

Malignant fibrous histiocytoma of the mesentery: report of two cases and review of the literature

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SUMMARY: Malignant fibrous histiocytoma of the mesentery: report of two cases and review of the literature.

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Malignant Fibrous Histiocytoma (MFH) rarely affects the abdomen and only a few cases arising in the mesentery have to date been discovered. In this paper, two cases of MFH of the mesentery are described and a review of the literature is reported.

RIASSUNTO: Istiocitoma fibroso maligno del mesentere: analisi di due casi e revisione della letteratura.

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L'Istiocitoma Fibroso Maligno (IFM) solo di rado colpisce l'addome e, fino ad oggi, solo pochi casi di origine mesenteriale sono stati riportati. In questo articolo gli Autori descrivono due casi di IFM del mesentere con una revisione della letteratura.

KEY WORDS: Malignant fibrous histiocytoma - Abdomen - Mesentery - Soft tissue sarcomas.
Istiocitoma fibroso maligno - Addome - Mesentere - Sarcomi dei tessuti molli.

Introduction

The term Soft Tissue Sarcomas (STS) refers to a group of rare malignant tumours arising in the extra-skeletal connective tissue (1). Malignant Fibrous Histiocytoma (MFH) is the most frequent STS in adults, as a rule primarily affecting the limbs, rarely the abdomen. In case of abdominal involvement, the mesenteric origin is exceptional to date only a few cases having been described. We report two cases of MFH of the mesentery.

Case reports

Patient n. 1

An 88-year-old female was admitted with a four-week history of progressive abdominal distension, mild abdominal pain, abdominal fullness, dyspnoea, and nausea. At physical examination, the abdomen was distended and a 15 cm palpable mass was found, extending from the lower epigastric to the periumbilical area, and accompanied by ascites. At palpation, the mass was, smooth, lobulated, firm, and mildly tender.

An abdominal ultrasound scan and a total body computed tomography were performed, showing a discrete, inhomogeneous mass with alternated lower density fluid-like and increased density vascularised areas (Fig.1), while both liver and lungs were clear. Blood tests showed mild anaemia (Hb=11.4 g/dL, Ht=33.4%) and increased CA-125 (= 980 U/ml, normal values < 30 U/ml).

At laparotomy, the mass originated from the mesentery and involved 45 cm of the small bowel, also infiltrating an adjacent bowel loop and the greater omentum. A double bowel resection with radical excision of the tumour was performed. No liver or other distant metastases were found. The neoplasm was encased in a pseudocapsule, measured 12 x 9 x 7 cm, and weighed 4 kg. On the cut section the mass was fleshy, white-grey, and had a soft consistency. Microscopically, there was a complex structure, with fascicles of spindle cells, sometimes showing a storiform growth pattern, separated by epithelioid areas. Myxoid areas composed by stromal cells showing different degrees of differentiation were also present (Fig. 2). The cells had fusiform nuclei, sometimes with rounded edges and mainly eosinophilic cytoplasm. In other areas the cells had a vacuolated appearance, or showed monstrous and gigantic nuclei. Mitotic index was high, with 15 mitoses/10 HPF. The small bowel showed multiple infiltrations. A diagnosis of pleomorphic type MFH was made, which, according to the International Union Against Cancer, was classified stage IV A, poorly differentiated (G3) (2).

Post-operative course was uneventful, and the patient was discharged home 10 days after surgery. However, four months later she presented abdominal recurrence with liver metastases and died after two months.

Patient n. 2

A 63-year-old female was admitted with a four-month history of progressive abdominal distension, weight increase (6 kg), and dyspnoea. At physical examination, there was a distended, hypo-

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mobile abdomen, while at palpation there was a large, painless, lobulated, firm mass, extending from the right flank to the right iliac fossa.

Computed tomography showed a 13x17x 19 cm lesion.

At surgery, the neoplasm consisted of three masses originating from the mesentery, each weighing respectively 0.9, 1.5, and 6.2 kg, which were all removed. Histology showed some areas with fascicles of spindle cells variously oriented, while other areas had storiform growth features, with plump spindle cells mixed with giant pleomorphic cells, some of which multinucleated and containing intensely eosinophilic droplets (Fig.3). A diagnosis of MFH, storiform-pleomorphic type was made also in this patient.

Post-operative course was normal, and the patient was discharged home 8 days after surgery. After 12 months, the patient is well and has no signs of recurrent disease.

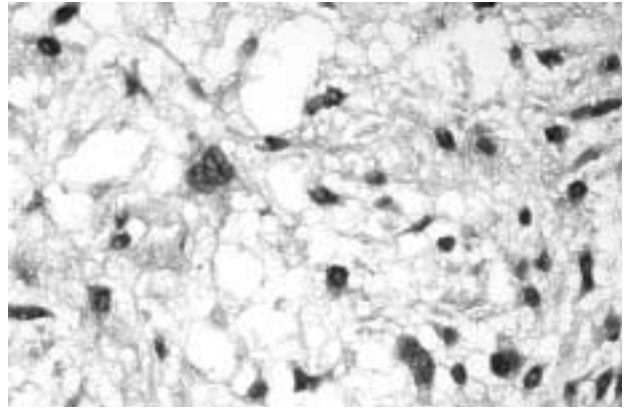


Fig. 3 - Giant pleomorphic cells some of which multinucleated and containing intensely eosinophilic droplets (H&E x250).

Discussion

STS are rare, representing only 1% of all human

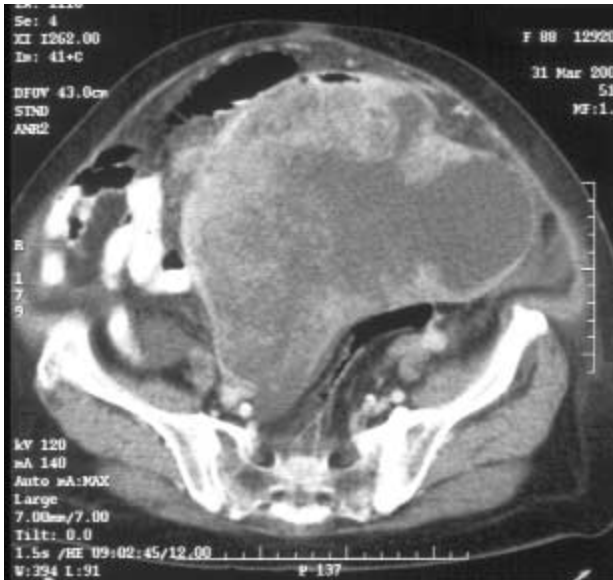


Fig. 1 - Abdominal computed tomography showing a discrete, inhomogeneous mass with alternated lower density fluid-like and increased density vascularised areas.

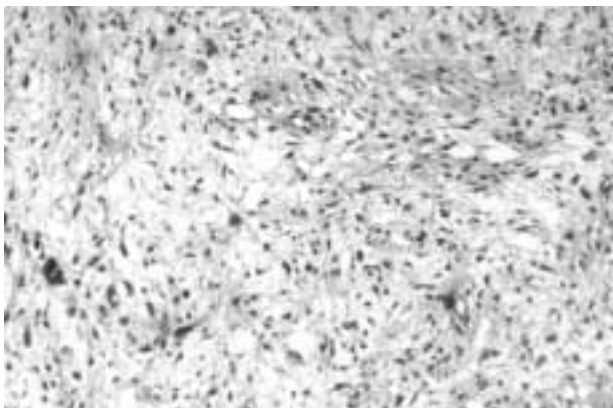


Fig. 2 - Myxoid areas composed by stromal cells showing different degrees of differentiation (H&E x 100).

malignant neoplasms. Among all STS, MFH are the most frequent, with highest incidence in the sixth and seventh decades of life (3). MFH was first identified in 1963 (4), and is characterised by pleomorphic, storiform, or stellate elements, all deriving from mesenchymal cells, which explains possible primary involvement of any tissue (5). Previously to its identification, cases of MFH were either classified as pleomorphic liposarcoma or as rhabdomyosarcoma. The male to female ratio is 2:1. Five main morphologic types of MFH have been identified, which, in decreasing order of frequency, are: 1. storiform-pleomorphic; 2. myxoid; 3. giant-cell; 4. angiomatoid; 5. inflammatory. Of note, is that the inflammatory type most commonly affects the retroperitoneum and exceptionally the limbs. Aetiology of MFH is unknown most STS arising *de novo*, and only few affecting areas of previous radiation exposure (3, 6, 7), fracture (8), or bone infarct (9-11). Up to 13% of these patients develop synchronous tumours, although this figure is probably biased by the advanced age of this population and, therefore, it is of no statistical significance (9). Most frequently the limbs are involved (68% of cases), followed by the abdomen and retroperitoneum (16%) (3), (5).

There are not known risk factors for the development of abdominal or mesenteric MFH. Signs and symptoms of MFH are non-specific and mainly related to site, size, and to its speed of growth, which, similarly to other tumours, may increase during pregnancy (12). Paraneoplastic syndromes in MFH have only rarely been reported (3, 13-15). When limbs are interested, the tumours are usually discovered at an early stage, due to the clinical findings and to the involvement of muscles and tendons. Abdominal MFH, on the contrary, grow slowly and remain clinically silent for a long time, with non-specific signs and symptoms, mainly consisting of mere sense of abdominal weight and tension, which consorts with the huge dimensions of these abdominal lesions when they are eventually

removed and implies a later diagnosis and worse prognosis (16, 17). Furthermore, the absolute lack of specific symptoms makes pre operative definitive diagnosis practically impossible, while blood results and instrumental work-up is of no use to differentiate between MFH and other sarcomas. Preoperative work-up necessarily implies the assessment of metastases in order to optimise surgical treatment. Metastases to lymph nodes are difficult to ascertain but seem relatively rare (4-17%)(18,19), while pulmonary (90%), bone (8%), liver (1%), and bone secondaries (21-57%) occur more frequently and are related to size, grading, site, and maybe type of primary MFH (3, 17, 20-22).

Macroscopic features vary in relation to site of development, abdominal lesions appearing as huge, lobulated lesions, in contrast with limb lesions which, as a rule, are smaller, being discovered at an earlier stage, and have, sometimes, a fusiform appearance (17). Furthermore, while abdominal MFH appear macroscopically well delimited and are, sometimes, encased in a pseudocapsule, MFH affecting limbs (in 2/3 of patients located within the muscles) often expand microscopically along the fascial planes or along the muscular fibres, which explains the high incidence of local recurrences (up to 80% of cases). On the cut section, the neoplasm may show different features in relation to the main component, varying from a yellowish appearance in the inflammatory type (due to xanthomatous cells) to a brownish colour in the haemorrhagic forms, in which bleeding can also be so massive to turn the tumour into a fluctuating lesion, such as in cystic haematoma (3).

Prognosis mainly relies upon staging of the disease, which, in turn, depends from histological grade, number of mitoses, bone, vessel, or nerve infiltration, and metastases. Other important variables are size of the tumour, and possible site and type (17,19). Five-year survival rate is 82% for MFH smaller than 5 cm, 68% for lesions between 5 and 10 cm, and 51% for tumours bigger than 10 cm. Histological grade is also important for prognosis: 5-year survival rates decreasing from 80 to 60% in relation to good or moderate differentiation.

If tumour size and histological grade are conjointly taken into account, at one extreme there is a 5-year survival rate of 93% for lesions smaller than 5 cm and with low level of malignity, and at the other of 41% for those tumours bigger than 10 cm and with high level of malignity (17). The weight on prognosis of MFH histological type is debatable. Some authors considering the histological variant irrelevant (23,26), others attributing a different prognosis to each type, in relation to lower tendency to metastasise of some forms, such as the inflammatory type (3).

Treatment of MFH mainly consists of surgical removal, and in case of abdominal lesions the treatment of choice is *en bloc* excision. If radical surgery is not possible, metallic clips should then be inserted within the operative field to better target later radiotherapy. In case of MFH of the limbs, even if the lesion is macroscopically circumscribed, at least 2 cm of apparently clear tissue should be removed and, if needed, amputation performed, in order to achieve radical resection of the tumour, should microscopic infiltration along muscles and tendons occur. As a matter of fact, later recurrences would be difficult to treat and of ominous significance.

In presence of distant metastases, while there is no indication to treat multiple secondaries, surgical removal of single pulmonary metastasis has sometimes produced good results. In case of MFH of the limbs, surgical treatment of metastases to regional lymph nodes has been beneficial, and routine removal of regional lymph nodes has therefore been recommended (19).

Both chemotherapy and radiotherapy do not have precise indications or standardised modalities of administration. Some researches have shown MFH to be radio- and/or chemo-resistant (17,27-32), while others have proven beneficial results (33-41). Such conflicting results are probably related to the rarity of this condition, which makes it difficult to perform controlled clinical trials and to compare homogenous subsets of patients. At present, uncertainty of the results and advanced age of these patients do not warrant their employment, which is probably only justified in cases selected for age and clinical stage.

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