ORIGINAL ARTICLE

Superficial myxofibrosarcoma: Assessment of recurrence risk according to the surgical margin following resection. A series of 21 patients

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KEYWORDS
Myxofibrosarcoma; Diffuse infiltrative pattern; Recurrence.

Summary

Introduction: Superficial myxofibrosarcomas are malignant connective tissue tumors, whose frequent recurrence influences the local and vital prognosis. Even when resection seems to be macroscopically complete it is very often microscopically contaminated. The aim of this study was to evaluate recurrence in relation to the surgical margins and to compare, when possible, tumor size, evaluated clinically and macroscopically by the pathologist.

Materials and methods: This was a single center study of 21 patients, mean age 67 years old, treated for superficial myxofibrosarcoma. The number, date and location of recurrence were collected for each patient. A clinical and pathological measurement was made of the longest axis of the tumor in each case of recurrence.

Results: Fifty-seven percent of patients presented with recurrent tumors. The mean number of recurrences was 1.4 per patient (1–8). The surgical margins were wide in four cases, marginal in two cases and incomplete/intralesional in 15 other patients with a rate of recurrence of 25, 50 and 67% respectively. The size evaluated during the preoperative clinical examination (14 cases) was underestimated by a mean 2.4 cm compared to the macroscopic pathology assessment. The preoperative size on MRI (5 cases) was also underestimated by a mean 1.3 cm.

Conclusion: Superficial myxofibrosarcomas are tumors that are difficult to resect completely because they are infiltrative, a feature that is often underestimated before surgery. Surgical
Introduction

Superficial myxofibrosarcomas are malignant connective tissue tumors, which usually progress slowly [1]. Nevertheless, the rate of recurrence is very high in these tumors, influencing the local and vital prognosis. Recurrence is usually local characterized by extension along the fascias and the hypodermal passageways around the nodule [2,3]. Although surgical resection may seem complete to the surgeon it is often found to be incomplete by the pathologist. One possible explanation is that the size of the tumor is underestimated clinically and on MRI because of the highly infiltrative and poorly differentiated tumor proliferation in adjacent subcutaneous tissue. It is therefore difficult to precisely define the extent of surgical resection that will be necessary [4].

The aim of this study was to evaluate the rate of recurrence in relation to the surgical margins and to compare, when possible, the size of the tumor measured clinically and macroscopically by a pathologist. Because this was a retrospective study we could not measure the largest axis of the tumor based on the extent of tumoral invasion detected on microscopic analysis, which is the usual tumor sampling procedure, so that this variable could not be precisely determined.

Materials and methods

Materials

This was a continuous retrospective series of patients treated for superficial myxofibrosarcoma (supra-aponeurotic) between 2001 and 2010. All patients underwent surgery in the same center for all procedures.

Methods

The number, date and location of recurrences were collected for each patient.

This included noting the size of the largest nodule along its longest axis at diagnosis and for each case of recurrence. Depending upon the available information, the size was determined clinically, on MRI and by macroscopic pathological assessment of the resected tumor:

- clinical measurement was obtained by the surgeon during the preoperative assessment;
- the longest axis of the tumor was measured on MRI in the following sequences: axial, coronal and sagittal T1 and T2-weighted sequences;
- macroscopic pathological assessment was based on the longest axis of the tumor.

The tumor grade, defined according to the National Federation for the Fight Against Cancer (Fédération Nationale de Lutte Contre le Cancer [FNCLCC] [5]) and the quality of resection according to the Ennekking classification (intraleisional, marginal, wide) [6] were obtained for each resected tumor.

The series

This series included 21 patients (11 women, 10 men), mean age 67 years old (38–85) at the first surgical procedure (Table 1). The tumor was located on the lower extremities in 11 cases (52%), upper extremities in eight cases (38%) and on the trunk in two cases (10%). A tumefaction was discovered fortuitously in all patients except one who presented with signs of compression of the ulnar nerve in the elbow.

All patients underwent planned surgery whose goal was to obtain clean surgical margins of at least 1 cm. After surgery all patients underwent postoperative radiotherapy at a dose of between 54 and 60 Grays. One patient also underwent neoadjuvant chemotherapy due to diffuse subcutaneous tissue infiltration.

Pathology results showed grade 1 myxofibrosarcomas in five cases, grade 2 in eight and grade 3 in eight cases. The tumor was limited to the dermis and hypodermis in all cases (Fig. 1). Although resection seemed to be complete at surgery in the 21 tumor samples that were analyzed, it was found to be wide in three cases, marginal in two cases and intraleisonal in 16 cases. Scar revision surgery was performed in all recent cases of intraleisonal resection once the pathological results were received.

Results

Twelve patients (57%) presented with recurrence, which was always local on the periphery of the initial area of resection. There were a mean 1.4 recurrences per patient (1–8): in the 12 patients with recurrence, eight had one or two recurrences, two had three recurrences, and two had four or more recurrences (Fig. 2). Recurrence occurred after a mean 10.5 months (1–29 months). The initial tumor was grade 1 in four cases, grade 2 in four cases and grade 3 in four cases. Resected tumors from the first recurrence were one grade higher than the initial tumor in 58% of cases. In particular, in grade 1 tumors, the recurrent tumor was one grade higher in 100% of the cases.

Two of the patients with recurrent tumors presented with distant metastases associated with the recurrent tumor.
Superficial myxofibrosarcomas: recurrence after resection

Table 1  Clinical features of the 21 patients.

<table>
<thead>
<tr>
<th>Age</th>
<th>Gender</th>
<th>Tumor location</th>
<th>Surgical margin</th>
<th>Grade</th>
<th>Number of recurrences</th>
<th>Metastases</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>38</td>
<td>F</td>
<td>Buttocks</td>
<td>R2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>59</td>
<td>F</td>
<td>Knee</td>
<td>R1</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>80</td>
<td>F</td>
<td>Popliteal fossa</td>
<td>R2</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>81</td>
<td>F</td>
<td>Back</td>
<td>R2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>5</td>
<td>62</td>
<td>M</td>
<td>Leg</td>
<td>R0</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>57</td>
<td>F</td>
<td>3rd finger</td>
<td>R2</td>
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<td>0</td>
</tr>
<tr>
<td>7</td>
<td>43</td>
<td>F</td>
<td>Forearm</td>
<td>R2</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>8</td>
<td>76</td>
<td>M</td>
<td>Forearm</td>
<td>R2</td>
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<td>1</td>
</tr>
<tr>
<td>9</td>
<td>59</td>
<td>M</td>
<td>Back</td>
<td>R2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>10</td>
<td>77</td>
<td>M</td>
<td>Knee</td>
<td>R2</td>
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<tr>
<td>11</td>
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<td>M</td>
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<td>1</td>
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<tr>
<td>12</td>
<td>67</td>
<td>F</td>
<td>Forearm</td>
<td>R2</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>13</td>
<td>68</td>
<td>M</td>
<td>Arm</td>
<td>R2</td>
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<tr>
<td>14</td>
<td>73</td>
<td>F</td>
<td>Leg</td>
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<tr>
<td>15</td>
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<td>Leg</td>
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</tr>
<tr>
<td>16</td>
<td>61</td>
<td>M</td>
<td>Leg</td>
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<tr>
<td>17</td>
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<td>F</td>
<td>Knee</td>
<td>R2</td>
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<tr>
<td>18</td>
<td>70</td>
<td>M</td>
<td>Shoulder</td>
<td>R2</td>
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<td>1</td>
</tr>
<tr>
<td>19</td>
<td>79</td>
<td>M</td>
<td>Leg</td>
<td>R2</td>
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<td>2</td>
</tr>
<tr>
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<td>85</td>
<td>M</td>
<td>Arm</td>
<td>R2</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>21</td>
<td>67</td>
<td>F</td>
<td>Wrist</td>
<td>R2</td>
<td>2</td>
<td>1</td>
</tr>
</tbody>
</table>

R0: absence of residual tumor; R1: microscopic tumor remains; R2: macroscopic tumor remains.

(pulmonary, liver and bone). They were discovered during the first recurrence in one case and the third in the other case. The latter died 6 months after the last surgical procedure for recurrence and the discovery of metastases. These patients received adjuvant chemotherapy as well as revision surgery.

The surgical margins were wide in 4/21 patients, marginal in 2 and intraleisional in 15 cases and recurrence occurred in 25, 50 and 67% respectively. The surgical margins in the 29 other tumor samples, resected due to recurrence, were wide in seven cases, marginal in two cases and intraleisional in 20 cases with a rate of new recurrence of 14, 50 and 75% respectively. Out of the total of 50 resected tumor samples (including initial and recurrent tumors), recurrence was 18, 50 and 71% respectively.

The results of this series were not influenced by histological grade or age. The rate of recurrence in relation to the histological grade was 80, 50 and 50% for grades 1, 2 and 3 respectively. The mean age of patients with recurrence was 66.2 and of those without was 65.6.

Evaluation of tumor size

Clinical measurement of the longest axis of the main nodule was available retrospectively in 14 of the tumor samples and a preoperative MRI was available in five cases. Clinical

Figure 1  Myxofibrosarcoma of the leg. Sagittal T2-weighted MRI with comet tail appearance.

Figure 2  Number of patients in relation to the number of recurrences.
measurement was underestimated a by a mean 2.4 cm (0–11) compared to macroscopic pathology results. The MRI measurement was also underestimated by a mean 1.3 cm (0–7.7) compared to macroscopic pathology results (Figs. 3 and 4).

Discussion

For several years certain authors have defined myxofibrosarcomas as a distinct tumoral entity [7]. This entity has been recognized since 2002 and is now included in the World Health Organization tumor classification [8].

Myxofibrosarcomas are one of the most frequent sarcomas in the elderly with a peak incidence in patients between 61 and 70 years old [9]. They are usually located on the lower extremities. These are malignant connective tissue tumors involving cutaneous and subcutaneous tissue in two thirds of the cases. In other cases the fascia, underlying muscles and even the bone may be involved. Angervall et al. reported local recurrence in 50–60% of cases, with no relationship to histological grade [7].

On the other hand Willems et al. [1], in a series of 32 myxofibrosarcomas and Fukunaga and Fukunaga [10] in the pathological assessment of one case, have already shown that low-grade tumors frequently increase in grade during local recurrence and may metastasize. For Ferguson et al., a diagnosis of myxofibrosarcoma may even be predictive of an increase in histological grade during any eventual recurrence [11]. We reached the same conclusions since 58% of recurrences were a grade higher than that of the initial tumor and two patients presented with distant metastases. Nevertheless, because of the small number of patients it was not possible to show any correlation between the progression of tumor aggressivity and the number of recurrences.

Myxofibrosarcomas are characterized by their significant multidirectional spreading pattern along the fascial planes [9,12,13]. This is seen as a hypersignal on T2-weighted MR images which usually has a comet tail appearance, and which has been clearly described by Kaya et al. [4]. According to these authors, this characteristic infiltration is found in 80% of the cases of myxofibrosarcoma. Nevertheless the hypersignal on T2-weighted images is not constant: in a certain number of cases, MRI shows a local lesion and spreading along the fascias is identified by histological analysis of the tumor sample. This probably explains the high rate of contaminated or marginal surgical margins in resected tumors (78% of the primary tumors and recurrent tumors in our series).

Our rate of recurrence (57%) is comparable to that reported in the literature: 52–61% [2,7,9,12,14]. For Merk et al. [12] the rate of recurrence may be influenced by age (more recurrence in elderly patients), histological grade and the quality of resection [15,16]. In our series, as in others [15–19], the rate of recurrence logically varied in relation to the quality of the surgical margins. On the other hand unlike Lin et al. [15] and Gronchi et al. [16], we did not find any correlation with the histological grade, which has also been noted by several authors [18–23]. Age was also not a factor that influenced the rate of recurrence (65.6 vs. 66.2).

Nevertheless there are two important observations in our study. First, the significant difference in the rate of recurrence between wide and contaminated surgical margins (18 vs. 71%), which emphasizes the importance of obtaining the most complete resection possible at the outset (the high rate of recurrence even with wide margins should be noted [18%]). Myxofibrosarcomas are therefore difficult tumors to control even when appropriate treatment is provided. At the same time it is impossible to establish a statistical correlation between the quality of the surgical margins and recurrence in this study for two reasons. First this tumor is rare, therefore there were very few patients included in the study, making it impossible to obtain a correlation. Second, surgical management of marginal resection changed between 2001 and 2010: initially patients did not systematically undergo revision surgery if pathology results showed resection to be marginal, while this is now systematic. These observations are a reminder of how important the first biopsy is; when the diagnosis of myxofibrosarcoma is confirmed, particular attention should be paid to making sure that surgical margins are wide enough.

Normally T2-weighted MRI is the best technique to identify the extent of tumoral invasion. At the same time, Kaya et al. [4] have shown that MRI is not sufficient to identify
tumoral infiltration in these cases. We reached the same conclusions in our study, which showed that the size of the tumor was underestimated by a mean 1.3 cm on MRI compared to pathology results. However, there were not enough MRIs in our study to define a safe surgical margin that ensures that healthy tissue has been reached. Our results do not provide more information on this issue than the study by Kaya et al. [4] who recommend resection of all of the tissue with a hypersignal. To determine the ideal surgical margins, a study would have to be performed to evaluate tumor size with MRI and on pathology, which is difficult because of the low incidence of this tumor.

Conclusion

It is difficult to obtain complete resection of superficial myxofibrosarcomas during the initial surgical procedure, because the invasive spreading of these tumors is often undiagnosed before surgery. This tumor should be resected as completely as possible during the first surgical procedure because of the high risk of recurrence. Thus, surgical treatment of these tumors must include surgical margins that are much wider than those suggested by the clinical evaluation and MRI. It is therefore important to perform a biopsy first to confirm the diagnosis and plan on wide resection. Indeed in many cases, tumor infiltration identified on T2-weighted MRI sequences underestimated actual tumoral infiltration. Even after complete resection, the risk of recurrence is high. In case of marginal or incomplete resection, revision surgery of the scar should be systematically performed.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

References