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Undifferentiated Pleomorphic Sarcoma with Multiple Metastases: A Case Report

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Abstract | **Case Report**

The undifferentiated pleomorphic sarcoma (UPS) is a rare type of mesenchymal neoplasm based on the absence of a specific line of differentiation under histological examination and techniques such as immunohistochemistry. Very little is known about the management of this entity, and surgery is yet the first line of treatment being other methods still unsatisfactory. We report a peculiar case of death of a 77-year-old man presenting upper gastrointestinal bleeding as one of the first symptoms of UPS with numerous metastases to the bones, skin, hemithorax and stomach. This case brings interesting reflections from the clinical, histopathological and radiological point of view.

Keywords: Malignant fibrous histiocytoma, Sarcoma, Cancer, Pathology.

INTRODUCTION

The High-grade Undifferentiated Pleomorphic Sarcoma (UPS), first described in 1961 by Kauffman and Stout as malignant fibrous histiocytoma (MFH) [1], is a rare entity, with a frequency of 1-2 cases per 100,000 people [1, 2], but among soft tissue sarcomas, is the most common of adulthood. There is a slight predominance in males from the sixth and seventh decades of life [3]. The MFH was classified into three subtypes: pleomorphic, inflammatory and giant cells. However, by the 2002 World Health Organization (WHO) classification of bone and soft tissue tumors, pleomorphic HFM was renamed UPS [4].

The UPS usually forms a fast-growing, painless, histopathologically solid structure characterized by spindle-shaped and pleomorphic tumor cells, with storiform pattern and growth, no line of differentiation and a variable amount of histiocytes which seem to be just reactive, and play no role in the etiopathogenesis of the lesion or indicate a distinct prognosis.

Immunohistochemistry is generally positive for CD68 (focal), keratin, actin, desmin, EMA, CD99, and CD34, but UPS is still a diagnosis of exclusion [2, 5]. Most high-grade UPS originate from the retroperitoneum and extremities with more common metastasis to the lung and long bones, especially metaphysis and diaphysis [2, 4]. We present an uncommon case of UPS with numerous metastases: to the humerus, left hemithorax and stomach, discovered after upper gastrointestinal bleeding.

CASE PRESENTATION

A 77-year-old white man, former college professor, married, reported to the Emergency Department, with upper and lower digestive hemorrhage and shoulder pain. Denied the use of tobacco and alcohol. Denied any family history of malignancy. The patient had no fever and showed stable vital signs and a nuisance general appearance, but the physical examination revealed a subcutaneous lesion on the lateral face of the right thigh. Soft tissue ultrasonography of the thigh displayed a hardened lesion without invasion of the muscular plane, difficult to measure and compatible with a heterogeneous septation-lobed solid lesion, with a distance between skin and lesion ranging from 0.1 to 0.4 cm from the skin.

At first, it was performed an upper digestive endoscopy, which showed remarkable and intense enanthematous pangastritis, with intramural lesions in the stomach and duodenum, related to a possible metastasis. The multiple lesions presented ulcerated apices, measuring between 5 and 15cm (biopsy over

biopsy), located in the antrum and especially in the body.

He had a limited range of motion on his right upper limb due to severe pain in proximal 1/3 of the humerus, with no phlogistic signs or fistulas. At the anteroposterior radiography, it was observed a lytic aspect lesion - fracture of the diaphysis, without soft tissue invasion, well delimited, without calcifications or periosteal reactions (Figure-1). The patient also presented a dense mass in the upper 1/3 of the left hemithorax, about 5cm, painless and not adhered to the deep planes. Other imaging exams such as magnetic resonance imaging and computed tomography were performed to assess the extent of the lesions. Given a large number of metastasis sites and the advanced degree of the disease, we take the right thigh as the probable primary site of the disease, as it usually presents in extremities and this was the location where the patient noticed the appearance of the first nodule.

Routine laboratory tests revealed severe anemia treated with blood transfusion. Transaminases, albumin, total protein, magnesium, sodium, and calcium levels were below laboratory reference levels. The C-reactive protein, beta-2 globulin, globulin, and urine summary levels were elevated.

Biopsy specimens of the nodular lesion in the left pectoral region, the fragments of the right humerus bone lesion and the elevated gastric lesions showed malignant neoplasia composed of atypical, irregular, rounded, spindle-shaped cells, associated with extensive necrotic areas. The lesions were predominantly diffuse and pleomorphic, with no morphological pattern or cytological differentiation line. The nuclei were large, crowded and pleomorphic, including vesicular, elongated, spindle-shaped, and occasionally bizarre and multinucleated giant cells. Immunohistochemical reactivity showed positivity to vimentin and CD99, but negativity AE1 / AE3, Actin HHF35, Sarcomeric Actin, SMA (Smooth Muscle Actin), CD31, CD34, Desmin, Caldesmon, FLI-1, HMB45, Melan-A, PSA, CD68 and S100. Reaction with Ki67 marked 4% of nuclei (Figure-3). The conclusion was a high grade undifferentiated pleomorphic sarcoma with multiple metastases.

The medical team aiming to allow greater mobility and pain management referred in the patient`s right upper limb, fixation surgery was performed, using an intramedullary osteosynthesis. The orthopedic procedure was associated with physical therapy, and the patient presented pain reduction and movement evolution during the hospitalization period. In the case of our patient, the therapeutic actions were based on the identification of symptoms and relief, enabling a better quality of life.

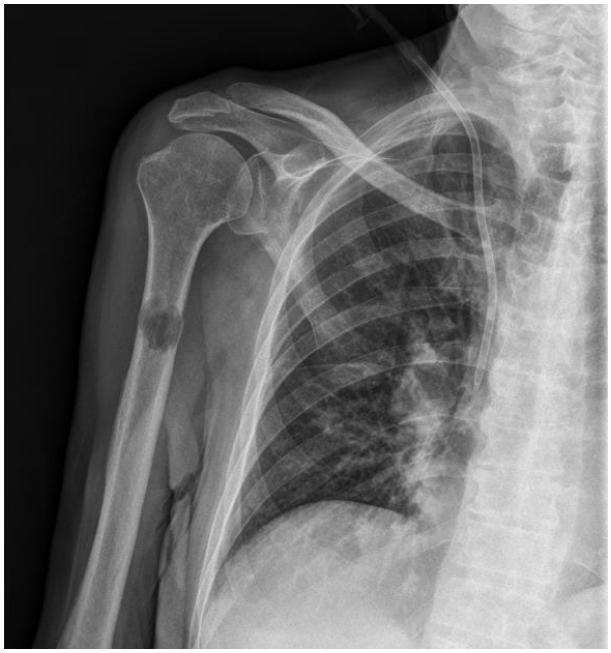

Fig-1: Right shoulder radiograph. Lytic lesion in the proximal diaphysis humerus with pathological fracture and adjacent soft tissue gases

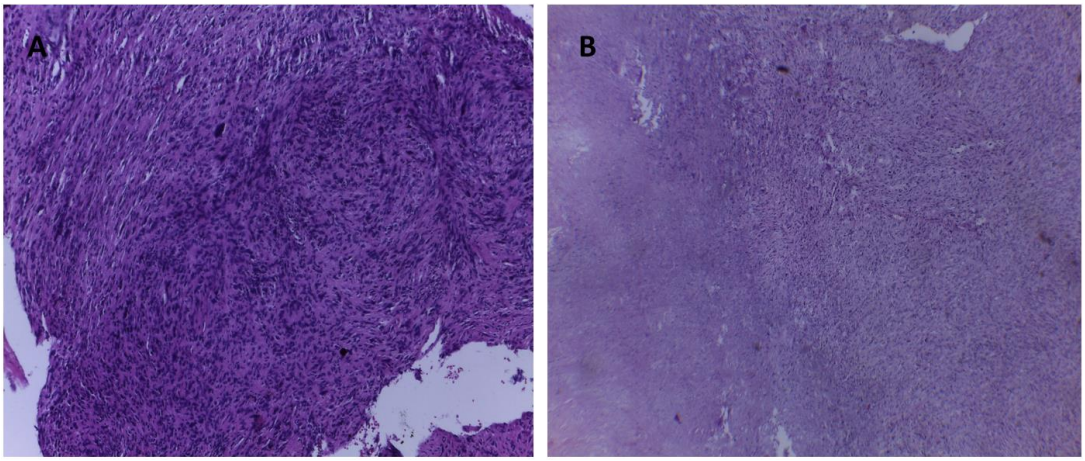

Fig-2: (A) Gastric biopsy. A poorly differentiated mesenchymal tumor presenting large malignant cells forming pleomorphic-storiform areas. (B) Skin biopsy. A poorly differentiated mesenchymal tumor showing storiform pattern and ample zones of necrosis (H&E, original magnification × 100)

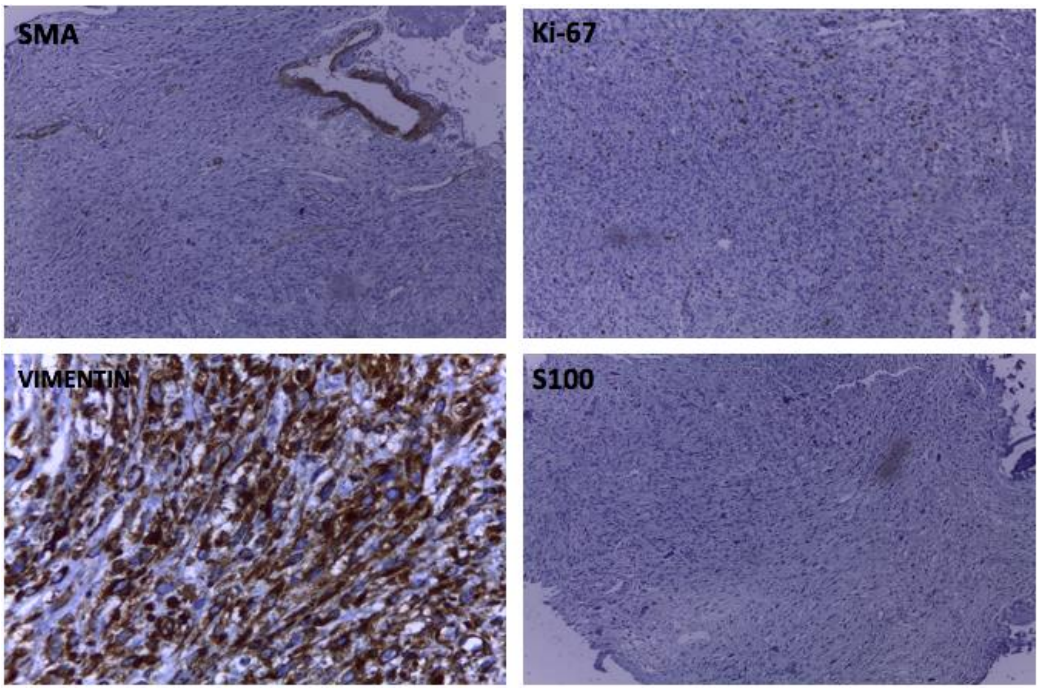

Fig-3: Immunohistochemical analysis. The malignant cells show strong positivity to vimentin. The S100 and SMA expression was negative. Reaction with Ki67 marked 4% of nuclei

DISCUSSION

Sarcomas are rare and represent 1% to 11% of neoplasms, with UPSs being only 5% of sarcomas [3-5]. This malignant neoplasm can occur anywhere in the body, but rarely occurs in bones and other organs. In general, high-grade UPS is considered an aggressive sarcoma, clinically presenting fast-growing, painless, soft-tissue solid-looking lesions with poor prognosis, with a reported 2-year survival rate of 60% and a survival rate of 5 years of 47% [2, 4, 6].

It is worth mentioning that the study through imaging exams was essential for the attempt to delimit the extent and location of the lesions. Most tumors show different nonspecific signal strength on CT and MRI images. The CT may help assess bone destruction and soft tissue lesions. However, magnetic resonance imaging is considered to be the best tool to identify soft tissue extension and compression of adjacent tissues.

The UPS is a diagnosis of exclusion based on the absence of a specific line of differentiation after careful histological examination and use of ancillary techniques such as immunohistochemistry. Some differential diagnoses should be considered and excluded before making the final diagnosis, such as melanoma, poorly differentiated carcinoma, dedifferentiated liposarcoma, pleomorphic liposarcoma, pleomorphic leiomyosarcoma, myxofibrosarcoma, pleomorphic rhabdomyosarcoma, and malignant peripheral nerve sheath tumor.

Surgical resection with sufficient margin is the first-line treatment, according to the National Comprehensive Cancer Network (NCCN) Soft Tissue Sarcoma Guidelines, and amputation is required in cases of limb involvement [7]. Broad excision associated with radiotherapy it is recommended due to its high propensity for local recurrence (exceeding 31%) and metastasis [2, 8-10]. The combination of chemotherapy, radiotherapy or hyperthermia has been used for unresectable tumors and has obtained unsatisfactory results. While the combination of cisplatin, ifosfamide, and adriamycin to reduce metastasis was used to reduce metastases [11-13]. The severity of the lesions and the present advanced metastatic disease in our patient indicated that curative treatments were inadequate, and targeting quality of life supportive care [14].

The presence of metastatic disease is usually associated with a poor prognosis, which in our patient's case is supposed to be due to the delayed histopathological diagnosis of the lesion on the lateral aspect of the thigh. As already mentioned, the occurrence of metastases is rare, for example, pulmonary metastases observed in only 5% of patients [15].

CONCLUSION

We present a well-illustrated advanced case of UPS with numerous metastases, accompanied by upper gastrointestinal bleeding. The case arouses attention, from the histopathological point of view, by the wide negativity of markers and low Ki67. While from the radiological point of view by a large number of lesions. Besides, the disease represents a diagnostic challenge, which takes time, due to diagnostic exclusions. The diagnosis became possible only through the clinicopathological correlation and

immunohistochemical technique. The metastatic UPS remains an extremely rare malignancy without standardized treatment and poor prognosis and given the advanced state of the disease, complete surgical excision was not an option, being adopted palliative care. Further investigation and data collection are needed to better understand this rare entity.

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