Desmoplastic fibroma of bone: Amorphological and immunohistochemical characterization

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Abstract

Background: Desmoplastic Fibroma (DF) of bone is a locally aggressive and infrequent benign neoplasm. Recently was described a role of vascular endothelial growth factor in the interstitial fibrotic processes.

Case presentation: A 13-year-old female presented with pain, swelling and limitation of movements in right forearm. An osteolytic lesion at the distal end of the right radius was shown, with pathologic concentration of Technetium 99 and slight enhancement of soft tissue lesion employing computerized axial tomography. The surgical biopsy showed nodular formations of hyalinized collagen fibers arranged in thick bands with few well-differentiated interstitial fibroblasts / myofibroblasts, focally expressing VEGF-A.

Conclusion: The intramedullary neoplastic proliferation is limited by the cortical bone, provoking compression of the intratumorally micro-vessels, favoring both, the extracellular matrix and VEGF-A synthesis. Future research should include therapeutic intervention with anti-CD117 and anti-VEGF-A drugs, with the aim of limiting tumor growth, facilitating the complete surgical excision of the neoplasm.

Keywords: desmoplastic fibroma; vascular endothelial growth factor; hyalinization; neoplasm progression.

Introduction

Desmoplastic fibroma (DF) of bone is an infrequent and locally aggressive benign neoplasm, representing 0.06% of all bone neoplasms and 0.3% of benign neoplasms in this location [1]. In pediatric population, the occurrence of this entity is lowest than 1% of bone neoplasms. The entity was described in 75% of males’ cases, being the lower jaw (22%), femur (15%), pelvic bones (13%), radius (12%) and tibia (9%) the predominant locations [2,3]. Radiologically presents a circumscribed lytic lesion, without peripheral sclerosis or periosteal reaction [4,5]. Microscopically, the entity is described as a proliferation of spindle or stellar cells, with little cytological atypia and abundant stromal collagen [6]. On the other hand, a role of vascular endothelial growth factor (VEGF) in the interstitial fibrotic processes was recently described [7].

Due to the unusual nature of this entity in pediatric population, our objective was describing the histopathology findings, emphasizing the immunohistochemical expression for VEGF-A and its relationship with fibro-sclerotic process.

Report of the case

A 13-year-old female presented with pain, swelling, limitation of pronosupination movements in right forearm and a pre-
The authors confirm that they have parental consent to publish the information presented in this paper. The importance of communicating the findings obtained was emphasized to improve the pathogenetic understanding of the entity and the best therapeutic approach to this infrequent pathology.

**Figure 1:** In this zone, the cell population was organized in short interlocking fascicles, eventually vorticial (H&E, 100X).

**(1B):** The neoplastic fusiform cells demonstrated capability for destroy trabecular and cortical bone, extending beyond the radius (H&E, 100X).

**(1C):** In this sector, the neoplasm underwent transition with others that showed a gradual increase of stromal collagen, until reaching areas with keloid-like appearance (H&E, 100X).

**(1D):** The neoplastic stroma shows increase of collagen fascicles, frequently hyalinized, rounded by fibroblast/myofibroblast neoplastic cells (H&E stain, 100X).

**(1E):** The area illustrated by this picture represent stromal zones occupied by undulated collagen bundles, surrounded by scarce cellular component (H&E, 100X).

**(1F):** This histologic image shows the cellular characteristics of the neoplastic cells, organized in short fascicles, fusiform or rounded cytoplasm configuration and hyperchromatic nuclei. In this area, the neoplastic stroma was lax, with edematous aspect (H&E stain, 400X).
DF is an infrequent entity, which has traditionally been associated with microscopically similar extra-abdominal desmoid tumors [8]. In the diagnostic differentiation, it is important to determine the precise location of both processes [9]. A common histological component is the presence of hyalinized or sclerosing collagenous matrix, with low cell density in these areas, being a characteristic observed in various benign and malignant processes. There is evidence that supports the complex interrelation between neoplastic cells and the surrounding extracellular matrix (ECM), which promotes the transdifferentiation of fibroblasts to myofibroblasts, the degradation and new synthesis of extracellular components (remodeling), angiogenesis, proliferation, and expansion of neoplastic cells [10]. In addition, focal groups of CD117 positive cells were observed, describing a membranous immunohistochemical pattern, indicative of stem cells, probably of bone marrow origin, suggesting an alternative source of fibroblasts and myofibroblast, beyond the transdifferentiation phenomenon. CD117 encodes a membrane receptor tyrosine kinase that is expressed in gastrointestinal stromal tumors (GISTs) but not in smooth muscle or neural tumors of the gastrointestinal tract. Mutations in c-kit leading to the constitutive activation of thymosine kinase are believed to have a role in the tumorigenesis of the overwhelming majority of GISTs. There have been several reports of KIT immunostaining in a limited number of soft tissue tumors other than GISTs, including metastatic melanoma, clear cell sarcoma, angiosarcoma, extraskeletal Ewing sarcoma, and desmoid fibromatosis, at times with conflicting results. In this sense, CD117 positive cells could be facilitate increase of extracellular hyalinized matrix and, indirectly, the VEGF-A production. Whether c-kit inhibitors might provide therapeutic benefit to the subset of patients with desmoplastic fibroma whose tumors show immunoreactivity for c-kit remains to be determined [11]. On the other hand, in our case, we also observe an increased extracellular matrix, that included hyalinized collagenous matrix at medullary space of bone. The hyaline collagen fibers were surrounded by activated myofibroblasts, which expressed α-SMA. Also, these areas showed lower vascularity by the reduction of CD34 immunostaining compared to sectors expanded beyond the bone. The fibroblasts/myofibroblasts cells were increased in sites of cortical bone rupture, with extension towards the soft tissue’s neighbors. These sectors showed the highest cellular density of the neoplasia, where myofibroblasts and endothelial cells showed nuclear immunolabelling for Ki67 (Immunohistochemistry for Ki67, 200X). This small / medium size CD117+ cells (F) showed a typical membranous pattern of immunolabling (insert), forming focal groups near of small vessels in cellular zones of the neoplasia (Immunohistochemistry for CD117, 400X).

In liver diseases, the hypoxia is a condition that link between the fibrogenic, angiogenic and carcinogenic phenomena [19]. For this reason, we hypothesize, at least in this case, that the initial intramedullary neoplastic proliferation is limited by the cortical bone, provoking compression of the intratumorallymicro-vessels in certain zones, decreasing the blood and oxygen supply. This situation favoring the expansion of ECM by accumulation of interstitial hyalinizing collagen, probably due the participation of the transcription factor hypoxia inducible factor-1 (HIF-1), activating the system fibroblast / myofibroblast and increasing the collagen deposition [20]. Then, the mechanical collapse of the tumor vessels, promotes VEGF-Asynthesis, angiogenesis, and neoplastic expansion, especially in areas of...
cortical bone destruction and extension on extraosseous soft tissue.

Finally, we accept the limitation of this hypothesis, however, we believe that it’s a starting point for future research that includes therapeutic intervention with anti-CD117 or anti-VEGF-A drugs, with the aim of limiting tumor growth, facilitating complete surgical excision of this aggressive neoplasm.

**Declarations**

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**References**


