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Adult Head and Neck Sarcomas: Rare Localization with Difficult Therapeutic Management

Karima Oualla[1]*, Nawfel Mellas[1], Fatimazahra El'mrabet[1], Samia Arifi[1], Afaf Amarti[2], Siham Tizniti[3] and Omar Elmesbahi[1]

[1]Department of medical oncology, Hassan II University Hospital, Fez, Morocco
[2]Department of pathology, Hassan II University Hospital, Fez, Morocco
[3]Department of radiology, Hassan II University Hospital, Fez, Morocco

Abstract

Background: Head and neck sarcomas are very rare tumors, accounting less than 1% from all malignancies of this region. They represent a heterogeneous group of tumors with distinct prognostic features. There have been significant improvements in characterizing these sarcomas using traditional morphologic assessments and immunohistochemical analysis, but treatment management is still a big challenge. Prognostic factors are essentially tumor grade, margin status and tumor size. Surgery remains the mainstay of treatment, despite the anatomic constraints, followed by radiation therapy.

Aim: to show the rarity of the head and neck localization, and describe epidemiologic, clinico-radiological, histological features, treatment management and the evolution of these tumors.

Methods: It is a retrospective descriptive study conducted in the department of medical oncology at Hassan II University Hospital between January 2007 and December 2011, including all patients with histologically proven melanoma of the anorectal area.

Results: 10 cases were collected, that represented 7 % from all sarcomas reported at the study period. Five men and 5 women, the mean age was 34 years (range: 17-65years). Local imaging was performed by MRI in six cases and CT scan in 4 cases. It had showed locally advanced disease in 7 cases and among them 6 patients had a metastatic disease at the staging. Lung was the site of predilection of metastases. Histological analysis with the support of immunohisto-chemestry showed diverse histological subtypes. For the 3 cases with localized stages, the mainstay treatment was based on surgery followed by radiation therapy in one case with unclear margins. For metastatic stages, first line of chemotherapy was mainly based on: doxorubicin, ifosfamide, and cisplatine for osteosarcoma. Evolution was marked by disease controlee and remission in 2 patients who underwent surgery with clear margins. Unfortunately by recurrence in patient operated with unclear margins and by rapid progression for metastatic stages leading to death.

Conclusion: Adult head and neck sarcomas are very rare tumors with poor prognosis, high aggressiveness and rate of recurrence. They are frequently diagnosed at advanced stages. Treatment management is still a big challenge given to the difficulty of surgery and modest response to chemotherapy.

Keywords: Head and neck; Sarcoma; Surgery; Margins; Radiotherapy; Chemotherapy; Prognosis

Introduction

Head and neck sarcomas are rare tumors, accounting for only 1% of all head and neck malignancies and 5% of all sarcomas [1,2]. They are a heterogeneous group of neoplasms according to their origin site that can be bone, muscle, vessel, nerve, fat and fibrous tissue. Most common histological types are: osteosarcoma, rhabdomyosarcoma, pleomorphic sarcoma and angiosarcoma [3,4]. The treatment depended on histological type, grade, stage and operative considerations according to the site. They are characterized by high rate of local recurrence and lower overall survival rate because of anatomic constraints limiting functional resections rather than difference in biologic behavior and tumor histology. Given to their management difficulties, they must be treated in multi-disciplinary approach.

Methods

It is a retrospective descriptive study conducted in the department of medical oncology at Hassan II University Hospital between January 2007 and December 2011, including all adult patients with histologically proven sarcoma of the head and neck area.

Results

Ten cases of head and neck sarcomas were collected, that represented 11% from all sarcomas reported at the study period. Five men and 5 women, the mean age was 34 years (range: 17-65years). Symptoms were very diverse according to the site of tumor. Local imaging was performed in all patients, and was by MRI in six cases and CT scan in 4 cases (Figures 1-3). It had showed locally advanced disease in 7 cases and among them 6 patients had a metastatic disease at the staging. Lung was the site of predilection of metastases, followed by bone, lymph node, and then adrenals in one case. Regarding histological

***Corresponding author:** Karima Oualla, Department of medical oncology, Hassan II University Hospital, Fez-3000, Morocco, Tel: 00 212 676 61 02 67; Fax: 00 212 535 61 37 25; E-mail: karimarauf@hotmail.com

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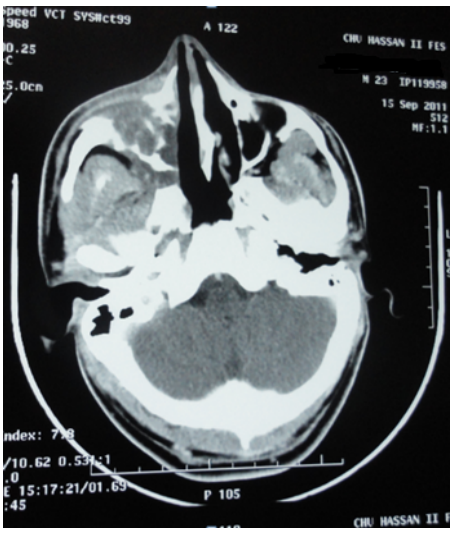

Figure 1: Cranio-facial CT scan showing locally advanced rhabdomyosarcoma of the maxillary sinus.

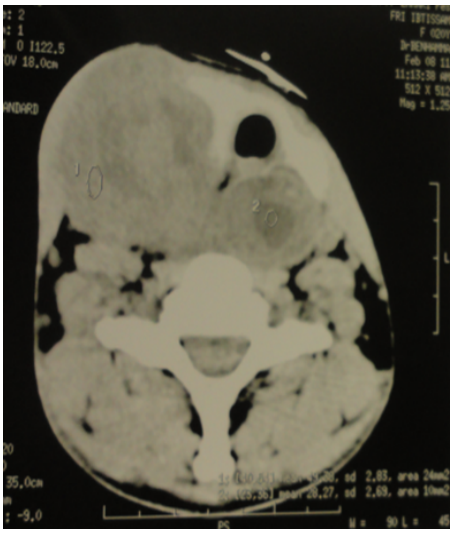

Figure 2: Cranio-facial CT scan showing locally advanced fibrosarcoma of the oro-phatynx.

features, biopsies had showed diverse subtypes. Table 1 shows the patient distribution according to age, gender, site of origin, histological subtype, initial stage, metastatic sites, treatment and evolution.

Discussion

Head and neck sarcomas are relatively rare tumors, accounting 1% of all head and neck malignancies and 4 to 10% of all soft tissue sarcomas [5]. Nevertheless, they represent an important group of tumors and are associated with significant morbidity and mortality. Their rarity makes rigorous study of their clinical behavior very difficult [6]. As a result, management of these timors, is drawn only from retrospective case series. There are several histological subtypes of sarcoma (Table 1) which present with a variety of clinical and biological characteristics. That is consistent with our results, where we found 7 histological subtypes among 10 patients. Scan and/or MRI are used to evaluate the extent of the primary lesion the regional lymphnodes and distant metastases. The commonest site for metastases was the lungs which was also the commonest cause of death. In our series also, lung was the predilection of metastases. Mendenhall et al. suggested that patients should undergo a chest CT before treatment and also suggested that in the absence of pulmonary metastases, other distant metastases are highly unlikely [7].

Surgery in the form of wide excision is the primary modality of management of all adult soft-tissue sarcomas. In extremity sarcomas, wider resections are generally possible due to adequate soft tissue around the tumors and the same is generally achieved without significant cosmetic and function deficits. The local recurrences are less than 10% and majority of the deaths in non-head and neck sites are due to metastatic disease. In comparison, because of the relatively small space of the head and neck region, anatomical constraints and proximity to vital structures, surgical removal of head and neck sarcomas often cannot achieve the ideal "wide" resection margins that are preferred in other anatomic sites. The others important considerations include the potential for morbidity related to breathing, swallowing, and speaking, and the significant cosmetic deformity that may follow maxillo-facial resections. Patients with head and neck sarcomas therefore frequently experience local relapses and succumb to it, many times without distant metastatic disease [7,8].

The local recurrence rates for high-grade soft tissue sarcomas after surgical excision have been reported to be as high as 50% in the literature [3,9,10]. Intralesional or marginal surgical margins are also risk factors of recurrence [8,11]. Therefore, surgery must be made in way to maximise the margins that can be achieved at the time of the first surgical procedure, if necessary by going back and doing a further wide excision if the initial margins prove positive.

These data are consistent with our results, where we found that 2 patients who underwent surgery with clear margins had no recurrence after 2 and 4 years respectively.

When patient develop local recurrence, further excision should be considered, and clear surgical margins should always be aimed for. Regarding adjuvant treatment, radiotherapy should be considered to decrease the risk of local recurrence and should be recommended for all high-grade tumors, tumors more than 5 cm, and in case of close or

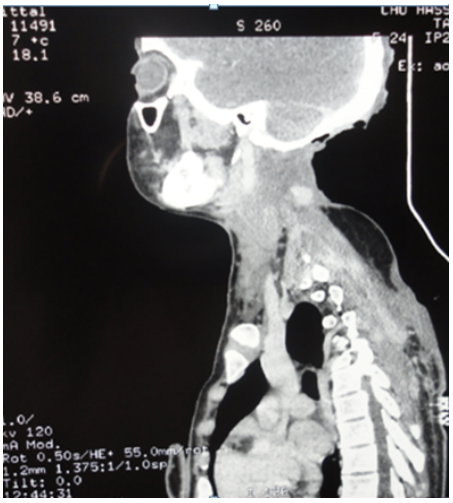

Figure 3: Radiological aspect of leimyosarcoma of the neck on CT scan.

Site of origin	Gender	Age	Histology	Initial stage	Metastatic site	Treatment	Evolution
Maxillary sinus	M	23	Rhabdomyosarcoma Grade III	Metastatic	Lung	Chemotherapy: ifosfamide, doxorubicin	Disease progression, 2nd line by docetaxel
Infra-temporal Fossa	M	17	Rhabdomyosarcoma Grade II	Metastatic	Lung, bone	-	Pulmonary embolism leading to death
Nasal cavity	M	20	Rhabdomyosarcoma Grade III	Metastatic	Lung	Chemotherapy: ifosfamide, doxorubicin	Disease progression and death
Neck	F	34	Léiomyosarcoma Grade II	Metastatic	Lung, lymph nodes	Chemotherapy: doxorubicin	Disease progression
Conjonctiva	M	29	Léiomyosarcoma Grade I	Localized	-	Resection R0 + Chemotherapy: ifosfamide, doxorubicin	No recurrence after 4 years
Mandible	M	30	Osteosarcoma Grade III	Locally advanced	-	Resection R2 + Chemotherapy: cisplatine, doxorubicin	Disease progression , 2nd line by cisplatine+etoposide
Larynx	F	44	Chondrosarcoma Grade II	Localized	-	Surgery: total laryngectomy R1 + radiation therapy	Local and distance recurrence after 4 months + Pulmonary embolism leading to death
Oropharynx	F	28	Fibrosarcoma Grade III	Metastatic	Lung, bone	Chemotherapy: ifosfamide, doxorubicin	Disease progression, base supportive care
Neck	F	38	Fibromyosarcoma Grade I	Metastatic	Lung, lymph nodes	Chemotherapy: doxorubicin	Progression , 2nd line by ifosfamide
Thyroid	F	65	carcinosarcoma	Localized	-	Total throidectomy R0	No recurrence after 2 years

R0: resection with microscopic clear margins
R1: resection with microscopic involved margins
R2: resection with macroscopic involved margins

Table 1: Patients distribution according to: age, site of origin, metastatic site, histological subtype, treatment and evolution.

positive margins [11-13]. In the case of low-grade, deep, tumor size >5 cm, radiation therapy should be discussed in a multidisciplinary fashion, considering the anatomical site and the related expected sequelae versus the histological aggressiveness.

The other role for radiation in the management of soft-tissue sarcomas is in cases of unresectable tumors, where in it is used as a primary modality and at times with chemotherapy. But unfortunately it is more in a palliative strategy.

Concerning chemotherapy, it did not produce a survival benefit in the treatment of sarcomas. However, there is 10% of benefit of chemotherapy on recurrence-free survival [14]. Adjuvant chemotherapy is not used in histological subtypes known to be insensitive to chemotherapy. If the decision is made to use chemotherapy as upfront treatment, it may well be used preoperatively, at least in part. A local benefit may be gained, facilitating surgery. If used, adjuvant chemotherapy should consist of the combination chemotherapy regimens proven to be most active in advanced disease [15]. Therefore, surgery with clear margins remains the mainstay of treatment of localized disease, and it must be performed by a surgeon specifically trained in the treatment of this disease. The wide excision is followed by radiotherapy when it is indicated. Radiation therapy is not given in the case of a truly compartmental resection of a tumor entirely contained within the compartment.

Standard chemotherapy is based on anthracyclines as first-line treatment [16]. There is no formal demonstration that multi-agent chemotherapy is superior to single-agent chemotherapy with doxorubicin alone in terms of OS. However, a higher response rate may be expected, in particular in a number of sensitive histological types. Therefore, multi-agent chemotherapy with adequate-dose anthracyclines plus ifosfamide may be the treatment of choice, particularly when a tumor response is felt to be able to give an advantage and patient performance status is good. In angiosarcoma, taxanes are an alternative option, given their high antitumor activity in this specific histological type [17]. An alternative option is gemcitabine ± docetaxel.

Doxorubicin plus dacarbazine is an option for multiagent first-line chemotherapy of leiomyosarcoma, where the activity of ifosfamide is far less convincing on available retrospective evidence.

After failure of anthracycline-based chemotherapy, or impossibility to use it, Patients who have already received chemotherapy may be treated with ifosfamide, if they did not receive it previously. Ifosfamide with high dose may be indicated for patients who have already received standard-dose ifosfamide [18].

Trabectedin is a second-line option in léiomyosarcome, liposarcoma and [19]. Its clinical benefit was also obtained in other histological types.

One trial showed that gemcitabine+docetaxel is more effective than gemcitabine alone as second-line chemotherapy, but data are conflicting and toxicity is different [20].

Gemcitabine was shown to have antitumor activity in leiomyosarcoma also as a single agent.

Dacarbazine has some activity as second-line therapy (mostly in leiomyosarcoma). The combination of dacarbazine and gemcitabine was shown to improve the OS and PFS over dacarbazine in a randomized trial and is therefore an option in leiomyosarcoma [21].

A randomized trial showed a benefit in PFS averaging 3 months for pazopanib given up to progression to advanced, previously treated, soft tissue sarcomas patients excluding liposarcomas [22].

For osteosarcoma, Curative treatment of high-grade osteosarcoma consists of chemotherapy and surgery. Compared with surgery alone, multimodal treatment of high-grade localized osteosarcoma increases disease-free survival probabilities from only 10-20% to >60%. In general, chemotherapy is administered in peri-operative strategy. The extent of histological response to preoperative chemotherapy predicts survival [23-25]. Doxorubicin, cisplatin, high-dose methotrexate, ifosfamide, and etoposide are frequently used as the basis of treatment.

In our series, patients who underwent resection with involved margins presented disease recurrence. For patients with metastatic disease, they mainly received chemotherapy based on anthracyclines and ifosfamide but response was very modest and disease had progressed in short time.

Conclusion

Adult head and neck sarcomas are very rare tumors with poor prognosis that can present management difficulties. Complete resection with negative margins followed by adjuvant radiation and possibly chemotherapy in selected cases potentially decreases local recurrences and improves survival. These tumors are best managed in a multi-disciplinary setting.

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Competing Interest

Authors have declared that no competing interests exist.

Authors' Contribution

All authors had participated to the study, each one in his field, and they all read and approved the final manuscript.

Consent

All patients were agreed and had consent to participate to this work.

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