CASE REPORT

Difficulties of diagnosis in retroperitoneal tumors

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Abstract
Retroperitoneum is a large space where the primary and metastatic tumors grow silently before clinical signs appear. Retroperitoneal sarcomas represent 10% to 15% of all soft tissue sarcomas. This group, retroperitoneal soft tissue sarcomas is associated with a very poor long-term survival rate, difficulty in diagnosis and complete surgical removal with a rim of normal tissue around the tumors. Liposarcoma is the most frequent retroperitoneal sarcoma. MFH is the second most common retroperitoneal sarcoma. The diagnosis in retroperitoneal sarcomas is clinical, radiological and histological. Our case presents a MFH with the difficulties of clinical, radiological and histological diagnosis. The initial diagnosis is based on the imaging findings, which offer information on the composition, density, extent and relation to the adjacent organs and structures, with the identification of displacement of the kidney. The definitive diagnosis is established by the pathology findings. The proportion of local recurrence rates of MFH after initial local excision ranges between 16% to 52%.

Keywords: retroperitoneal tumors, MFH, IHC, CT exam.

Introduction
The retroperitoneal space is limited anteriorly by the peritoneal covering, posteriorly by posterior abdominal wall, superiorly by the 12th rib and vertebra, inferiorly by the base of the sacrum and iliac crest, and laterally by the site borders of the quadratus lumborum muscles. It contains: connective tissue, the adrenals, kidneys and ureters, aorta and its branches, inferior vena cava and its tributaries and lymph nodes [1].

The retroperitoneum is the place of non-neoplastic conditions such as: inflammatory processes from the kidneys, large bowel, appendix, pancreas, infection from a tuberculous vertebra which form cold abscess, malakoplakia, hemorrhage, benign retroperitoneal cysts, idiopathic retroperitoneal fibrosis (Ormond’s disease) and tumors.

Primary tumors of the retroperitoneum can be of many types: neoplasms arising in the kidney, adrenal gland, retroperitoneal lymph nodes (malignant lymphomas). The retroperitoneal soft tissue sarcomas are also presented in this location, as liposarcoma, lipoma, malignant fibrous histiocytoma, leiomyosarcoma, rhabdomyosarcoma, fibrosarcoma, vascular tumors, peripheral nerve tumors, synovial sarcoma, alveolar part sarcoma, extraskeletal osteosarcoma. Retroperitoneal teratomas in children can occur. Retroperitoneal germ cell tumors in adult can occur in this location or can represent metastasis from gonads tumors.

Metastatic tumors may appear in the retroperitoneal space because of local extension or lymph node involvement [2].

Symptoms secondary retroperitoneal neoplasms are vague and appear late in the course of the disease caused by compression of the organs and obstructive phenomena. Diagnosis is made by radiological methods (ultrasonography, CT exam, MRI) and after surgery, histological.

Liposarcoma is the most frequent retroperitoneal sarcoma. It is particularly prone to arise and grow in the perirenal region.

MFH is the second most common retroperitoneal sarcoma and the differential diagnosis includes: malakoplakia, sarcomatoid renal cell carcinoma, liposarcoma [2].

Malignant fibrous histiocytoma (MFH) is an aggressive sarcoma. O’Brien and Stout, in 1964, recognized MFH as the most common soft tissue sarcoma of the late adult life. The MFH occurs in: lower extremity (49%), upper extremity (19%), retroperitoneum and abdominal cavity (16%), thigh (30%) [3]. It has been estimated that only approximately 3–7% of these tumors occur in the head and neck region. The diagnosis of MFH is radiological and histological [2, 4]. MFH is sub-classified based on histologic appearance into: storiform-pleomorphic, myxoid, giant cell, inflammatory and angiomatoid type [5].

The most favorable prognosis is associated with the angiomatoid and myxoid type of MFH, whereas a poorer prognosis is reported with giant cell variant. The storiform-pleomorphic and inflammatory MFHs fall between these two extremes. Various prognostic indicators have been identified: depth of the tumor invasion, tumor size, anatomic location and histologic features [6].

Surgery is the treatment of choice for MFH, with adequate margins of normal surrounding tissues is required for a favorable prognosis [7].
The proportion of local recurrence rates of MFH after initial local excision ranges between 16% to 52% [2, 4].

**Patient, Methods and Results**

A 44-year-old white female patient presented a short history of painless in right lumbar region. The physical examination revealed no anomalies except for the palpation of increased consistency in the right renal fossa. An abdominal X-ray study was therefore carried out revealing a large density increment with mass effect in the right side of the abdomen. Ultrasound showed a right renal mass measuring approximately 8 cm in diameter. Native CT exam revealed a large tissue mass with fine microcalcifications, occupying the posterior portion of the right kidney and extending to the capsule (Figure 1).

Operatory biopsy was represented by right kidney, 14/9/6 cm with a tumor of 7 cm in size, mediorenal located and another biopsy, 13/2 cm, which had a tumoral aspect, was removed from retroperitoneum. A new operation, six months later, showed a tumoral relapse.

Hematoxylin–Eosin (HE) stained sections demonstrated a tumoral cells proliferation with fusiform cells, pleomorphic cells, giant cells in both operatory biopsies. The first microscopical diagnosis was MFH vs. dedifferentiated liposarcomas. The next immunohistochemical algorithm was made: vimentin (Figure 2), actin muscle, CD68 (Figure 3), CD34 (Figure 4), S100, CK AE1/3, CK8/18, CK7, Factor XIII, desmin, MIB-1.

The S100 reactive cells comprised less than 10% of the lesional cells, histiocytes express weak to moderate cytoplasmic to Factor XIIIa, desmin negative, etc.

![Figure 1 – CT native: A solid mass with microcalcification amorphous in right kidney.](image1)

![Figure 2 – MFH: Vimentin (ob. ×10).](image2)

![Figure 3 – MFH: CD68 (ob. ×20).](image3)

![Figure 4 – MFH: CD34 (ob. ×20).](image4)

The radiological diagnosis in our case was CT exam which offer information on the composition, density, extend and relation to the adjacent organs and structures.

Abdominal-pelvic computed axial tomography with intravenous contrast injection revealed a large tissue mass occupying the posterior portion of the right kidney and extending to the capsule. The tumor was heterogeneous with hypodense and hyperdense areas, fine microcalcifications, and showed intense contrast enhancement (Figures 5 and 6). Invasion of the inferior vena cava or right renal vein was not found (Figure 7). The lesion measured about 8.5/6.5/7.5 cm. There were
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no adenopathies. The rest of the exploration showed no alterations.

Grossly operatory biopsy was represented by a tumor measuring 7 cm medior enal located, flashy with aspect, with necrosis and adherent by fatty renal tissue.

The second operatory biopsy had the same grossly aspect, measuring 13/2 cm.

HE staining showed a pleomorphic tumoral cell proliferation (fusiform cells, giant cells) necrosis areas, atypical mitosis (Figure 8).

Histological diagnosis, in this stage, was MFH vs. leiomyosarcoma, sarcomatoid carcinoma, etc.

A battery of immunohistochemical stains were then conducted to provide a definitive diagnosis: vimentin intense positive in tumoral cells, actin focal positive in tumoral cells, S100 negative, CD68 negative in tumoral cells, positive in macrophage, CD34 negative in tumoral cells, without tumoral embols in the vessels, AE1/3 negative, CK8/18 negative, CK7 negative, Factor XIIIa positive (Figures 2–4).

The final diagnosis was for malignant fibrous histiocytoma.

MFH may arise from the renal parenchyma but the relation of the given tumor to the kidney cannot be judged. The fatty capsule can be the site of origin. The retroperitoneal soft tissue is a more common site of MFH.

Discussion

Malignant fibrous histicytoma is the commonest primary malignant soft-tissue tumor of the extremities and retroperitoneum in adults.

The average age at diagnosis is 50 years, but all age groups are affected [1, 2, 4]. Many patients clinically present with a painless mass that has been evident for several months.

The tumors have a high recurrence rate after resection, and 50% have already metastasized (lung, liver, bone, lymph nodes) by the time of diagnosis [2].

The clinical manifestations are depending upon the size of the tumor and are very unspecific [2, 4, 8]. The lesion can grow to a large size, due to their retroperitoneal location, before causing symptoms – this contributing to delay the diagnosis of the disease [4].

Nevertheless, the most common symptom is pain in
The initial diagnosis is based on the imaging findings, which offer information on the composition, density, extend and relation to the adjacent organs and structures, with the identification of displacement of the kidney, the ureter or bladder in relation to the tumor [7, 9].

Invasion of the inferior vena cava or renal vein usually is not found. This distinguishes malignant fibrous histiocytoma from advanced renal cell carcinoma [2, 7].

Although malignant fibrous histiocytoma is clinically and radiologically indistinguishable from the renal carcinoma [8, 9], the condition should be suspected in the presence of certain radiological features: (a) tumors measuring over 10 cm in size at the time of diagnosis, with no invasion of the renal parenchyma or renal vein or vena cava; (b) tumors showing various intensities in the MRI images (areas that appear hypodense in T1- and T2-weighted sequences, reflecting the fibrous components; areas the appear hypodense in T1- and hyperdense in T2-weighted sequences, reflecting cystic degeneration, necrosis or regions with abundant histiocytic cell) [4, 7, 10]; (c) tumor with hypodense areas corresponding to multilocular cystic degeneration, and hyperdense areas corresponding to calcifications in CT scans [7, 8].

The definitive diagnosis is established by the pathology findings. Macroscopically, these are large and multilobulated tumors, of a yellow-gray color, with hemorrhagic areas containing necrotic zones [2, 5].

Retropertioneal MFH usually presents with constitutional symptoms, including fever, malaise, and weight loss [4, 8]. The tumors are often larger than 10 cm in diameter at the presentation and may cause displacement of the bowel, kidney, ureter and/or bladder [10–12].

MFH was regarded as the most common soft tissue sarcoma of the late adult life for almost 25 years [8, 13]. Serious doubts have been raised about the existence of MFH as a specific entity. Adult between 50–70 years sometimes in the retroperitoneum. Some of the tumors arise at the site of previous radiation therapy, at the site of surgical scar. Macroscopically, these are large multinodular gray-white tumors. These tumors share common histological features: pleomorphic tumor cells, bizarre multinucleate or Reed–Sternberg like cells may be present. Similar features are noted in metastatic carcinoma from large bowel, lung or kidney, in irradiated osteosarcoma, other sarcomas (e.g., leiomyosarcoma), T-cell lymphoma, histiocytic lesions, xanthogranulomatous pyelonephritis [16].

Giant cell MFH is usually located in the skeletal muscle of the extremities. Superficial tumors (subcutis or fascia) have a better prognosis than deeply situated (subfascial) tumors. Microscopic features are: multinodular tumoral cells composed by fibroblasts, histiocytes and osteoclast like giant cells, focal osteoid or bone formation present at the periphery, stromal hemorrhage is present, cell display pleomorphism and mitotic figures are conspicuous. When neoplastic osteoid and bone formation is prominent, it is justifiable to call the lesion giant cell variant of soft tissue osteosarcoma. Leiomyosarcoma with osteoclast like cell is a subgroup of this variant. Differential diagnosis must to be made with carcinoma (lung, thyroid, pancreas), other sarcomas with giant cells, rarely melanoma [5, 16, 17].

Myxoid MFH is usually located in the extremities (mostly subcutaneous in location) and are associated with better prognosis. Microscopically, the tumor has a gelatinous appearance: hypocellular area containing: hyperchromatic spindle or stellate cells, delicate blood vessels are prominent. The tumor cells resemble lipoblasts but contain acid mucin and not lipid in the cytoplasmic vacuoles (pseudo-lipoblasts). Differential diagnosis: myxoid liposarcoma, intramuscular myxoma, angio-myxo-sarcoma, low-grade fibromyxoid sarcoma, mixoid variants of nerve sheath tumor and smooth muscle tumor (immunohistochemistry plays an important role in establishing the final diagnosis) [14, 18, 19].

Storiform-pleomorphic MFH (Figure 9), this variant probably embraces well-defined sarcomas of various types with largely anaplastic features (e.g., pleomorphic leiomyosarcoma, rhabdomyosarcoma, liposarcoma). The tumor is usually located in the deep fascia or substance of the skeletal muscle of the extremities and sometimes in the retroperitoneum. Some of the tumors arise at the site of previous radiation therapy, at the site of surgical scar. Macroscopically, these are large multinodular gray-white tumors. These tumors share common histological features: pleomorphic tumor cells, bizarre multinucleated cells, storiform pattern, inflammatory cells composed of lymphocytes, plasma cells, eosinophils and xanthoma cells [6, 17, 19].

Angiomatoid MFH (Figure 10) has a slow growing nodular or cystic tumor; microscopic features are represented by solid nets of fibroblast like and histiocyte like cells, large blood filled cystic spaces and areas of hemorrhage, lymphoplasmacytic infiltrate is present. Immunohistochemistry shows: desmin positive, muscle actin (HHF-35) positive, SMA negative, CD68 usually positive [14, 20–23].

MFH is a neoplasia of mesenchymal origin with two well-defined cellular types: histiocytic and fibroblastic. The diagnosis is histological and the differential diagnosis is especially important with pleomorphic sarcomas. MFH tends to appear in the fifth and the sixth decades of life.
Any primary malignant tumor in the soft tissue of the extremities or retroperitoneum presenting after the age of 45 years is most likely MFH. In younger patients, the most frequent diagnosis would be liposarcoma. Because of the great tolerability of retroperitoneal space, these tumors have a long asymptomatic evolution that is correlate with its dimensions. Abdominal MFH is difficult to diagnose, even CT-scan and MRI offer a lot of information for diagnosis; surgical exploration is the most important step for evaluation of retroperitoneal tumors. The treatment of choice is surgical with wide resection margins to allow local control of the disease and if distance metastases are seen, chemotherapy is also advisable. Because of its aggressive nature, radical excision of MFH is the recommended treatment. Prognosis of MFH is usually poor.

Conclusions

Primary malignant tumor in retroperitoneum after age of 45 years is most MFH. The great dimension of retroperitoneal MFH is correlated with tolerability of this large retroperitoneal space. Diagnosis in abdominal MFH is difficult; it requires CT-scan, MRI and histological examination.

References


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