INTERNAL MEDICINE - PEDIATRICS

PROLONGED FEVER WITHOUT OBVIOUS ETIOLOGY FINALLY DIAGNOSED AS HIGH-GRADE SOFT TISSUE SARCOMA

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PROLONGED FEVER WITHOUT OBVIOUS ETIOLOGY FINALLY DIAGNOSED AS HIGH-GRADE SOFT TISSUE SARCOMA (Abstract): Sarcomas represent a challenge to clinicians as they are rare and diagnosis is often delayed. Soft tissue sarcomas are relatively uncommon cancers, the incidence is estimated about 1% from all malignant tumors. Due to aggressive biological behavior of pleomorphic undifferentiated sarcoma diagnosis must be made as quickly as possible. MRI is the standard imaging modality for investigating possibly malignant masses. Excisional biopsy appears to be necessary for differentiating soft tissue sarcoma from expanding hematoma. FDG PET scans may be helpful in specific circumstances (as was the situation in our case, because the lesion is composed from two components: an area without precise edges and a necrotic-cystic area). Keywords: SOFT TISSUE SARCOMA, FDG PET SCAN, PROLONGED FEVER, EXCISIONAL BIOPSY.

The large majority of soft tissue tumors are benign, with a very high cure rate after surgical excision. Soft tissue sarcoma (STS) incidence is estimated about 1% of malignant tumors, life-threatening being the main problem, the diagnosis and treatment representing a significant challenge due of more than 50 histological subtypes of soft tissue sarcomas which often have specific characteristics in clinical presentation, prognosis and treatment (1).

Undifferentiated high grade sarcomas are usually present in patients aged over 40 years, predominance beings around the age of 60-70 years, rare examples may be encountered in adolescents and young adults. Preponderance it's a little bit higher in men versus women, approximately 1.2:1(2).

STS distribution according to the anatomic area as follows: head and neck 8.9%, trunk 17.9%, upper extremities 13.1%, lower extremities 46.4%, retroperitoneum 12.5%, mediastinum 1.3% (3). In the extremities, STS it's presenting most often as a painless lump or swelling, usually 5-10 cm in diameter, located in muscle (4). In order to be able to differentiate between various types of sarcomas and discriminating through the newly diagnosed low-grade and high-grade sarcomas, a high sensitivity it's required and this may be achieved by combining metabolic and morphological information of FDG PET/CT imaging (5). These combined images have been already used for multiple purposes: biopsy guidance, response assessment, grading, and follow up in STS (6).

Among the most often used systems for classification we notice: French grading and the National Cancer Institute grading,
Prolonged fever without obvious etiology finally diagnosed as high-grade soft tissue sarcoma which are based on histologic type and subtype, tumor necrosis, and mitotic activity. Further evolution to metastatic disease is given by histological grading which is also an important prognostic factor (7).

**CASE REPORT**

A 67 years old Caucasian female, without significant medical history, was admitted with prolonged fever (up to 39°C), chills, sweats, diffuse myalgia, fatigue, persistent inflammatory syndrome, weight loss (10 kg in last 5 months) and a recent appearance of a pain in left thigh without swelling. The medical investigations performed before admission: thorax scanner, bone scintigraphy, abdominal ultrasound and transthoracic cardiac echography were negative. The patient was treated during 15 days with corticosteroids (Medrol 12 mg/d), but without symptomatic improvement.

Clinical examination reveals pain on deep palpation in the left trochanter without local swelling. Vital parameters were normal except the fever.

Laboratory investigations show the following results: CRP 148mg/L, hemoglobin 10,2g/dL, ferritinemia 840,4µg/L(normal value between 30 to 400), serum iron 16µg/dL, hypoalbuminemia 20,9g/L. Bacteriological analyzes of urine and blood were negative.

Due to the fact that the patient began to invoke a pain in left thigh we chose to do some investigations to discover the etiology. A pelvis and femur radiography reveals no bone lesions. A bone scintigraphy shows on the precocious images an intake at the soft tissue of the left thigh. We continued investigations with a hip ultrasound which revealed a heterogeneous formation of 112 mm on 40mm which occurs vascularized.

We followed with an MRI exams which detected a lesion of 10 cm containing two components: a fleshy area without precise edges and a necrotic-cystic area, suspicious of malignancy (rhabdomyosarcoma), as illustrated in the following two figures:

![Fig. 1. MRI of the thigh: coronal cut, T2-weighted. The lesion at the vastus lateralis muscle occupying a major part of this muscle, that seems not to cross the vast intermediate aponeurosis, showing a double signal: the cranial part appears fleshy (yellow arrow) and caudal part appears necrotic-cystic (red arrow) well delimited by a fibrous membrane (blue arrow).](image1)

![Fig. 2. MRI of the thigh: axial cut, T2-weighted. The lesion in the vastus lateralis muscle occupying a major part of this muscle.](image2)
We have continued the investigations with a FDG PET scan which revealed us a voluminous lesion very hypermetabolic. We proceeded to the surgical excision of the mass which led us to the diagnosis of soft tissue sarcoma.

**DISCUSSION**

Unexplained prolonged fever is characterized by a higher temperature than 38.3°C (101°F) lasting more than 3 weeks for no apparent reason after clinical examination and routine tests.

The main causes of prolonged fever (except patients with a known HIV positive serology) are: infections (20 to 35% of cases), malignancies (10 to 15% of cases), autoimmune conditions (20 to 30% of cases) and miscellaneous (5 to 15% of cases) (8). In rare cases, soft tissue sarcoma can cause general symptoms such as: fever, chills, sweats, weight loss, fatigue. Soft tissue sarcoma in its early stages may grow without any signs or symptoms, pain or soreness appear when it presses against nearby nerves and muscles.

The first imaging test is a X-ray, followed by an MRI which is the most helpful test to image soft tissue tumors as it provides very important information about the mass such as the size, location, and proximity to neurovascular structures but the diagnosis of a tumor cannot be made by MRI alone. MRI cannot be done to patients with metal implants or pacemakers, in those cases a CT scan may be an option.

Rhabdomyosarcoma is part of tumors of the musculoskeletal tissue for which the performing of a 18F-fluorodeoxyglucose (FDG) PET-CT is indicated in order to stage the high-grade sarcomas (9). Considering the suspicion of rhabdomyosarcoma and that the lesion has several components, to avoid the risk of false negative result at biopsy we opted to continue investigations with a FDG PET scan due its direct relationship to tissue metabolism. The highest FDG uptake areas in a tumor reflect the most biologically aggressive areas with the probability of malignant behavior.

Below we present PETAC axial and axial CT images which have been fused to obtain a third image which shows a voluminous lesion very hypermetabolic.

![PETAC axial and axial CT images](image)

**Fig. 3.** Fusion between Positron Emission Tomography with Carbon-11 Acetate axial and CT axial images.

The standard uptake value (SUV) used in Fluorodeoxyglucose (FDG) imaging, has the capability in helping to distinguish between benign and malignant lesions, high SUV uptake may predict for an aggressive
histology. Because the lesion was intense hypermetabolic (SUVmax=49.6) we decided a total excision of the mass.

Fig. 4. Fused axial PET/CT images showed tracer uptake in a bulky soft-tissue mass in the left vastus lateralis muscle as indicated by red arrow

In case of mass suspicious of malignancy, the FDG PET image used in conjunction with other imaging can guide the surgeon to the most appropriate area to get biopsy tissue for diagnosis because the most biologically aggressive areas of a tumor have the highest FDG uptake (10).

Only the biopsy can provide a specific histological diagnosis of pleomorphic sarcoma which cannot be obtained by radiologic imaging. There are three procedures to obtain biopsy: fine needle aspiration (FNA) is not recommended as a primary diagnostic modality, core needle biopsy but several cores should be taken to maximize diagnostic yield and excisional biopsy.

After analyzing of surgical fragments, the anatomopathological result concludes the following diagnostic: Soft Tissue Sarcoma undifferentiated High-Grade 3 in the classification FNCLCC (Federation Nationale des Centres de Lutte le Cancer).

When the diagnosis of sarcoma is made, it is important to determine if a tumor is isolated (localized) or has spread (metastatic) by way of PET scan, which nowadays has become a routine exam in the extension evaluation of STS. Sarcomas can develop distant metastases and the most common site is the lung with the observation that if a pulmonary nodule is discovered after the patient has been diagnosed with a sarcoma, this one may be a metastasis of sarcoma. Rarely metastases may occur in the skin, soft tissues, liver, and lymph nodes (11).

Once the diagnosis of Soft Tissue Sarcoma has been confirmed, an individual treatment plan is made for each patient. Sarcoma treatment requires a multimodality approach and hence a team of physicians will participate in a patient’s care. There are essentially three main types of treatment: surgery, radiation, chemotherapy.

Adjuvant chemotherapy is among the treatments that can reduce the risk of developing subsequent systemic metastasis in addition to achieving a good local control in case of high grade sarcomas, greater than 5cm (12).

In our case, after surgical excision of the tumor (with healthy margins of resection) were not found metastases in tests performed. Due of large size of the tumor (10 centimeters) and because there were no metastases found corroborated with a good health condition of the patient, we had considered appropriate to administrate an adjuvant chemotherapy by Adriamycin 3 sessions of intravenous continuous infusion over 3 days every 3 weeks followed by a complement of radiotherapy.

CONCLUSIONS

In prolonged fever of unknown origin we can expect sometimes an infrequent diagnosis, so the presumptive diagnosis should not remain obtuse, but must keep a wide vision to avoid missing the rare diagnosis and particularly aggressive as in our case. Diagnostic steps must be well structured in order to reach the diagnostic as quickly as possible to discover the disease in its earliest stages.
to improve the survival prognosis. While some imaging scans such as CT and MRI isolate organic anatomic changes in the body, PET is capable of detecting areas of molecular biology detail (even prior to anatomic change).

The high diagnostic accuracy of FDG-PET and PET/CT has been well documented for several neoplasms, with a consequent rapid increase in the utilization and acceptance of PET imaging in the clinical setting.

REFERENCES


