Cardiac metastasis in malignant fibrous histiocytoma

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ABSTRACT

يعتبر الورم النسيجي الليفي الخبيث (MFH) سرطان عدواني ذو خلية مغزلية، وهو أكثر أورام النسيجية الطرية شيوعاً بين المسنين. يصيب في بادئ الأمر الأطراف. لديه انتشارا عالي ويمكنه الانتشار في مختلف الأحشاء بما في ذلك الكبد والرئة والعظام والدماغ. ولكن يعتبر الانتشار في القلب نادراً للغاية. نذكر هنا حالة لرجل يبلغ من العمر 50 عاماً، شخصت بورم نسيجي ليفي خبيث في الذراع اليمنى، وأصيب بانتشار للورم النسيج الحشوي للرئة وآفة كتلة في الأذين الأيسر. تدهورت حالة المريض ومن ثم توفي.

Malignant fibrous histiocytoma (MFH) is an aggressive spindle cell cancer and is the most common soft tissue tumor in the elderly, primarily affecting the extremities. It has high metastatic potential and can spread to various viscera including liver, lung, bone, and brain; however, cardiac metastasis is an extreme rarity. Here, we present a 50-year-old male, diagnosed as pleiomorhphic storiform MFH a of right arm who developed parenchymal pulmonary metastases and a mass lesion in left atrium. Patient had a downhill course and eventually succumbed.

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Although metastases of soft tissue sarcoma are site specific yet no site is immune and atypical and unusual presentations can be identified. The formation of metastatic foci is a continuous process, and newer lesions appear depending on tumor duration and tumor burden. Malignant fibrous histiocytoma (MFH) can spread to various viscera including liver, lung, bone, and brain, however, cardiac metastasis is an extreme rarity. The patient under discussion had a soft tissue MFH which eventually spread to lungs and left atrium as was seen in contrast enhanced computed tomography of chest and 2D echocardiography.

Case Report. A 50-year-old male presented with one year history of painful progressive swelling on the medial aspect of right arm of 6 months duration. Clinical examination showed 10 cm x 10 cm, nontender, firm, immobile swelling with normal overlying skin. Excision biopsy revealed MFH (pleomorphic storiform) (**Figure 1**). Staging work up did not show any metastasis. The patient was administered 4 courses of intensive combination chemotherapy consisting of injection Ifosfamide 5 gm/m^2 d1-d5 and etoposide 325 mg/m^2, d1-d3 every 3 weeks. Further, chemotherapy was abandoned as patient developed acute hepatitis B (HbsAg positive). The follow-up CT scan of the chest (5 months later) was normal. Eight months later, he developed persistent cough, progressive dyspnoea and generalized weakness. Clinical examination revealed a performance status III (ECOG), drowsiness with a respiratory rate of 40/mt, pulse 120/mt, BP 120/80 mm Hg, raised jugular venous pressure, clubbing, mild pedal edema, bilateral pleural effusion, and hepatosplenomegaly, while as cardiovascular system examination was normal and there were no neurodeficit. Investigations showed hemoglobin 9.1 gm/dl (12 -16gms/dl), lactate dehydrogenase 930 U/L (240 -480 U/L), kidney function tests and electrolytes were normal, arterial blood gas revealed hypoxia. Chest x-ray showed multiple bilateral lung secondaries. The 2D echo Doppler echocardiography revealed a mass of variable echo texture in left atrium lying against the postero-superior margin. Patient was in sinus rhythm, and the left ventricular functions were normal. Computerized tomography chest revealed large filling defect seen within left atrium extending across the mitral valve with evidence of multiple parenchymal metastases and pleural effusion with mediastinal shift and compression of underlying left lung (**Figure 2**). No surgical intervention was possible

because of poor surgical risk. The patient was managed symptomatically until he expired.

Discussion. Malignant fibrous histiocytoma is a fibrohistiocytic group of soft tissue sarcoma, first described by Stout and Lates in 1967[1] and its ultra structural study was published by Merkow et al[2] in 1971. The tumor has a diverse histology, and majority of tumors are composed of spindle cells (fibroblasts) and round cells arranged in storiform and pleomorphic areas of giant and inflammatory cells. Five major morphologic types were described, viz; Storiform (pleomorphic), myxoid (myxofibrosarcoma), giant cell types (malignant giant cell tumor of soft parts), inflammatory type (xanthosarcoma, malignant xanthogranuloma) and angiomatoid.[3] The pathophysiology of MFH are far from settled, however, facultative transformation of tissue histocytes with fibroblast like cells is hypothesized. The most characteristic features of MFH are large number of multinucleated epuilis type giant cells of variable size which is ultimately associated with smaller histiocyte looking mononuclear cells and spindle shaped fibroblasts. Malignant fibrous histiocytoma cells express human leukocytic antigen-DR and fibroblastic associated antigens, but are negative for Leu-3, Leu-M3, OKM1 (histocytic markers) and T200 (a leukocytic common antigen).[4] Malignant fibrous histiocytoma was seen following irradiation of breast carcinoma, exposure to phenoxyacids, preexisting bone infarcts (intraosseous MFH), retinoblastoma, hodgkin's disease and multiple myeloma. Approximately 10% of patients with MFH had or subsequently developed a second neoplasm. The tumor was induced in experimental animals with tea extracts and with macrophages transformed with SV40 virus. The 2/3rd of MFH occurs in men and whites are more affected than blacks and orientals. It is the most common soft tissue sarcoma of late adult life (50-70 years). Diagnosis should be made in caution in patients less than 20 years of age. The tumors most frequently occur in lower extremity followed by upper extremity and retro peritoneum. Malignant fibrous histiocytoma are of considerable size, average size is larger than 10 cms. These tumors almost never present as metastatic disease without a clinically evident primary lesion, and this observation helps in the evaluation of isolated spindle cell neoplasm in lung and lymph node. Occasionally fever, leukocytosis with neutrophilia, or eosinophilia may dominate the clinical picture of the disease especially in inflammatory type of MFH, though seen in other types as well. Both eosinophilic chemotactic factor and eosinophilopoietic activity have been detected in tumor extracts of MFH; these symptoms usually remit following tumor removal. The treatment is surgery and about 1/3 of patients recur locally and more than half metastasize to lungs.

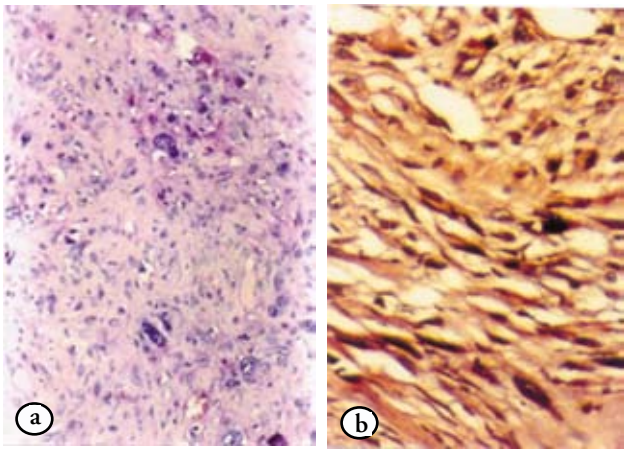

Figure 1 - Histopathology results **a**) High power microscopy revealing bizarre tumor giant cell in malignant spindle cell storiform of MFH (hematoxyline and eosine x 40). **b**) High Power photography showing malignant cells resulting, fibroblast, myofibroblasts, histiocytes and potential mesenchymal cells, with presence of bizarre nodules (Masson's trichrome stain x 40).

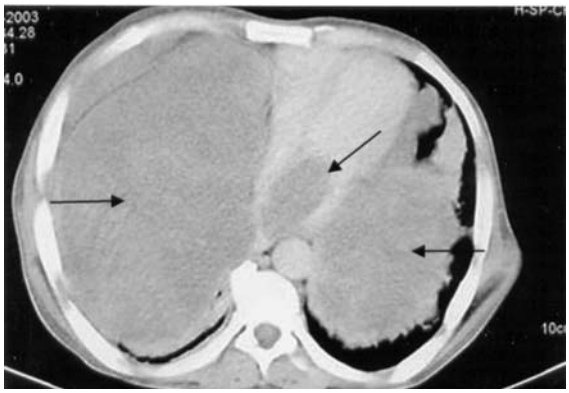

Figure 2 - Contrast enhanced CT chest showing multiple parenchymal metastases, left pleural effusion and a filling defect in the left atrium extending across mitral valve.

Malignant fibrous histiocytoma has a distinction of having primary cardiac origin, where it presents early (mean age 36 years) and with female predominance.[1] However no age is exempted. Primary MFH in the left atrium of a 72 year male and a 16 year old boy have been reported.[5,6] The tumor arises mainly from left atrium; however, while reviewing the literature, Armed Forces Institute of Pathology (AFIP) has reported a series of 14 cases, the tumor location has been from right ventricle in 4 cases, left ventricle 2, right atrium 2, left atrium 4. Primary site could not be determined in 2 cases.[7]

The clinical features are due to mass effect, impeding the chamber filling and outflow. In AFIP series, 80% had more than one symptom[8] Nearly half of the patients had cardiac murmurs, pleuritic chest pain,

fever, and dyspnoea, had non-specific electrocardiogram change, chronic cardiac failure, and a small percentage had cyanosis, dyspnoea, embolic phenomena, weight loss, fever, malaise, and chest pain. Synchronous/ metachronous visceral metastases can occur in liver, bone, brain, pleura, nevertheless, the spread to heart is rare. Lee and Fisher[8] reported a case of solitary cardiac metastasis from MFH of the scalp.[8] A case has been reported of a patient with pulmonary metastasis of MFH with left atrial infiltration via pulmonary vein, an extreme rare occurrence.[9] The median survival after diagnosis has been 1 month to 48 months. Surgery is the mainstay of treatment irrespective of nature of origin, however, in some patients, chemotherapy and radiotherapy have been instituted postoperatively achieving high degree of palliation. The tumor is uniformly fatal, and the survival is between 1-4 years after onset of symptoms. Majority of the patients recurred within 4-10 months after resection. Survival is predicted by the histological subtype, depth of tumor invasion, location (distal versus proximal) and the presence of metastasis.[10]

The spread is hematogenous, although a retrograde spread from lungs to heart can also occur. The organ tropism of tumors in general and soft tissue tumors in particular is known. Several hypothesis proposed to include a preferential growth of tumour cells induced by local factors/hormones in the target organs, special recognition of signals on the endothelial cells and the tumour cell response to soluble factors, diffusing locally out of target organs.[11] Such chemo kinetic and chemo tactic mechanisms besides expression profiling of tumours, biologic behavior and gene expression, hypothesizes the metastatic ability, and overall prognosis. The unique cardiac metastatic presentation of MFH awaits further analysis in future by a large series to unveil the gaps in the overall management.

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