removed to avoid local recurrence and the patient was offered no adjuvant therapy. The metastatic work-up including bone scan and CT-scan of the thorax were essentially normal and we expect long term survive in this case. The behavioral of this tumor is unpredictable. Some may recur and metastasis has been reported in lung, brain [18] and involvement of the bone marrow [20].

However, it appears that the metastatic rate is less than 5% [18]. Because its location, some tumors are difficult to remove and the patients can die because of uncontrolled local growth. The diagnosis, especially on biopsy may be difficult. Although the myxoid pattern may also cause confusion with myxoid liposarcoma, no lipoblasts are present.

Conclusions

Primary renal inflammatory myofibroblastic tumor is an extremely rare neoplasm of uncertain biological potential. The preoperative diagnosis of IMT remains difficult, despite progress in medical imaging and often requires surgical exploration. The diagnosis is based on a correlation of radiological and histological findings.

Typically, the IMT is characterized by the expression of vimentin, smooth muscle actin and cytokeratins. There are some predictors for aggressive behavior and metastatic potential of IMT, which include presence of ganglion like cells, cellular atypia, aneuploidy and p53 overexpression. Surgery remains the main stay of treatment.

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