International Journal of Medical Science and Clinical Research Studies

ISSN(print): 2767-8326, ISSN(online): 2767-8342

Volume 05 Issue 03 March 2025

Page No: 487-491

DOI: https://doi.org/10.47191/ijmscrs/v5-i03-15, Impact Factor: 8.188

Involutive Congenital Tufted Angioma, an Atypical Case Presentation

Ivanna Ocampo Carrasco[1], Eder F. Rios Bracamontes[2], Diego I. Rodríguez Mendoza[3], Guadalupe Castro Mosqueda[4], Andrea G. Navarro Ortega[5]

[1]Hospital General de Zona 1, Villa de Alvarez, Colima, and Department of Internal Medicine, Orcid: 0009-0007-4315-3954
[2]Hospital General de Zona 1, Villa de Alvarez, Colima, and Department of Internal Medicine, Orcid: 0000-0002-4660-7372
[3]Hospital Civil de Guadalajara Fray Antonio Alcalde, Guadalajara, Jalisco, Department of Pediatric Dermatology
[4]Hospital Civil de Guadalajara Fray Antonio Alcalde, Guadalajara, Jalisco, Department of Pediatric Dermatology
[5]Hospital General de Zona 1, Villa de Alvarez, Colima, Department of Internal Medicine

ABSTRACT

A case is presented of a 3-month-and-15-day-old male patient referred for a consultation due to a congenital 'red spot' on the left abdomen, where a linear erythematous-violaceous plaque with gray areas, indurated texture, and fine hairs was observed.

An ultrasound was requested, revealing findings consistent with an infiltrative lesion. A biopsy was performed, and the lesion was reported as compatible with tufted angioma, reactive for immunohistochemical markers CD31, CD34, and D2-40. A description of the case is provided, along with a bibliographic review, emphasizing the clinical presentation and diagnostic approach.

KEYWORDS: Tufted Angioma, Erythematous Infiltrative Lesion, Pediatric Dermatology, Hemangioma, Vascular Skin Lesions

ARTICLE DETAILS

Published On:
12 March 2025

Available on:
https://ijmscr.org/

INTRODUCTION

Tufted Angioma (TA) is a rare benign vascular tumor, first described in 1949 by Nakagawa (previously known as Nakagawa's angioblastoma), characterized by small glomerular capillaries with a tufted appearance and angiomatosis lobules in the dermis, associated with dilated lymphatic vessels. With a low incidence, it commonly presents in childhood, and the congenital presentation is uncommon.(1)

CLINICAL CASE PRESENTATION

A case is presented of a 3-month-and-15-day-old male patient referred for a consultation due to a congenital 'red spot' on the left abdomen.

On physical examination, a polymorphic dermatosis was found, localized to the left lateral abdomen, characterized by a linear erythematous-violaceous plaque with gray areas, measuring 18 x 6 cm, with diffuse borders, indurated texture, and an infiltrated appearance, as well as areas of fine hair.

An ultrasound of the lesion was requested, revealing a diffuse and irregular increase in echogenicity with hypoechoic foci, raising suspicion of an infiltrative lesion such as scleroderma versus morphea. A 3 mm punch skin biopsy was performed, with hematoxylin and eosin staining confirming a diagnosis consistent with tufted angioma. Histopathological examination revealed clustered capillaries in the dermis and subcutaneous tissue with a characteristic "cannonball" pattern. Immunohistochemical staining showed reactivity for CD31, CD34, and D2-40 markers. Given the lesion's involution, the patient was kept under observation, with no growth or complications noted during follow-up.

Clustered capillaries in the dermis and subcutaneous tissue with a characteristic "cannonball" pattern.

DISCUSSION

Tufted angioma (TA) is an uncommon benign vascular neoplasm, first reported in 1949 by Nakagawa as angioblastoma and later described in 1971 by MacMillan and Champion as progressive capillary hemangioma. Subsequently, Jones and Orkin in 1971 presented a series of cases with similar histopathological features, coining the term tufted angioma (1,2,3).

While tufted angioma is rare, it is not exceedingly so, though congenital presentation is unusual. Congenital tufted angioma (cTA) represents 10%-20% of all TA cases in older case series and up to 54%-78% in more recent studies (1,4).

Approximately 60%-70% of cases present before 5 years of age, with more than 50% of these appearing within the first year of life, though cases in adults have also been reported. Some cases are described with very early onset, but with lesions becoming evident only after a few days of life, suggesting they might actually be congenital cases that were not evaluated until the lesions became more pronounced. Some patients develop potentially serious complications such as Kasabach-Merritt syndrome (KMS) or chronic coagulopathy without thrombocytopenia (CCWT), which require treatment. Additionally, it is a neoplasm that lacks malignancy in its progression (1,3,9).

The pathogenesis of TA remains incompletely understood. Genetically, it has been associated with somatic mutations in the GNA14 gene and with increased factors that stimulate angiogenesis, such as IL-8. The latter contributes to the elevation of endothelial and vascular growth factors, promoting angiogenesis and the development of capillary lobules. The presence of lymphatic endothelial markers in the proliferating cells of these lesions suggests that these tumors possess, at least in part, a lymphatic endothelial immunophenotype. Furthermore, the expression of genes linked to lymphatic differentiation has been observed in various vascular tumors, such as Kaposi's sarcoma, Dabska-type hemangioendothelioma, kaposiform hemangioendothelioma, and tufted angioma. Although the detection of a single lymphatic differentiation marker may not be sufficient to distinguish one type of vascular tumor from another, the specific expression pattern within the tumor may do so (1,3,5,8,11).

One of the immunohistochemical markers being studied is VEGF-A, which is important in vascular angiogenesis and stains the proliferative phase of infantile hemangiomas. In a case series by Sadeghpour M. et al. (6), 9 biopsies of TA from 7 patients were analyzed, stained with hematoxylin and eosin, and markers such as D2-40, VEGF-A, GLUT-1, and HHV-8. It was expected that VEGF-A would primarily stain the capillary clusters in TA; however, both these clusters and the lenticular lymphatic vessels showed diffuse staining in all samples. Additionally, the epidermis also stained for VEGF-A. This suggests that, in TA, VEGF-A is not exclusively associated with a specific type of vessel (vascular endothelial or lymphatic) nor a particular cell (endothelial cell or keratinocyte). However, it has been proposed that epidermal keratinocytes may be a source of VEGF-A. Given the close interaction between capillaries and lymphatic vessels in TA (evidenced by some capillaries staining with D2-40), the diffuse VEGF-A staining pattern supports the hypothesis that TA may originate from a pluripotent cell type capable of differentiating into both lymphatic and vascular endothelial cells, or that it may be a lymphatic malformation with secondary foci of capillary proliferation (6).

Clinically, the presentation of TA is highly variable; it is suspected when a solitary, indurated, erythematous-violaceous vascular lesion with poorly defined borders is observed, although in certain cases, well-demarcated lesions can be seen. Presentations with extensive, multifocal lesions, ranging in size from 2 to 10 cm, are described, typically located on the neck, upper trunk, and extremities, though cases in other locations such as the face and oral mucosa have also been reported. These lesions often have a deep nodular component (which may extend into the subcutaneous tissue, fascia, and muscle), and while locally invasive, they never metastasize. Initially, they might be confused with a capillary malformation or segmental hemangioma. Therefore, biopsy is necessary to confirm the diagnosis of TA and differentiate it from other vascular proliferations (e.g., congenital hemangioma) and other non-vascular lesions. Generally, TA is an asymptomatic lesion, though it may cause local discomfort, warmth, inflammation, and can be slightly painful. The most serious complication is the Kasabach-Merritt phenomenon, characterized by platelet trapping in blood vessels and thrombocytopenia coagulopathy, leading to petechiae and ecchymosis, though this is rare in TA (1,3,8,10,12,13).

TA may present in three different clinical patterns: uncomplicated TA (the most common type), TA without thrombocytopenia but with chronic coagulopathy, and TA complicated by Kasabach-Merritt syndrome with thrombocytopenia. Differential diagnoses for this entity include other conditions such as congenital hemangioma, infantile hemangioma, vascular malformations, pyogenic granuloma, and, in adults, kaposiform hemangioendothelioma and Kaposi's sarcoma. To differentiate between other tumors or to assess the affected area, imaging techniques such as ultrasound or magnetic resonance imaging may be used (8).

Histopathologically, TA is characterized by well-circumscribed foci of capillaries grouped in the dermis and subcutaneous tissue. Each lobe consists of aggregates of endothelial cells arranged concentrically around the vessels of the dermal vascular plexuses, associated with dilated lymphatic vessels. No mitotic activity or atypia is found in the cells, and these capillary clusters give the angiomatosis structures a characteristic "cannonball" or "shotgun" pattern. These lobules are separated by normal dermis, with no inflammatory infiltrate observed, and some of these lobules protrude over the surrounding vascular walls, giving a characteristic semilunar morphology. Some entities that must be differentiated from this lesion include Kaposi's sarcoma, kaposiform hemangioendothelioma, and low-grade angiosarcoma, especially in adults. Kaposi's sarcoma shows spindle-shaped endothelial cells with slit-like spaces and the "promontory sign," while kaposiform hemangioendothelioma presents a lobular and infiltrative pattern, and differentiation from low-grade angiosarcoma can be made by the absence of atypia and mitotic figures (3,12).

Immunohistochemical studies reveal that the cells of the lobules express characteristic endothelial cell markers, such as CD31, CD34, WT1, and smooth muscle actin. The

peripheral dilated vessels in a semilunar shape show variable staining with podoplanin (D2-40), confirming their lymphatic origin. Histopathological analysis, complemented by immunohistochemistry, is essential to rule out other lesions, such as infantile hemangioma, vascular malformations, infantile myofibromatosis, and congenital dermatofibrosarcoma protuberans. Immunohistochemistry for GLUT1 is positive in 100% of infantile hemangiomas but not detected in vascular tumors such as TA (2,12).

Among the markers studied is Prox1, a nuclear transcription factor for lymphatic endothelial cells, which has been shown to promote aggressive behavior in KHE mouse models. In a study by Rimella Le Huu A. et al., overexpression of the Prox1 gene, a lymphatic endothelial transcription factor, was shown to promote aggressive behavior in KHE models. They analyzed 75 vascular lesions, finding that both KHE and TA share a similar endothelial immunophenotype, helping to differentiate these tumors from KHE and TA. The results suggest that Prox1 is a useful biomarker for confirming the diagnosis of KHE/TA and could be used as part of the immunohistochemical diagnosis (7).

There are no clear guidelines for managing congenital TA and early-acquired TA when there are no symptoms or complications. Most recommendations come from studies with small samples, individual case reports, or clinical experience of specialists. Browning et al. (4) noted that spontaneous regression is more common in congenital TA and in lesions arising within the first year of life compared to those that appear later. They also indicated that these lesions present fewer complications and a better prognosis. Therefore, the most appropriate initial strategy for treating congenital TA might be observation and follow-up before intervening (1).

Pharmacological treatment has mainly been indicated for cases where lesions are extensive or associated with KMS. Recently, a positive response to low-dose aspirin (2.2-5 mg/kg/day) has been reported in patients with extensive and/or symptomatic congenital TA, as well as in those with early TA without KMS. A reduction in lesion size, as well as improvement in their appearance and associated symptoms, was observed. Systemic corticosteroids are used as first-line therapy for TA associated with KMS, though they have a relatively low response rate and a high recurrence rate. Additionally, severe side effects, such as Cushing's syndrome and opportunistic infections, have been observed in several cases. Vincristine, an inhibitor of endothelial proliferation, presents as a promising option for treating TA associated with KHE, especially in cases of steroid-resistant KHE. Large-scale clinical trials have demonstrated the effectiveness of vincristine in treating KHE. Other therapeutic options, such as interferon, radiotherapy, embolization, antiplatelet agents (aspirin), propranolol, and sirolimus, which are used individually or in combination, are reserved for second- or third-line treatments. However, none of these treatments have shown uniform and reproducible effects (1,14).

In conclusion, although tufted angioma (TA) is a rare entity, its early diagnosis and appropriate treatment are critical to prevent serious complications and improve patient prognosis. The diversity in TA's clinical presentation, from asymptomatic lesions to those associated with Kasabach-Merritt syndrome (KMS), demands a careful diagnostic and therapeutic approach. Immunohistochemistry and histopathological analysis are essential tools for distinguishing TA from other vascular and non-vascular lesions, allowing for accurate identification and exclusion of alternative diagnoses, such as hemangiomas or vascular malformations.

Despite advances in diagnosis, the treatment of TA remains challenging, as no clear guidelines exist for how to manage it effectively in all cases. While observation and follow-up remain the first-line options, especially for congenital cases or those without severe symptoms, pharmacological therapies such as corticosteroids, aspirin, vincristine, and other antiplatelet agents are reserved for more severe or complicated cases. In summary, TA, though rare, requires special attention due to its complexities in diagnosis and treatment. Ongoing research into its pathogenesis, as well as the development of biomarkers and new therapies, is crucial for improving the quality of life of patients affected by this vascular neoplasm, minimizing complications, and optimizing therapeutic management.

REFERENCES

I. Feito-Rodríguez M, Sánchez-Orta A, De Lucas R, López-Gutiérrez JC, Ruiz-Bravo E, Baselga E, et al. Congenital tufted angioma: A multicenter retrospective study of 30 cases. Pediatr Dermatol [Internet]. 2018;35(6):808–16. Available from: http://dx.doi.org/10.1111/pde.13683

II. Osio A, Fraitag S, Hadj-Rabia S, Bodemer C, de Prost Y, Hamel-Teillac D. Clinical spectrum of tufted angiomas in childhood: a report of 13 cases and a review of the literature: A report of 13 cases and a review of the literature. Arch Dermatol [Internet]. 2010;146(7):758–63. Available from: http://dx.doi.org/10.1001/archdermatol.2010.135

III. Victoria Martínez AM, Cubells Sánchez L, Esteve Martínez A, Estela Cubells JR, Febrer Bosch I, Alegre de Miquel V, et al. Angiomas en penacho en la infancia. Serie de 9 casos y revisión de la literatura. An Pediatr (Barc) [Internet]. 2015;83(3):201–8. Available from: http://dx.doi.org/10.1016/j.anpedi.2014.10.018

IV. Browning J, Frieden I, Baselga E, Wagner A, Metry D. Congenital, self-regressing tufted angioma. Arch Dermatol [Internet]. 2006;142(6):749–51. Available from: http://dx.doi.org/10.1001/archderm.142.6.749

V. Le Huu AR, Jokinen CH, Rubin BP, Mihm MC, Weiss SW, North PE, et al. Expression of prox1, lymphatic endothelial nuclear transcription factor, in

Kaposiform hemangioendothelioma and tufted angioma. Am J Surg Pathol [Internet]. 2010;34(11):1563–73. Available from: http://dx.doi.org/10.1097/PAS.0b013e3181f6076f

VI. Sadeghpour M, Antaya RJ, Lazova R, Ko CJ. Dilated lymphatic vessels in tufted angioma: a potential source of diagnostic confusion. Am J Dermatopathol [Internet]. 2012;34(4):400–3. Available from: http://dx.doi.org/10.1097/DAD.0b013e318234e720

VII. Le Huu R, Jokinen A, Ruben CH. Expression of Prox1, lymphatic endothelial nuclear transcription factor, in kaposiform hemangioendothelioma and tufted Angioma Am. J Surg Pathol. 2010;34:1563–73.

VIII. Silva CM da, Schettini APM, Santos M, Chirano CAR. Tufted angioma. An Bras Dermatol [Internet]. 2017;92(5):742–3. Available from: http://dx.doi.org/10.1590/abd1806-4841.20175896

IX. Tufted angioma: A picture not to forget. J Am Acad Dermatol [Internet]. 2018;79(3):AB304. Available from: http://dx.doi.org/10.1016/j.jaad.2018.05.1202

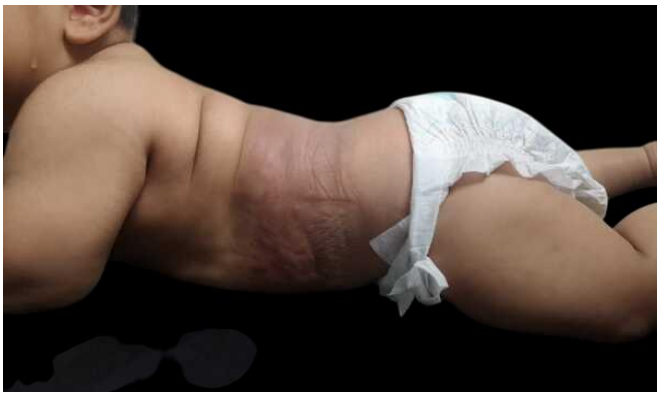
X. Goss JA, Greene AK. Congenital vascular tumors. Otolaryngol Clin North Am [Internet]. 2018;51(1):89–97. Available from: http://dx.doi.org/10.1016/j.otc.2017.09.008

XI. Lim YH, Bacchiocchi A, Qiu J, Straub R, Bruckner A, Bercovitch L, et al. GNA14 somatic mutation causes congenital and sporadic vascular tumors by MAPK activation. Am J Hum Genet [Internet]. 2016;99(2):443–50. Available from: http://dx.doi.org/10.1016/j.ajhg.2016.06.010

XII. Rambhia KD, Khopkar US. Tufted angioma. Indian Dermatol Online J [Internet]. 2016;7(1):62–3. Available from: http://dx.doi.org/10.4103/2229-5178.174313

XIII. Pfister BK, King EC, Samet JD, Gulliver J, Wolf SF. Tufted angioma of the index finger middle phalanx. J Am Acad Orthop Surg Glob Res Rev [Internet]. 2022;6(7). Available from: http://dx.doi.org/10.5435/JAAOSGlobal-D-21-00301

XIV. Liu XH, Li JY, Qu XH, Yan WL, Zhang L, Yang C, et al. Treatment of kaposiform hemangioendothelioma and tufted angioma. Int J Cancer [Internet]. 2016;139(7):1658–66. Available from: http://dx.doi.org/10.1002/ijc.30216



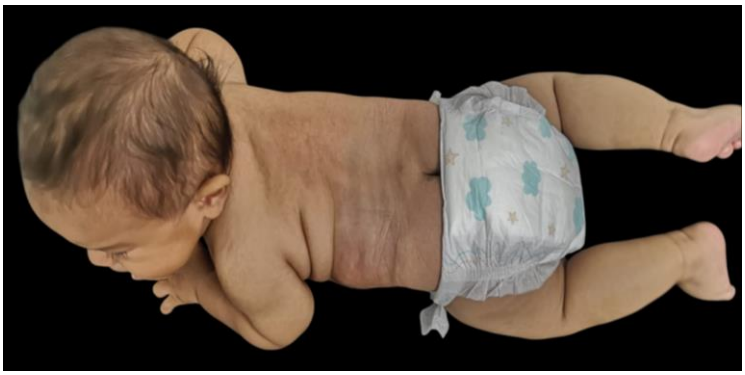
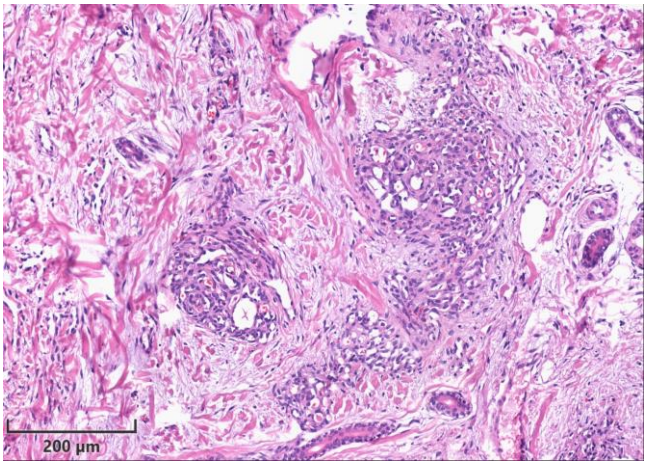


Image 1 and 2: clinical presentation of a linear erythematous-violaceous plaque compatible with tufted angioma



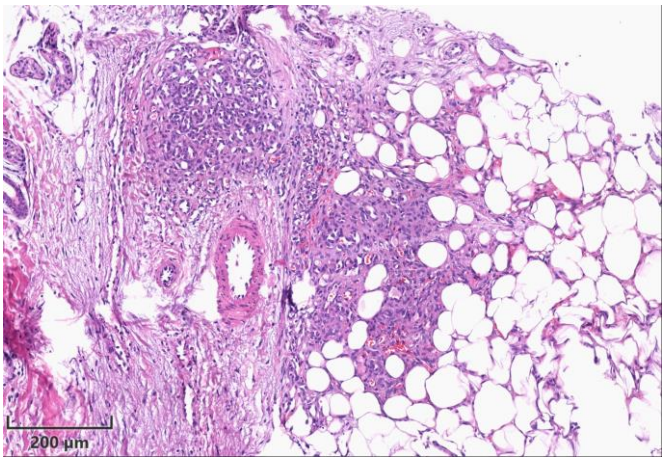


Image 3 and 4. Skin biopsy at 10X magnification showing angiomatous structures with a characteristic "shotgun pellet" or "cannonball" pattern in the dermis and hypodermis.

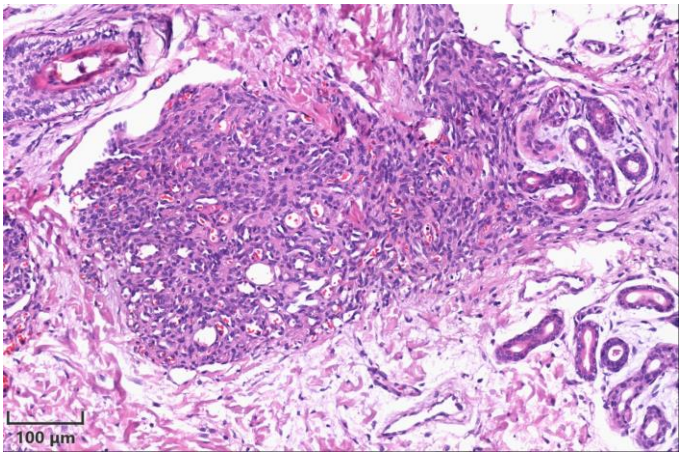


Image 5. Skin biopsy at 100X magnification showing angiomatous structure with a characteristic "cannonball" pattern in the dermis, without the presence of mitosis or cellular atypia.

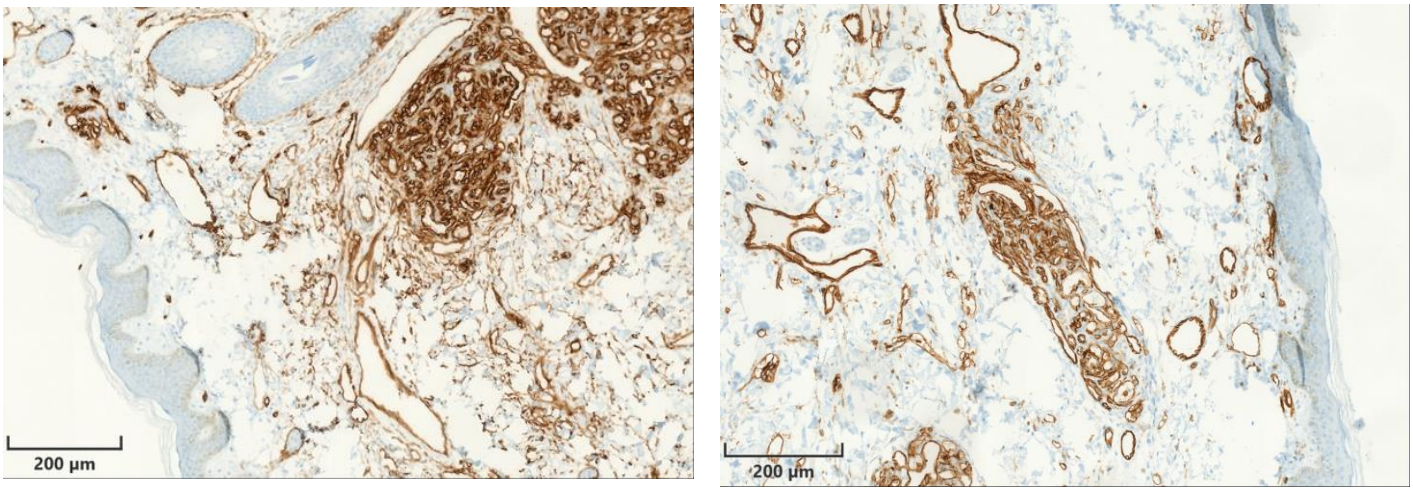


Image 6 and 7. SSkin biopsy at 10X magnification showing immunohistochemical staining reactive for CD31, CD34, and D2-40 markers.