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Clinical characterization of the Dermatofibrosarcomas at Barretos Cancer Hospital in São Paulo

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ABSTRACT

Introduction: Dermatofibrosarcoma (DFSP) is a rare neoplasia from mesenchymal tissues in the skin. It has a high potential for local invasion and a high rate of recurrence after the surgical excision. It appears as a hardened plaque of violaceous color, asymptomatic, which evolves with protuberant nodules. There are few Brazilian studies on DFSP. Therefore, patient's characterization could contribute to future therapeutic studies. **Objective:** To characterize patients with this cancer and describe their clinical and demographic characteristics; to describe adopted therapeutic, recurrence rate and survival. **Methods:** Retrospective observational study which analyzes data of the medical record of Barretos Cancer Hospital. The variables were analyzed in terms of the average, median and frequency. The Fisher's exact test and the Chi-square test were used to identify associations among the variables. Analysis of cancer survival with no recurrence were made through confection of Kaplan-Meier curves and the log-rank test. **Results:** There were 69 patients, 52.2% male and 71% white. The average diagnosis age was 42 years old. Regarding education, elementary school incomplete was 37.7%. The main location of the primary tumor was the trunk (34.8%). Conventional surgery was chosen in all cases of primary tumor and 7.2% underwent adjuvant radiotherapy, of which 36.2% presented local recurrence. Among the patients that had never been treated, the recurrence rate was 9 (24.3%) and the distant recurrence was observed in only one case. The previous treatment, before the hospital treatment, was a variable related to recurrence (p=0.014). Disease-free survival had an average of 23.4 months. **Conclusion:** Conventional surgery used in all cases obtained, in most cases, stabilization or cure of the disease. The recurrence rate was high, however, it was possible to be controlled. Also, only one patient died because of the disease, confirming the low but deadly potential of the dermatofibrosarcomas.

Keywords: Dermatofibrosarcoma; DFSP; Neoplasia of soft tissues; recurrence; survival; protuberans.

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INTRODUCTION

The dermatofibrosarcoma protuberans (DFSP) is a rare cutaneous soft tissue sarcoma with high potential of local invasion and high rate of local recurrence after surgical excision and it rarely leads to metastasis.[1]

The Dermatofibrosarcoma comes from fibroblasts, histiocytic (inactive and fixed macrophages, with retracted pseudopods with ovoid shape), or from a neuroectodermal origin. The causes of the disease are trauma, surgical scars, burn scars, places of multiple immunizations. [2]

The most prevalent places are the trunk, chest, shoulders, and proximal extremities.[2,3] At first, it appears as a hard plaque of violaceous color, reddish-brow and asymptomatic. As years go by, protuberant nodules are developed inside the plaque. [1]

The incidence of dermatofibrosarcoma is estimated of 0,8-5 cases in a million of people every year, it does not have a significant discrepancy among men and women and usually occurs in people from 20 to 50 years old.[3]

There are cytogenetic changes involving the chromosomes 17 and 22. There is fusion of the gene that codifies collagen of alpha-1 type, with the platelet-derived growth factor beta polypeptide (PDGFB gene) which is a tyrosine kinase receptor.[1, 4]

It appears in the microscope with fusiform dermal cells proliferation infiltrating the subcutaneous fat and with a honeycombed appearance.[1] It is composed of cells with large nucleus, rarely presenting a hemosiderin deposit, inflammatory infiltrates, foamy histiocytes and giant cells. It presents little pleomorphism and low degree of mitosis figures.[5]

The dermatofibrosarcoma diagnosis is through clinic, histopathological confirmation and mainly immune histochemical. This last analysis can be useful in differential diagnosis once the cells show a positive marking for CD34 and negative for the Factor XIIa - stabilizing factor of fibrin.[1]

It is necessary to carry through an excisional or incisional biopsy. If the lesions (nodules or plaques typical of DFSP) are very extensive or deep in the soft tissues, it is necessary to rule out lung metastasis through computerized tomography, even though it is really rare. [6]

The standard treatment for dermatofibrosarcoma is surgical. When the diagnosis is not made in the correct way, the conventional surgery performed has a chance of recurrence in 60% of the cases, reducing to 20% when the margins are superior to 4 cm. Even for patients with low-grade DFSP with negative margins, the local recurrence rate was 7% in a 5-year period. Alternatively, the excision through Mohs micrographic surgery (MMS) provides a recurrence rate of only 1.6%, considered the best for the DFSP treatment.[1, 2, 7]

The Mohs technique consists of the removal of several layers of neoplastic tissue which are mapped and examined using special coloration, making it possible to observe the side and deep margins of the tumor in the microscope. Therefore it is a procedure highly specialized that requires a considerable training and a specialized auxiliary team, which limits its wide application.[7]

Radiotherapy can also be used in cases where the tumor is inoperable or clear margins are not possible, or even after or multiple previous recurrences.[1,4,8] There is no known effective chemotherapy treatment.[7]

For follow up, clinical examinations are advised every six months for five years and annually thereafter. In a recent systematic review of MMS in the DFSP, the average recurrence time was 68 months.[1]

As a rare neoplasia, there are few studies and knowledge among non-specialists, making a direct impact in diagnosis and proper treatment.

Therefore, here we provide relevant clinical information and descriptive analysis where, in Brazilian literature, the subject is practically absent. The characterization of a real population will be very useful for the therapeutic planning and evaluation of results in a real-world scenario.

OBJECTIVES

To characterize patients with dermatofibrosarcoma of Barretos Cancer Hospital – Brazil and to describe the clinical and demographic characteristics of the disease, treatment, recurrence and survival rates of the patients.

METHODS

It is a retrospective study that analyzes clinical and demographic data as: sex, skin color, education, diagnosis age, tumor localization, histological subtype, treatment methods, recurrence, survival and the disease's current status of the dermatofibrosarcoma patients treated from January 2005 to December 2015 in Barretos Cancer Hospital. Patients with lack of minimum clinical data in their medical records were excluded from this research.

The continuous variables were analyzed in terms of average, median, standard deviation and eventual measures of dispersion. Discrete variables were described in their frequencies. The Fisher's exact test or the Chi-square test were used to identify associations among the discrete variables. The analysis of cancer survival with no recurrence was made through confection of Kaplan-Meier curves and the log-rank test. For practical purposes, the value of statistical significance for all the calculations was 95% (p=0.05).

ETHICAL ASPECTS

This is an observational study that uses the analysis of data from the patients' medical records. The research was submitted to the Ethics Committees in Research and approved by it. Submission number: 25441019.7.0000.5437. Moreover, the authors declare absence of conflict of interests.

RESULTS

There were 74 patients with dermatofibrosarcoma treated in Barretos Cancer Hospital from 2005 to 2015. Five patients were excluded for not presenting minimum relevant information. Three of the five excluded patients did not present data like recurrence date, diagnosis date, treatment date and so on. Two of the five were not treated in the hospital and had incomplete information. At the end, the total analysed were 69 patients.

Sociodemographic, histopathological, and clinical characteristics

The discrete variables analyzed according to frequency show that the majority was male 36 (52.2%) and white skin 49 (71%). Regarding education, 37.7% of the patients has an incomplete elementary school level of education. Table 1 shows sociodemographic characteristics of the patients.

The histological subtypes were not classified in most of the cases (78.3%). The main location of the tumor was the trunk: in 24 cases (34.8%). All the histopathological and clinical characteristics are presented in Table 2.

Continuous variables, such as age at diagnosis and surgical margin, were analyzed with the following results obtained: average age of 42.15 years old, (6 years old to 74.65, standard deviation of 15.66). Average margin of 13.65mm, (1mm to 50mm standard deviation of 9.78).

All patients underwent a conventional surgery in the primary tumor and 5 (7.2%) received adjuvant radiotherapy. None of them received systemic treatment.

Among the 69 patients admitted in hospital, 30 (43.5%) had previous treatment outside Barretos Cancer Hospital and 37 (53.6%) did not. These data are shown in Table 3.

Table 1 – Sociodemographic characteristics of patients with Dermatofibrosarcoma at Barretos Cancer Hospital.

	Variables	Frequency n (%)
Sex	Female	33 (47.8%)
	Male	36 (52.2%)
Skin color	White	49 (71%)
	Black	6 (8.7%)
	Mixed race	14 (20.3%)
Education	Illiterate	1 (1.4%)
	Elementary school incomplete	26 (37.7%)
	Elementary school complete	5 (7.2%)
	High school incomplete	3 (4.3%)
	High school complete	15 (21.7%)
	Higher education incomplete	5 (7.2%)
	Higher education complete	12 (17.4%)
	Graduation	1 (1.4%)
	Not answered	1 (1.4%)
		Total: 69 (100%)

Table 2 – Clinical characteristics of patients with Dermatofibrosarcoma at Barretos Cancer Hospital.

	Variables	Frequency n (%)
Tumor location primary	Upper limbs	4 (5.8%)
	Head and neck	17 (24.6%)
	Trunk	24 (34.8%)
	Lower limbs	15 (21.7%)
	Shoulder	9 (13.0%)
Histological Subtype	Giant cell fibroblastoma	2 (2.9%)
	Fibrosarcomatous	9 (13.0%)
	Myxoid	4 (5.8%)
	Unknow	54 (78.3%)
		Total: 69 (100%)

Table 3 - Previous treatment of DFSP treated at Barretos.

Previous Treatment	Frequency n (%)
Yes	30 (43.5%)
No	37 (53.6%)
Unknow	2 (2.9%)
	Total: 69 patients

Characterization of the patient's recurrence

The main objective of the study was to evaluate the tumor recurrence. Therefore, pertinent questions about the recurrence of the disease were added to the collection form. Among the 69 observed patients, 25 (36.2%) had local recurrence, 1 (1.4%) had distant recurrence, and 43 (62.3%) did not recur. Among those patients who did not have previous treatment, that is, untreated people, there were 37 patients, and the recurrence rate was 9 (24.3%).

Local recurrence was detected in 25 patients 25 (36.2%). All underwent new surgical resection and 4 (16%) received adjuvant radiation therapy. Of these patients, 7 were negative margins and disease free (28%). 12 (48%) positive margins but clinically without progression and under surveillance; 5 (20%) had DFSP progression; and 1 (4%) without information. These results are presented in Table 4.

The patients´ status at the last verified information was 47 (68.1%) alive and disease-free 10 (14.5%) lost follow-up, 6 (8.7%) was alive with the disease, 5 (7.2%) dead from other causes and one (1.4%) dead from dermatofibrosarcoma.

Clinical and demographics characteristics of the primary tumors associated to recurrence

The recurrence was compared with variables as sex, color, localization of the primary tumor, surgical margins, and previous treatment. The previous treatment was a variable associated with the recurrence, as it is shown in Table 5.

Disease-free survival

The disease-free survival of the patients was analyzed with a mean follow up time of 23 months (3 to 83 months). The median disease-free survival was 23.4 months (3.5-83.9 months).

Disease free survival was also analyzed in comparison with the previous treatment, with the mean result of 13 months average for the patients with previous treatment and 38 months for those without previous treatment (P=0.009), as shown in figure 1 and figure 2.

Table 4 – Treatment of recurrent cases (n): responses.

	Variables	Frequency (%)
Response to treatment of the recurrence	Not evaluated	1 (4%)
	Complete response	7 (28%)
	Stable disease	12 (48%)
	Progression of the disease	5 (20%)
		Total 25 patients

Table 5 - Local recurrence according to clinical and demographic variables.

	With local recurrence (%)	With no local recurrence (%)	Total
Sex			
Female	12 (36.40%)	21 (63.60%)	33 (100%)
Male	14 (38.90%)	22 (61.10%)	36 (100%)
			P=0.513
Local			
Upper limbs	7 (53.80%)	6 (46.20%)	13 (100%)
Lower limbs	6 (40%)	9 (60%)	15 (100%)
Trunk	7 (29.20%)	17 (70.80%)	24 (100%)
Head and neck	6 (35.30%)	11 (64.70%)	17 (100%)
			P=0.523
Color			
White	19 (38.80%)	30 (61.20%)	49 (100%)
Mixed race	4 (28.60%)	10 (71.40%)	14 (100%)
Black	3 (50%)	3 (50%)	6 (100%)
			P=0.663
Margin			
Up to 20mm	28 (75.70%)	57.10%	
More than 20mm	9 (24.32%)	66.70%	
			P=0.459
Previous treatment			
Yes	16 (53.30%)	14 (46.70%)	30 (100%)
No	9 (24.30%)	28 (75.70%)	37 (100%)
			P=0.014

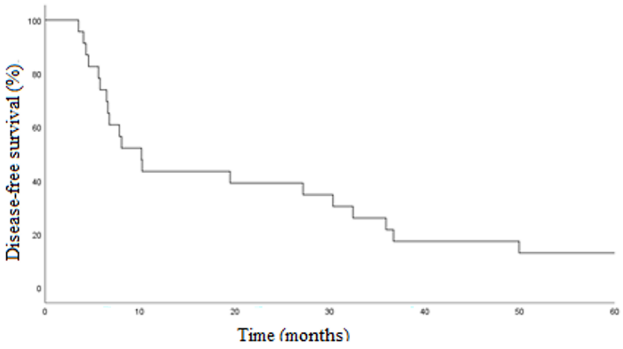

Figure 1 - Kaplan Meier curves showing the disease-free survival.

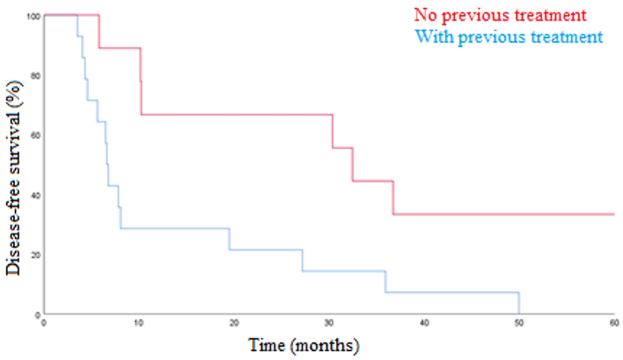

Figure 2 - Kaplan Meier curves of disease-free survival, with the previous treatment as comparison factor (p=0.009).

DISCUSSION

Dermatofibrosarcoma, in our reality does not differ among sex, education, skin color and the average diagnosis age. The trunk was the predominant location of the primary tumor, however, there was a large number of patients with head and neck tumors, as observed by Molina et al.[9]

Among all the clinical and demographic variables tested according to the recurrence, the only one that was associated was the previous treatment. Thus, previously treated patients with recurrence who looked for treatment at the hospital may be a study selection bias. Patients who treated only at the Barretos Cancer Hospital had a lower recurrence rate than those treated at other hospitals before.

The average time of recurrence, according to literature, is 68 months. In our study, the follow-up time average of the patients was 71 months. That is, it was a significant time to evaluate the recurrence of the disease.

CONCLUSION

This study presented information in agreement with the current literature regarding sociodemographic and clinical characteristics.

The clinical characterization of recurrences in patients with Dermatofibrosarcoma enable the analysis of important data. The recurrence is high, but controllable. The conventional surgery was used in all the recurrence cases and the disease was stabilized or cured in most cases. Only one patient died from the disease, confirming the local aspect of its development.

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