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Result of treatment of Ewing's sarcoma (About 05 cases)

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Abstract:
Introduction: *Ewing sarcoma is a small round cell malignant bone tumor with a high metastatic potential.*
Materials and methods: *From 2013 to 2016, 05 cases of Ewing sarcoma are collected at the Department of Orthopedic Traumatology 2 of the CHU Hassan 2 in Fez. The average age of our patients was 26 years. The most frequent localization was found in the lower limbs, which were affected in 80% of the cases. Diagnostic delay ranged from 4 to 12 months Pain and swelling were the main telltale signs. The initial radiological assessment included a standard radiology and an MRI that were performed for all our patients. The surgical biopsy was performed for all our patients and showed a round cell tumor. The outcome of the extension showed pulmonary metastases in two patients. All our patients were referred to the oncology department to begin neoadjuvant chemotherapy under the Euro Ewing protocol two patients underwent conservative surgical treatment, while in two other cases the treatment was radical and consisted of transfemoral and transtibial amputation.*
Results: *With the exception of one case that did not benefit from surgery. The evolution was marked by complete remission of a single patient seen which can be explained by the absence of the majority of the factors of bad prognosis and the good response to the chemotherapy as well as a good surgical management responding to the principle of carcinological resection. The unfortunate development of our fourth patient -who died- was probably due to the delay in diagnosis, the presence of pulmonary and pleural metastasis and initial volume of the tumor mass.*
Keywords: *Malignant tumor, Ewing's sarcoma, surgery, therapeutic technique*

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I. Introduction:

Ewing's sarcoma is a primary malignant bone tumor, which preferentially preferred the child and adolescent [1].

It can reach all the bones of the skeleton, and perhaps even grow exclusively in the soft parts. Radiologically, it is a lytic lesion, of aggressive appearance, with a development often important in the soft parts, well visible in a magnetic resonance imaging.

In the absence of treatment, the fatal evolution is rapid with the appearance of distant metastases, pulmonary or bone. The current treatment is based on the combination of multidrug therapy and local treatment, sometimes by radiotherapy or more rarely by radiotherapy alone.

The most recent protocols attempt thanks to high-dose chemotherapies with autologous stem cell grafting to improve outcomes in forms of poor prognosis. Recent advances in research can give hope for new treatments in the future.

II. Materials and Methods:

Over a period of 3 years between 2013 and 2016, 5 cases of Ewing's sarcoma were collected and managed in the B4 trauma department .Our work is a retrospective study of a series of 5 cases of Ewing's Sarcoma. Different parameters were exploited from the medical records of the traumatology unit of the concerned department. A pre-established exploitation document created for this purpose, is among the collection of epidemiological, clinical, paraclinical, therapeutic and evolutionary data.

III. Results:

Our study included 5 cases of Ewing's sarcoma treated over a period of 4 years. The initial radiological assessment included a standard radiology performed in all our patients with an MRI followed by a surgical biopsy. All our patients were referred to the medical department of medical oncology for neoadjuvant chemotherapy under the Euro Ewing protocol. Two patients underwent conservative surgical treatment versus radical amputation treatment in two other patients and one patient did not receive surgery the initial biopsy result was in favor of a round cell tumor in the entire series with an extension assessment that returned to lung metastasis in two patients.
The evolution was marked by a complete remission in two case, two cases lost sight of and the death of a single case.

Observation1:
20-year-old patient without antecedent who presented 4 months before his consultation knee bone-type pain with a painful mass of rapidly progression with fistulization on the surface.
X-ray of the left leg (Figure1): Permeativeosteolysis of stage 3 fibula according to Lodwick with discontinuous cortex and periosteal reaction spiculated in sunbeams and invasion of the soft tissues opposite.

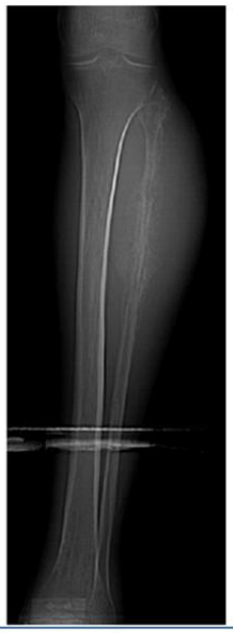

Figure 1: Percutaneous osteolysis of stage 3 fibula according to Lodwick with discontinuous cortex and pericosteal reaction spiculated in sunbeams and invasion of the soft tissues opposite

Scanner (Figure 2): Presence of an osteolytic tumor process centered on the proximal 1/3 of the epiphysis-diaphyseal fibula, heterogeneously enhanced after contrast, responsible for a periosteal reaction in grass fire (yellow arrow), invading the adjacent soft tissues (arrowhead) and sheathing the anterior tibial artery (blue arrow), measuring 87x100x167 mm.

MRI of the left leg (Figure 3): Aspect first evoking a malignant tumor

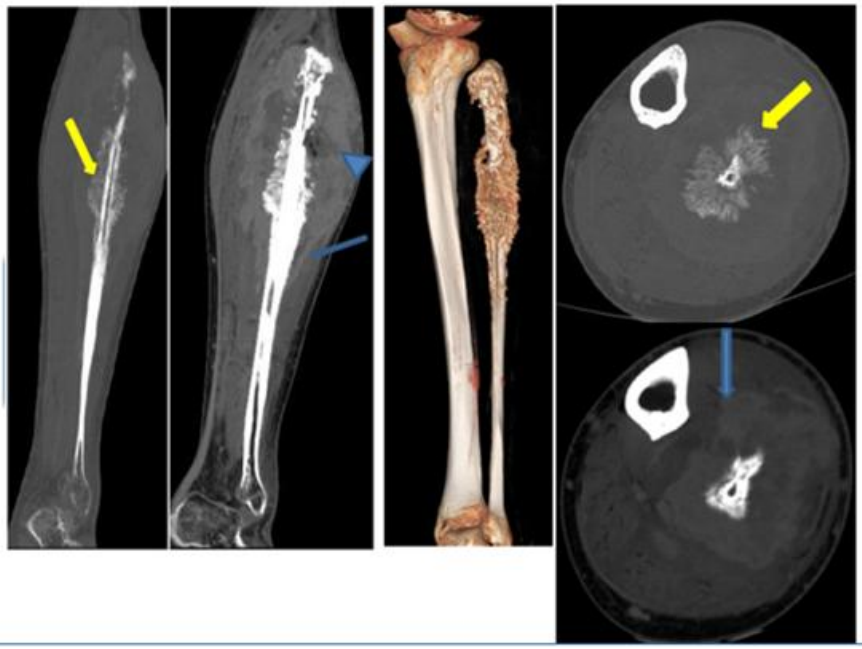

Figure 2 : Presence of an osteolytic tumor process centered on the proximal 1/3 of the epiphyso-diaphyseal fibula, raised heterogeneously after contrast, responsible for a periosteal reaction in grass fire (yellow arrow), invading the adjacent soft parts (head arrow) and sheathing the anterior tibial artery (blue arrow), measuring 87 * 100 * 167 mm

lesion a myxoidleimyosarcoma. The possibility of an aggressive dysmancer tumor is likely. To confront the data of the pathological examination.
Biopsy: Round cell malignant tumor prolapse first evoking IHC-confirmed Ewing / PNET sarcoma.
Extension assessment: Bilateral pulmonary nodules on CT TAP and hyper fixation of left ankle and left forefoot on scintigraphy.
Treatment: Neoadjuvant chemotherapy, Transfemoral amputation and adjuvant chemotherapy, then the patient was lost to follow-up 4 months later.

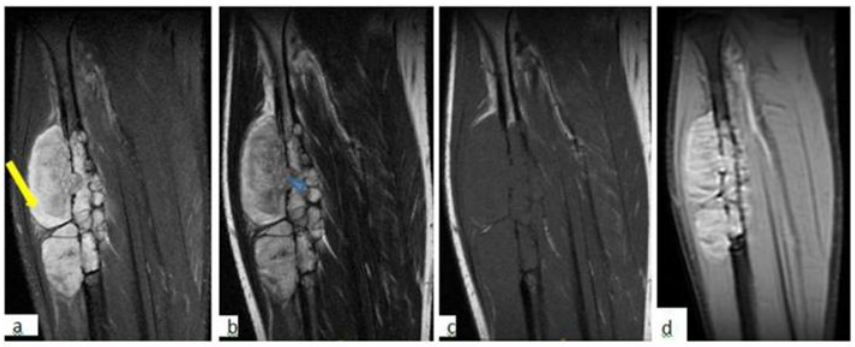

Figure 3 : MRI showing a diaphyseal intraosseous lesion process of the 1/3 superior-1/3 junction of the right fibula, measuring 78mm long and 25mm wide. This process is a hypo T1 signal, a discrete T2 hyper signal, which enhances itself heterogeneously after contrast. It is associated with a rupture of the cortical (arrowhead) and invasion of muscle PM (arrow) of the posterolateral box (posterior tibial nerve and long flexor hallucis muscle).

Observation 2
29-year-old patient with a history of epilepsy in childhood presents a year before his consultation a pain of the right leg without associated clinical sign.
X-ray of the right leg: Lodwick stage 2 osteolytic image at the level of the fibula diaphysis with pluri-lamellar periosteal reaction and invasion of the soft parts into a grass fire.
MRI of the right leg: Aspect in favor of a large fibular osteosarcoma with soft tissue extension.
Biopsy: malignant tumor process with round cells infiltrating bone and soft tissues. CD99 +, does not express: pancytokeratin AE1 AE3; EMA. CD45. Myogenin and PS 100.
Treatment: Neoadjuvant chemotherapy, external leg compartmental surgery, adjuvant chemotherapy. No tumor residue and complete remission at the end of chemotherapy (Figure 4).

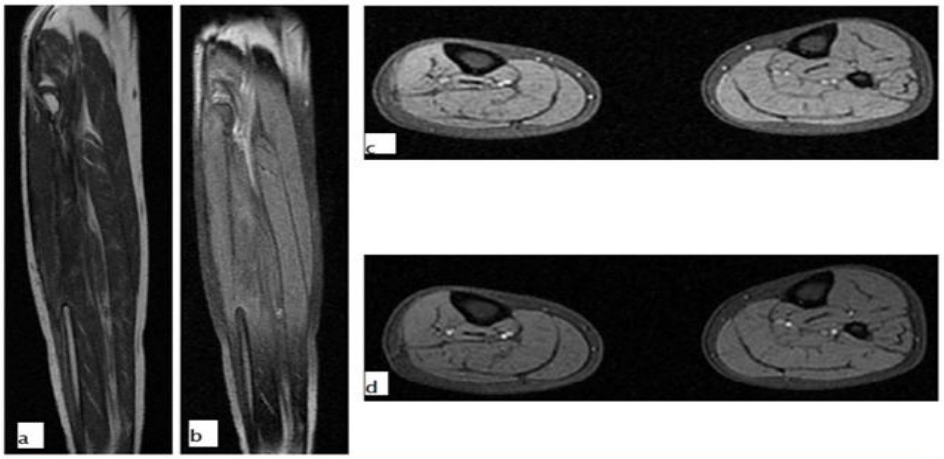

Figure 4 : MRI examination after the end of the adjuvant chemotherapy protocol Disappearance of intramuscular and aponeurotic formations of the anterolateral compartment of the right leg.
Absence of signal anomaly tibia and the rest of the fibula.
Absence of mass syndrome or pathological contrast enhancement.

Observation 3

36-year-old patient, chronic smoking, it has a mass of the right thigh of progressive evolution since 6 months.

X-ray of the right thigh: mixed osteolysis-osteocondensation image with periosteal multi-lamellar reaction and rupture of the cortex in places forming a Codman's spur with opacification of the soft parts testifying to an invasion at the level of the superior end of the femur at the trochanteric massive diaphysis junction.

MRI of the right thigh: in favor of a malignant tumoral lesion of the right thigh evoking an Ewing or other sarcoma (Figure 5).

Biopsy: Tumor proliferation with small round cells largely necrotic monotonous: CD99 +, NSE + PS100 + CD45 -confirming that it is a PNET.

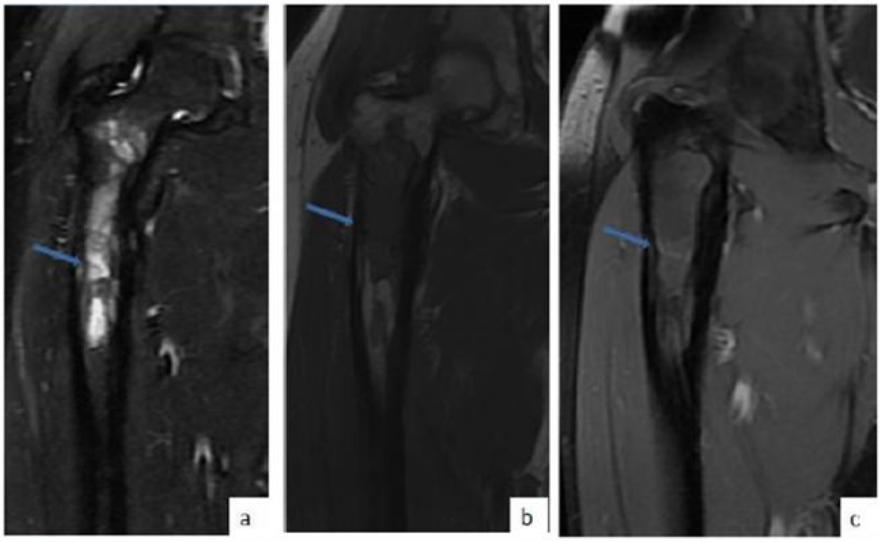

Figure 5 : MRI section showing the presence of a proximal cervico-diaphyseal lesion process of the right femur (arrow) with T1 hypointense T2 hypersignal, largely liquefied and having some areas of focal enhancement. This process extends moderately towards the soft parts opposite and in particular towards the vast intermediate muscle which is infiltrated, it does not extend towards the other muscular boxes, it remains at a distance from the superficial and deep vascular bundle.

Treatment: neoadjuvant chemotherapy, wide excision surgery (Figure 6) and adjuvant chemotherapy, the evolution was marked by the appearance of secondary locations for which the patient has benefited from palliative radiotherapy before being lost sight of.

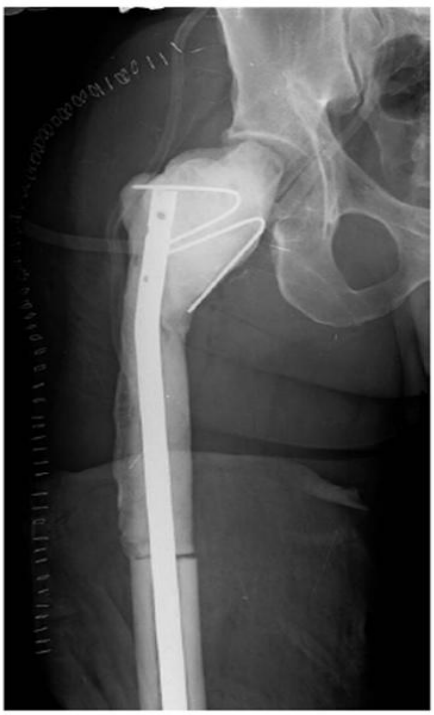

Figure 6 : Postoperative control radiology after tumor excision and spacer cemented spacer

Observation 4

25-year-old patient, with no history, presents a mass of the left shoulder rapidly increasing in volume for 1 year with pain and weight loss.

X-ray of the left shoulder: Geographic image with fuzzy boundaries without marginal sclerosis, stage 1c according to the Lodwick classification taking the scapula with its acromion with rupture of the cortex and invasion of the soft parts in a grass fire.

MRI of the left shoulder: diffuse muscular involvement of the soft parts of the shoulder with heterogeneous appearance of the scapula evoking a tumor in the first place (Figure 7).

Biopsy: histological and immunohistochemically appearance of a malignant round-cell tumor first suggestive of a tumor of the PNET / Ewing group: CD 99 positive.

Treatment: neoadjuvant chemotherapy with poor compliance

The evolution was marked by the appearance of pleural and

pulmonary secondary localization for which he had a palliative treatment, the patient died following a cardiopulmonary arrest on acute pulmonary edema complicated.

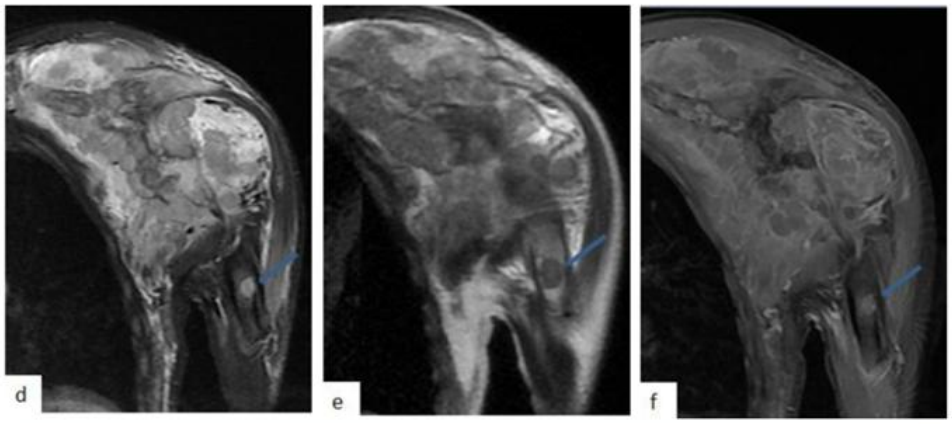

Figure 7 : Presence of a voluminous tissue process of the left shoulder, centered on the scapula which is completely invaded with its acromion. This process is an intermediate signal in T1 and T2, raised moderately and heterogeneously by the contrast medium, its boundaries are poorly defined and irregular. This mass invades all the muscles and tendons of the cap, as well as the acromioclavicular joint.
Presence also of a nodular lesion of the humeral diaphysis in relation to a skip metastasis (arrow).

Observation 5:

18-year-old patient, with no history, has bone pain in his left foot that has been evolving for 3 months. X-rayof the left foot: Osteolysis of the metatarsal diaphysis of the hallux permeative with blurred outline stage 3 according to Lodwick with pericosteal reaction spiculated in sunbeam and blistering of the cortical and invasion of the soft parts in a grass fire.

MRI of the left foot:tumor of the 1st metatarsal left 81 mm long axis with locoregional bone extension.

Biopsy: Histological appearance in favor of a round cell tumor evoking a priori round cell sarcoma (Ewing / PNET type); without formally excluding a lymphoma or plasmocytoma. IHC: immunohistochemically aspect compatible with Ewing / PNET type sarcoma (anti CD99).

Treatment: neoadjuvant chemotherapy then a transtibial amputation supplemented by adjuvant chemotherapy, No tumor residue and complete remission at the end of chemotherapy.

IV. Discussion:

Since his first description in 1921 by James Ewing [1] and he asked his question about its origin [2], it remains a rare tumor occupying 6-8% of primitive malignant bone tumors [6] with an incidence of 1.5 new cases / year / million inhabitants in France, 2 to 3 new cases / year / million inhabitants in the United States [7, 8] and a variable incidence in African or Asian populations [9].

Ewing's sarcoma occurs in 95% of cases between 4 and 25 years of age, with a peak frequency between 10 and 15 years [6, 7,8, 9]. In our series, the average age was 26 years old [18-36] with a purely masculine gender, which is contrary to the results of the literature with a sex of 1.5 [10]. In the literature, the notion of Preferred factors has been developed as the white race [11, 12], reciprocal translocation between chromosomes 11 and 22: t (11,22) [13, 14] and other toxic or infectious products [11,15].

The diagnosis is based on a procedure ranging from careful questioning to clinical examination, imaging and finally pathology [16,17]. Pain is the main symptom of this pathology [18]. The diagnoses are extremely variable and misleading, X-rays are indispensable for simple plain X-rays that may not be objective or osteolytic [19] classified according to the Lodwick classification [8,19,20], periosteal reaction [19, 21] or soft tissue extension [8,22] In our series, osteolysis and periosteal reaction were present in 80% of cases. MRI is the choice of choice in our context, especially compared to CT, it is more efficient in intramedullary invasion and the soft tissues display a T1 weighting and a heterogeneous reinforcement of T2 [23]. In our series, all of our patients had an MRI.

Based on the Enneking classification [24], 2 patients had a cleansing amputation: trans-femoral amputation (Case N1) and transtibial amputation (Case N5), 2 cases of compartmentectomy excision surgery of the anterolateral compartment of the leg (Case N2) and excision of the tumor (Case N3).

Currently, induction poly-chemotherapy is the basis of treatment whether it is neo-adjuvant [25, 26] or adjuvant [27]. Since 1999 a Euro-Ewing 99 protocol has been introduced [28]. In our series, all patients received neoadjuvant chemotherapy with different protocols:

• For cases N2 and N3 (initial non-metastatic patients): 06 courses of EMPTY.
• For the case N5 (non-metastatic patient): 03 courses of EMPTY.
• For case N1 (metastatic patient): 06 courses of VAC / IE.
• For case N4 (metastatic patient): 08 courses of VAI.

With regard to adjuvant chemotherapy, the protocols carried out included: Case N2 received 8 courses of VAI and case N3 received 6 courses of VAI the last Case n5 currently put under protocol type EMPTY. The usefulness of radiotherapy has been confirmed in some indications [29, 30,31] and in some authors [32, 33] it has been used in only one case of our series (Case N4).

In terms of survival rates of Ewing's Sarcoma, the combination of chemotherapy with surgery and sometimes radiotherapy seems to be the most effective at present [26, 34]. Several factors determine the prognosis of efficacy of the treatment such as the absence of metastasis. , tumor volume, good response of neoadjuvant chemotherapy [35] (evaluated by MRI) or Huvos classification [35]. The good response of the treatment with a positive evolution of the Case N2 can be explained by the absence of the majority of the factors of poor prognosis already cited: The absence of initial metastasis, the low tumoral volume, the good answer to the neo chemotherapy adjuvant same protocol as the Euro-Ewing 99: 6 cures of VACU, the absence of tumor residue on the post-surgical anatomopathologyexam of the piece and a grade 4 of the classification of Huvos .By cons, The unfortunate evolution of the case N4, who had Ewing's sarcoma of the unoperated left shoulder that ended in death due to PAO, is probably due to the presence of initial pulmonary and pleural metastasis and skips of humeral metastases. The high volume of the initial tumor and the poor response to neo-adjuvant chemotherapy, which was revealed by a re-increase in mass volume at post-chemotherapy CT.

V. Conclusion:

Ewing's sarcoma is a rare bone malignancy with a strong predilection in children and adolescents. His clinical picture is nonspecific, it usually includes pain and swelling. The diagnosis is made only by the demonstration by RT-PCR and / or FISH of a pathognomonic translocation of the Ewing tumor which involves the EWS gene with another gene of the ETS family.The determination of prognostic factors is mandatory, which will guide the therapeutic attitude to recall, the tumor volume, its initial site, the age of the patient and the histological response to induction chemotherapy. Its treatment is defined by the Euro-Ewing 99 protocol; it includes neoadjuvant chemotherapy, oncologic surgery, the combination or not of radiotherapy and adjuvant chemotherapy. Recent protocols attempt through high dose chemotherapies with peripheral stem cell transplantation to improve outcomes in forms of poor prognosis.

Declaration of no conflict of interest: I declare on my honor, and all participants in this study, that we have no affiliation (financial or otherwise) to disclose, with a for-profit or non-profit organization which can influence the results and analysis of this study.

What is known about this topic?

- Various protocols.
- Multidisciplinary management of Ewing sarcoma.

What does your study bring back?

- Study the therapeutic techniques, the evolutionary profile, the functional repercussion as well as the secondary effects of Ewing's sarcoma treatment.
- Tracing the experience of the Department of traumatology and orthopedics of university hospital center Hassan 2 B4 of Fez.
- Comparing our results with those of the literature.

Contribution of the authors:

- Mohammed Lahsika (Principal author): planning the study, exploitation of the archives, analysis of the results and writing of the manuscript
- Said Senhaji and Abdelhafid El Marfi: Exploitation of the archives, analysis of the results.
- Mohammed El Idrissi, Abdelhalim El Ibrahimi and Abdelmajid El Mrini: Critical review and final approval

Number of figures:7 figures.

Figure 1:X-ray of the leg showing osteolysis of the peroneus on Ewing's sarcoma.
Figure 2: Leg scan showing a periosteal reaction in the sunbeam.
Figure 3:MRI of the right leg with Aspect in favor of a large fibular osteosarcoma with soft tissue extension.

Figure 4:MRI of control after 3 months of the end of the chemotherapy showing a complete remission with absence of tumor residue.
Figure 5: MRI of the right thigh: in favor of a malignant tumoral lesion of the right thigh evoking an Ewing or other sarcoma.
Figure 6: Postoperative control radiology after tumor excision and spacer cemented spacer.
Figure 7: MRI of the left shoulder: diffuse muscular involvement of the soft parts of the shoulder with heterogeneous appearance of the scapula evoking a tumor in the first place.

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