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Dermatofibrosarcoma Protuberans; Case Report in a Pediatric Patient

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ABSTRACT

Dermatofibrosarcoma protuberans (DFSP) is a rare and locally aggressive mesenchymal neoplasm arising from the dermal and subcutaneous tissues. It typically manifests as a slow-growing, firm, protuberant or plaque-like lesion on the skin. DFSP predominantly affects young to middle-aged adults, with a slight predilection for females. This tumor exhibits a distinctive infiltrative growth pattern, characterized by tumor cells invading the surrounding tissues, including the deep subcutaneous layers and the underlying fascia.

Histopathologically, DFSP presents characteristic features, such as the presence of spindle-shaped tumor cells arranged in a "storiform" pattern, as well as the presence of a prominent "honeycomb" appearance due to the presence of multinucleated giant cells. Immunohistochemical staining is essential to confirm the diagnosis, with positivity for CD34 being a hallmark of DFSP.

Although DFSP rarely metastasizes, its extensive local invasion and high recurrence rate necessitate a wide surgical excision with clear margins as the mainstay of treatment. The use of Mohs micrographic surgery or adjuvant radiation therapy has demonstrated favorable outcomes in cases with challenging anatomical locations or microscopically positive margins. Imatinib mesylate, a tyrosine kinase inhibitor, has also emerged as a promising systemic therapy for advanced or unresectable DFSP, particularly cases with the COL1A1-PDGFB gene fusion, which represents the molecular hallmark of DFSP.

Early diagnosis and appropriate management are crucial to achieving optimal outcomes in DFSP. This article provides a comprehensive review of the clinical, histopathological, and molecular aspects of DFSP, highlighting the significance of a multidisciplinary approach to ensure accurate diagnosis and tailored therapeutic strategies for patients affected by this rare dermatological neoplasm.

KEY WORDS: Dermatofibrosarcoma, subcutaneous, mesenchymal, neoplasm

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INTRODUCTION

Dermatofibrosarcoma protuberans (DFSP) is a rare mesenchymal neoplasm belonging to the spectrum of soft tissue sarcomas. It is characterized by its locally aggressive behavior and distinctive infiltrative growth pattern within the dermal and subcutaneous tissues. DFSP commonly presents as a slow-growing, firm, protuberant or plaque-like lesion on the skin, posing diagnostic challenges due to its rarity and clinical resemblance to other benign or malignant skin lesions.[1,2]

First described by Taylor in 1890, DFSP represents less than 1% of all soft tissue tumors, rendering it an infrequent entity encountered in clinical practice. Its relatively indolent nature may lead to diagnostic delays, potentially resulting in delayed treatment and increased morbidity. DFSP most frequently arises in young to middle-aged adults, with a slight female predilection. Although it typically occurs on the trunk, limbs, or head and neck regions, its potential to involve deeper subcutaneous layers and fascial planes highlights the need for meticulous clinical evaluation and histopathological analysis to guide accurate diagnosis and therapeutic strategies.[1,2]

Histopathologically, DFSP exhibits characteristic features, including spindle-shaped tumor cells arranged in a "storiform" or cartwheel-like pattern, interspersed with "honeycomb" areas comprising multinucleated giant cells. While the diagnosis can be corroborated by immunohistochemical staining, the lack of specific molecular markers poses challenges in differentiating DFSP from other mesenchymal neoplasms. The molecular hallmark of DFSP involves the COL1A1-PDGFB gene fusion, which plays a crucial role in its pathogenesis and serves as a potential therapeutic target for advanced or unresectable cases.[2,3]

Given its infiltrative nature and potential for local recurrence, effective management of DFSP necessitates a multidisciplinary approach, involving dermatologists, surgical oncologists, and radiation oncologists. The mainstay of treatment involves wide surgical excision with clear margins, aiming to achieve complete tumor resection while preserving vital structures. In cases with anatomically challenging locations or microscopically positive margins, innovative techniques like Mohs micrographic surgery or adjuvant radiation therapy have been implemented to reduce the risk of local recurrence and improve patient outcomes.[3,4]
This comprehensive review aims to provide an in-depth understanding of the clinical, histopathological, and molecular aspects of DFSP, accentuating the significance of early and accurate diagnosis to facilitate timely intervention and optimize patient outcomes. Additionally, the evolving role of targeted therapies, particularly imatinib mesylate, in the management of advanced or unresectable DFSP underscores the potential for tailored treatment approaches, promising a brighter outlook for patients affected by this intriguing dermatological neoplasm.[3,4]

CASE REPORT

A 9-year-old female patient presents with a contusiform plaque of 1 year of evolution, anteromedial of the left shoulder. Accompanied by pruritus. Product of non-consanguineous parents. No history of trauma, bleeding, weight loss or any other symptoms. On physical examination there is no evidence of regional lymphadenopathy.8
The patient presented with localized monomorphous dermatosis, characterized by a 2x3 cm violaceous plaque with partially defined borders, of chronic evolution.(Fig.1) An excisional biopsy of the lesion was performed and the histopathological report showed: epidermis with orthokeratotic hyperkeratosis, formation of horny plugs, moderate regular acanthosis at the expense of the interpapillary processes and hyperpigmentation of the basal layer. In the superficial dermis there is a perivascular perivascular iflammatory infiltrate consisting of lymphocytes and histiocytes.

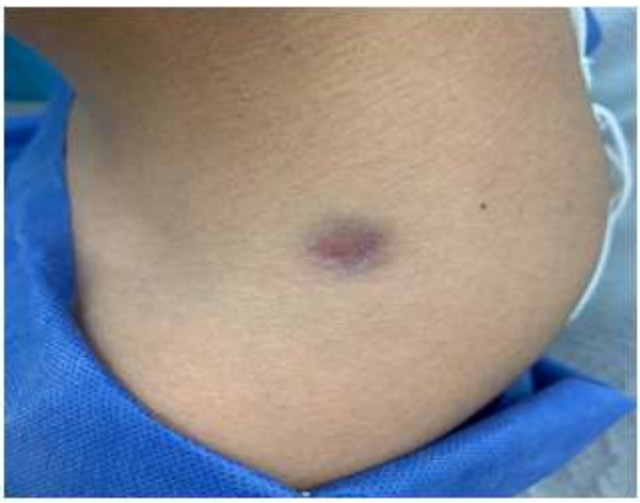

Figure 1. Dermatosis with violaceous plaque.

Throughout the thickness of the dermis there is circumscribed neoformation consisting of numerous spindle cells arranged in bundles that follow different paths and intermingle with collagen fibers, as well as the presence of melanic pigment. This neoformation infiltrates the subcutaneous cellular tissue in both lobules and septa. In the rest of the section there are areas of hemorrhage and vascular dilatation. Immunohistochemistry was performed with CD34 (+) and S-100(-) markers, so a diagnosis of DFSP was made.
A simple MRI of the shoulder was performed and no residual tumor was found.(Fig.2)

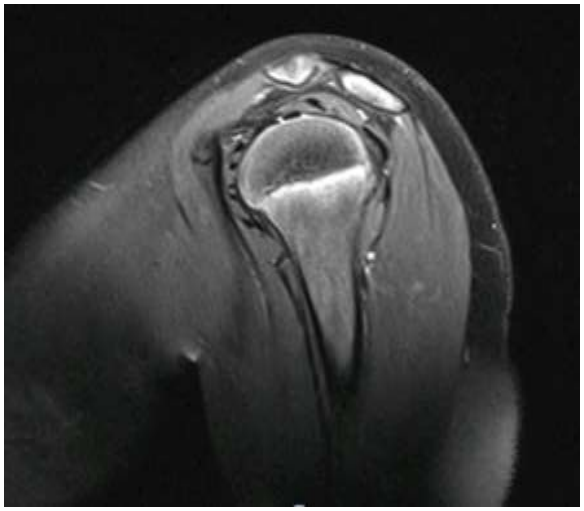

Figure 2. MRI Without alterations

DISCUSSION

It is an uncommon tumor, accounting for 2-5% of soft tissue tumors, with an incidence of approximately 0.8 to 5 cases per million inhabitants per year. It is of fibrohistiocytic origin, and although its stem cell is unknown, it is mostly CD34 (+) and it has been described in several studies that most cases occur due to a distinctive chromosomal rearrangement between chromosomes 17 and 22, in which a reciprocal translocation t(17;22) (q22;q13), or the production of a ring chromosome, producing the fusion of the alpha chain of collagen type 1 (COL1A1 gene in the 17q22 region) with the platelet-derived growth factor gene (PDGFβ). This genetic rearrangement has been found in up to 90% of these lesions, which are identified by cytogenetic analysis.[1,2]
This neoplasm is uncommon in pediatric patients, and when it occurs in them, it has a greater predilection for females. Its distribution by segments is 40-60% in the trunk, 20-30% in the extremities and only 10-20% in the head and neck. And even up to 20% is due to congenital forms. [3]
Since its clinical presentation depends on the time of evolution, initially the most common form is usually a firm, indurated, erythematous-violaceous or asymptomatic yellow-brown plaque, which slowly evolves into a violaceous nodular neoformation, with atrophic overlying skin, with the presence of telangiectasias. It tends to move freely towards the underlying tissues, and even invades them. Four

morphologic variants are described; nodular variant, atrophic plaque, keloid and sclerotic. [4]

Diagnosis is made by histopathological and immunohistochemical studies. Since up to 60% of tumors present local recurrences after excision. Complementary imaging studies can be used to assess the extension of the tumor, being the MRI of choice to see the depth and invasion of soft tissues, muscle fasciae or regional lymph nodes. Although 85-90% of these tumors are of low grade malignancy, [5]

DFSP is often confused in pediatric patients with other fibrohistiocytic neoplasms from which it must be differentiated, such as dermatofibromas, leiomyomas, neurofibromas, and fibrous hamartoma. [5,6]

The general characteristic of DFSPs on microscopy is a dense spindle cell component, with large nuclei and elongated cytoplasm, but a low degree of nuclear pleomorphism with low mitotic rate, located at the level of the dermis. All this cellular component is embedded in a stroma composed of collagen fibers and capillaries. An atrophic epidermis is usually seen in the layers overlying the tumor. The spindle cells are arranged in irregularly intertwined fascicles in a "storiform" pattern. As the tumor infiltrates the dermis, it acquires a "honeycomb" pattern due to its invasion through the septa, although its multilayered pattern of infiltration is what gives it the microscopic extension much wider than the macroscopic one, since it produces bands parallel to the epidermis, and causes the tumor to spread diffusely. In advanced stages, the tumor usually presents hemorrhagic and cystic degeneration. Necrosis is rare, and suggests a higher grade neoplasm. [6,7]

On immunohistochemistry, they usually express CD34 on immunostaining, which is present in their spindle cell component, but the presence of this finding is not very specific, since other neoplasms of fibrohistiocytic origin express this protein widely. It is a marker that is even possible to see in vascular and hematologic neoplasms[7]

Surgery is considered the treatment of first choice. It is mandatory to perform it with wide margins, 2 to 4 cm, and to corroborate that they are free, since microscopic extension is common, and goes far beyond the macroscopic margin. Mohs micrographic surgery reduces the recurrence rate and improves the prognosis, reporting a recurrence of 1.3% versus 20.7% in patients treated with conventional surgery. Radiotherapy cycles can be administered, since it is considered a radiosensitive tumor, but in most cases it is used as an adjuvant or neoadjuvant treatment. These schemes are preferred to reduce recurrences in patients operated with conventional surgery, since it lowers the rate to only 4%.[7,8]

Patients should be closely monitored despite complete remission of the disease, since in women, having had this neoplasm increases the risk of developing non-epithelial skin neoplasms and melanomas. Male patients do not have a higher risk of subsequent neoplasms. This is why a 6-12 months follow-up the first 3 years after diagnosis. [9,10]

CONCLUSION

It is important to take into account this neoplasm, despite its rarity in pediatric patients, as well as evidence of residual tumor. In our patient there is no evidence of residual tumor with excision of 2 cm, so it will be kept under surveillance to identify if she is a candidate for radiotherapy or neoadjuvant chemotherapy.

In conclusion, Dermatofibrosarcoma protuberans (DFSP) is a rare and challenging mesenchymal neoplasm characterized by its locally aggressive behavior and propensity for infiltrative growth within the dermal and subcutaneous layers. This unique tumor exhibits distinctive histopathological features, including spindle-shaped tumor cells arranged in a "storiform" pattern and the presence of multinucleated giant cells, which are crucial for its definitive diagnosis using immunohistochemical markers, particularly CD34 positivity.

Given its potential for relentless local invasion and high recurrence rates, successful management of DFSP relies heavily on a comprehensive, multidisciplinary approach involving dermatologists, oncologists, and surgeons. Wide surgical excision with clear margins remains the cornerstone of treatment, aiming to achieve complete tumor resection while preserving surrounding healthy tissues. In challenging anatomical locations or cases with microscopically positive margins, techniques like Mohs micrographic surgery or adjuvant radiation therapy have demonstrated promising outcomes, minimizing the risk of local recurrences.

The molecular basis of DFSP, mainly involving the COL1A1-PDGFB gene fusion, has unveiled potential therapeutic targets, with imatinib mesylate emerging as a promising systemic therapy for advanced or unresectable DFSP. Targeting the tyrosine kinase activity of the fusion protein has shown encouraging results, underscoring the potential of targeted therapies in enhancing treatment outcomes for patients facing more advanced disease stages.

Early and accurate diagnosis, along with appropriate and timely intervention, are paramount for optimizing clinical outcomes in DFSP. The rarity and complexity of this neoplasm necessitate continued research and collaboration to advance our understanding of its pathogenesis and potential therapeutic interventions. Ongoing efforts in clinical and translational research will further enhance our ability to provide personalized treatment approaches, thereby improving the prognosis and quality of life for individuals affected by this enigmatic dermatological malignancy.

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