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Case Report

Prolonged Local Control by Radiotherapy and Chemotherapy without Surgery in a Myxoid Liposarcoma Patient

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Abstract

This case report describes a non-surgical therapeutic strategy consisting of radiotherapy and chemotherapy resulting in prolonged local control of the primary tumor mass, in a myxoid liposarcoma patient with synchronous metastases at the time of diagnosis.

Keywords: Soft Tissue Sarcoma; Myxoid Liposarcoma; Radiotherapy; Local Control

Case Presentation

In February 2014, a 56 years old male patient was referred to us, for diagnosis and treatment of a 14 cm mass in the left gluteal muscles. Patient had noticed a mass in his left buttock over the last months prior to referral. There was slight pain while sitting on solid surfaces. His medical history revealed no prior abnormalities, his family history was without malignancies, he was not on any medication and he did not smoke. On physical examination we saw an otherwise healthy male, with a semi-solid, but mobile mass in his left buttock. The overlying skin was infiltrated and showed a 4 cm large ulcer and a fungating tumor (Figure 1A).

An MRI showed a sharply delineated mass in his left gluteus maximus muscle, enhancing after intravenous Gadolinium contrast administration. The neurovascular bundle was free (Figures 2A and B). A chest and abdomen CT scan revealed at least 5 pulmonary nodules between 5 and 7 mm in size in both lungs (Figure 3A). Furthermore in the left iliac lymph node chain, 3 enlarged nodes could be seen, the largest being 2.2 cm in diameter (Figure 3C). A biopsy showed a Myxoid Liposarcoma (MLS) without round cells. The cells were positive for the reciprocal chromosomal translocation t(12;16)(q13;p11), confirming the MLS diagnosis.

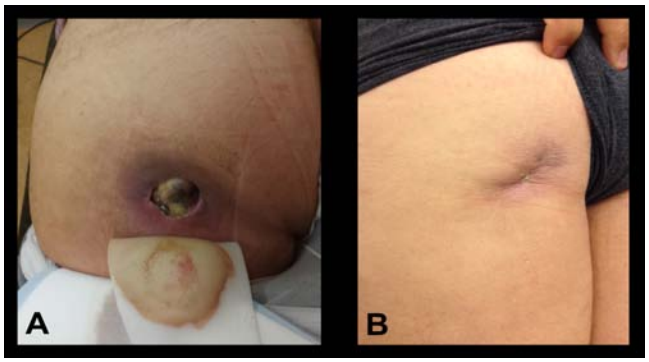

Figure 1: Figure 1A shows the left buttock with the ulcerating tumor mass at diagnosis. Figure 1B depicts the skin after RT, leaving a retracted scar with no visible late radiation effects to the normal skin.

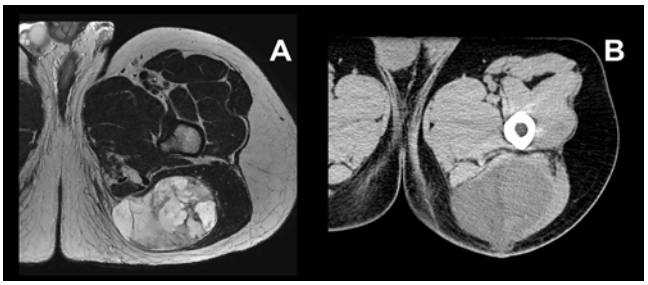

Figure 2: The primary sarcoma mass at diagnosis is shown, in Figure 2A, on T2 weighted MRI imaging and, in Figure 2B, on the planning CT-scan. For RT planning, patient was scanned in prone position. For easier visibility, the scan has been rotated 180 degrees. Note, that the ulceration was not present at the time of MRI evaluation prior to referral to our sarcoma hospital. However, ulceration was present at time of our first visit and is clearly visible at the CT scan.

Because his primary tumor was symptomatic but his metastatic pattern was designated as asymptomatic and low-volume, he was scheduled for radiotherapy (RT) on his primary tumor in March 2014. He received 25 fractions of 2 Gy by intensity modulated RT conform published guidelines [1]. He tolerated this regimen with mild (maximum grade 2) abdominal complaints, that completely resolved 2 weeks after RT.

Epicrisis

On re-evaluation, at the end of May 2014, patient was without pain and his primary tumor had almost completely resolved. The skin was healed, leaving a retracted scar (Figure 1B). However, there was clear progression in size of all lung- (Figure 3B) and parailiac lymphnode metastases, the largest node now being 3.3 cm. By the multidisciplinary sarcoma board, it was decided not to perform

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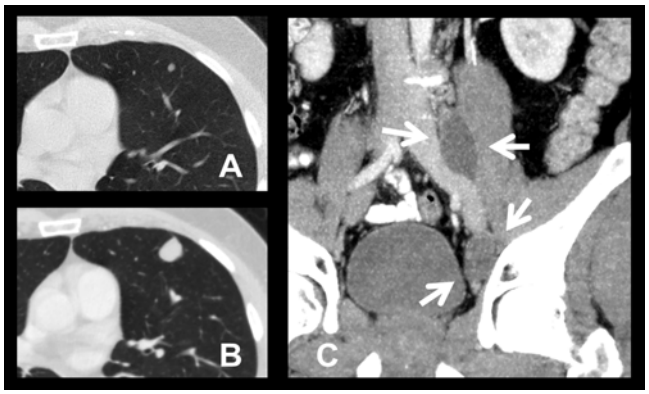

Figure 3: Figure 3A shows one of the pulmonary metastases at diagnosis. Figure 3B shows the same metastasis 3 months later indicative of significant progression in a relatively short observation period during which the patient was irradiated on his primary tumor. The white arrows in figure 3C highlight 2 of the 3 iliac lymph node metastases in a coronal CT maximum intensity projection.

surgery for 2 reasons: the good local palliation by RT and the systemic progression. Patient received single agent doxorubicin 75 mg/m^2 once every 3 weeks, starting in June 2014. Evaluation after 2 courses showed a good partial remission by RECIST criteria in all metastatic sites; the largest pulmonary nodules regressed from 17 mm to 9 mm and the largest lymphnode metastasis regressed from 33 mm to 20 mm. In October 2014, patient had completed a total of 6 courses. Further regression was appreciated after the 6th course as compared to after the 2nd course. There was ongoing local control of the irradiated primary tumor in his gluteal muscles. This may partly be explained by the additional good response on doxorubicin chemotherapy. Patient was re-discussed by the multidisciplinary sarcoma board where it was advised to carefully watch and wait.

The first sign of progressive disease was noted in May 2015 only at the site of the pelvic lymph nodes. He was observed for another 3 months. In August 2015, with ongoing scarification of the primary tumor and stabilization of the pulmonary metastases, only the parailiac lymphnode metastases further increased in size. Given the satisfactory response on RT (already for one and a half year) and in an attempt to postpone second line chemotherapy, patient was offered palliative iliac chain RT to a dose of 18 x 2 Gy.

Explanation of our policy

It is our local sarcoma tumor board protocol to start with conventionally fractionated RT on the primary tumor to a total dose of 50 Gy in 25 fractions in 5 weeks, in patients with *symptomatic* soft tissue sarcomas, with *asymptomatic* and *"low volume"* synchronous metastases at diagnosis. A re-evaluation of the primary tumor and all metastases after a 6 weeks observation period after completion of RT is planned. If, at that time, all metastases are stable in size and number, definitive surgery will be performed and chemotherapy postponed. If, however, as in this case, the metastatic spread is significantly progressive in these first 2-3 months, surgery will not be performed. Patient will be informed on the possibilities of systemic chemotherapy.

Discussion

Soft tissue sarcomas (STS) as a group of mesenchymal malignancies have a very low incidence. Among adults soft tissue sarcomas represent less than 1 % of all malignancies. In case of non-metastatic primary STS of the extremities and the chest- and truck wall, a combination of conservative surgery in combination with radiotherapy (RT) provides higher rates of local control as compared to surgery alone. The timing of RT is under debate. Preoperative RT results in an increased probability of wound complications [2]. However, other oncological endpoint rates, such as those for local control, metastasis free survival and overall survival, are either comparable to or are in favor of preoperative RT as compared to these rates after postoperative RT. Especially late functional morbidity is significantly worse after postoperative RT [2,3].

In general, STS are considered to be only moderately radiation sensitive. However, cell lines derived from sarcomas do not seem to be less radiation sensitive than those derived from epithelial malignancies [4]. Furthermore, relatively small sarcomas up to 3-5 cm in maximum diameter (estimated volumes of 15-65 mL) have been reported to be locally controlled by RT alone in more than 90% of cases, provided dose levels above 75 Gy are applied [5,6]. Myxoid liposarcomas (MLS) have been reported to be an exception [7-12]. During and shortly after 50 Gy preoperative RT in MLS, a substantial volume reduction can be observed [7,8]. Subsequently, almost always marked histopathological changes can be appreciated in MLS resection specimens after 50 Gy preoperative RT. This pathological response can be described as a fibrotic myxoid stroma containing wiry, non-lipogenic, hyalinized structures. Gross evidence of necrosis is uncommon. The classic delicate crow's feet capillary vasculature can still be identified [8,10]. Currently, a prospective phase II clinical trial is investigating the possibility to decrease the preoperative dose of RT to 36 Gy instead of 50 Gy in MLS and to investigate whether this dose provides lasting local control for (oligo-) metastatic disease(ClinicalTrials.Gov Identifier: NCT02106312).

In summary, this case report, the brief review of the literature and the availability of current accruing prospective clinical trials, underline the exquisite radiation sensitivity of MLS. This case report suggests that prolonged local control can be achieved by moderate doses of RT in MLS tumor masses. The application of RT in MLS should preferably be performed in the context of well-designed prospective clinical trials.

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