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Case report: myxoid atypical fibroxanthoma: a challenging diagnosis of a rare variant

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European Journal of Medical Case Reports
Volume 4(11):399–403
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https://www.discoverpublish.com/
https://doi.org/10.24911/ejmcr/173-1600450399

ABSTRACT

Background: Atypical fibroxanthoma is a cutaneous benign tumor of uncertain lineage, occurring more frequently in elder men, in sun-exposed or irradiated skin. It appears as a slowly progressing nodule, and it is treated by total excision. Several histological types have been described including the myxoid atypical fibroxanthoma.

Case presentation: A 73-year-old male presented at the plastic surgery department for excision of a single hard, centrally ulcerated, nodule on the right side of the scalp, 4.1 cm in maximum diameter growing slowly during the last years. The microscopical examination revealed a circumscribed, cellular tumor developing in the dermis. The cellular population consisted of spindle cells and histiocytes, without a specific growth pattern. Moderate cytologic and nuclear atypia were observed, combined with a relatively high mitotic rate. Also, many positive areas of myxoid degeneration detected with periodic acid Schiff and Alcian Blue stains were revealed. Immunohistochemistry showed positivity of the tumor cells for CD10, FXIIIa and focally for CD68, CD117, smooth muscle actin (SMA), and CD99. Tumor cells were negative for all the other assessed markers, including S-100 and Desmin. Ki-67 was 20%. Based on these morphological findings, the diagnosis of myxoid atypical fibroxanthoma was made.

Conclusion: Atypical fibroxanthoma is a benign lesion, the diagnosis of which may be proved difficult and challenging. Moreover, when we deal with a rare histologic variant, such as the atypical fibroxanthoma with myxoid change, only the strict application of histological criteria combined with the immunohistochemical findings can lead us to the correct diagnosis, excluding malignant, easily recurring, and metastasizing neoplasms.

Keywords: Atypical fibroxanthoma, myxoid change, case report, benign, cutaneous, histologic examination, immunohistochemistry.

Received: 18 September 2020 **Accepted:** 24 October 2020

Type of Article: CASE REPORT **Specialty:** Pathology

Funding: None.

Declaration of conflicting interests: The authors declare that there is no conflict of interests regarding the publication of this case report.

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Background

Initially described in 1963, atypical fibroxanthoma is a benign dermal tumor of uncertain lineage. It rarely shows local recurrences, and the local recurrences are scarce, usually concerning tumors that are not meeting the diagnostic criteria for atypical fibroxanthoma. It occurs more frequently in the seventh and eighth decade of life. The incidence is notably higher in men than women and it presents mainly in the sun-exposed areas of head and neck region, such as the scalp, nose, cheeks, and ears. Solar and therapeutic irradiation is a strong predisposing factor and mutation in TP53 gene caused by ultraviolet radiation has been demonstrated. Also, patients with xeroderma pigmentosum may develop this type of lesions at a young age. The gross appearance of atypical fibroxanthoma is not distinctive, and the preoperative diagnoses may include basal cell carcinoma, squamous cell carcinoma, pyogenic granuloma, or cutaneous angiosarcoma. Macroscopically they have polypoid or nodular configuration, reddish color, they usually measure <2 cm, and they may be crusted or ulcerated. Histologically these lesions are composed of pleomorphic cells, with mainly epithelioid and spindle morphology. However, except the classical, other variants have been described such as spindle-cell clear cell, osteoid, osteoclastic, chondroid, pigmented, and granular cell, making the differential diagnosis challenging. Also, few atypical fibroxanthomas with myxoid change have been reported. It should be noted that, the lesion should not include areas of necrosis, lymphovascular invasion or extension in the underlying soft tissues beyond the dermis [1].

Case Presentation

A 73-year-old male presented at the plastic surgery department for excision of a single hard, centrally ulcerated, cutaneous nodule on the right side of the scalp, growing slowly during the last years. The patient did not mention any comorbidities. Plastic surgeons considered that it was representing a basal cell carcinoma, or a cutaneous squamous cell carcinoma and excision of the tumor followed. We received a fusiform / elliptical skin excision measuring

6.5 × 5.5 cm and total depth of dermis and subcutaneous tissue 2.1 cm, with a centrally ulcerated reddish firm protruding lesion on the epidermis, occupying a surface area of 4.1 × 3.7cm. Also, we received in separate containers samples of the same patient labeled as "pericranium" and "bone shaves of scalp", in which we found two whitish and hemorrhagic firm tissue segments measuring from 0.5 to 0.9 cm in diameter. Fixation in 10% formalin was followed.

The microscopical examination revealed a well circumscribed, non-encapsulated, highly cellular tumor of the upper and lower dermis. The cellular population consisted of spindle cells and histiocytes. It was mostly composed of atypical spindle cells, mainly without a specific growth pattern and only focally presenting a fascicular pattern. Moderate cytologic atypia (nuclear enlargement and pleomorphism) and hyperchromasia, in combination with high mitotic rate (10-15 mitoses/high power field) were observed, making the morphology of the neoplasm worrisome (Figures 1–4). Also, sclerotic stroma and many positive areas of myxoid degeneration were detected with periodic acid Schiff and Alcian Blue (Figure 5) stains. It should be noted that there was no evidence of infiltration of the separately sent specimens.

The immunohistochemistry assay revealed diffuse positivity of the tumor cells for CD10 (Figure 6) and FXIIIa (Figure 7) as well as focal positivity for CD68 (Figure 8), CD117 (Figure 9), SMA, and CD99. Tumor cells were

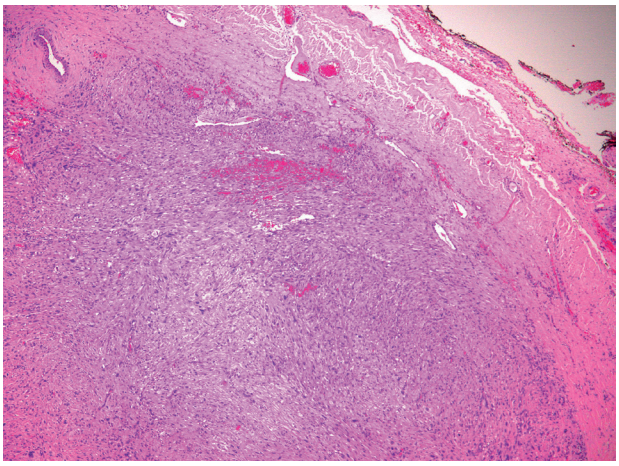


Figure 1. *Hematoxylin–eosin stain (4×).*

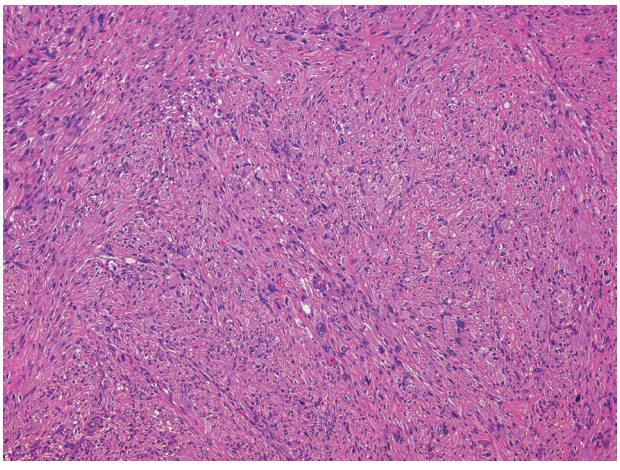


Figure 2. *Hematoxylin–eosin stain (10×).*

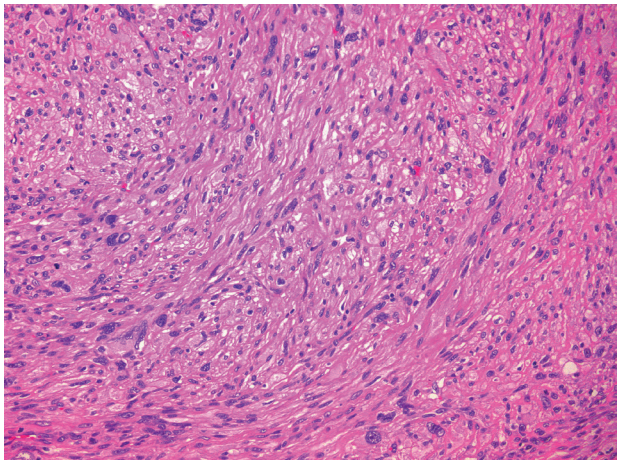


Figure 3. *Hematoxylin–eosin stain (20×).*

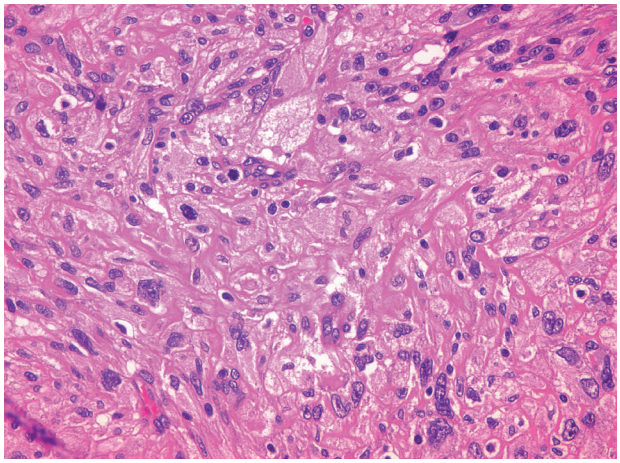


Figure 4. *Hematoxylin–eosin stain (40×).*

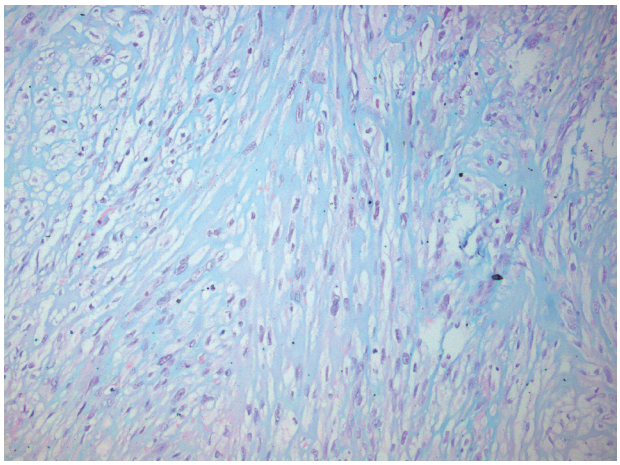


Figure 5. *Alcian Blue stain highlighting myxoid degeneration (20×).*

negative for S-100 (Figure 10), Melan-A, SOX-10, epithelial membrane antigen, p40, CK5/6, CD31, CD34, and E-twenty-six (ETS)-related gene (ERG). Staining for cell proliferation rate was heterogeneous and relatively increased, at around 20% (Figure 11). Based on the morphological findings, taking in consideration, the extended myxoid degeneration areas in the tumor and the results of the immunohistochemical assay, the diagnosis of myxoid atypical fibroxanthoma (atypical fibroxanthoma with myxoid change) was made. The patient remains disease free approximately 1 year.

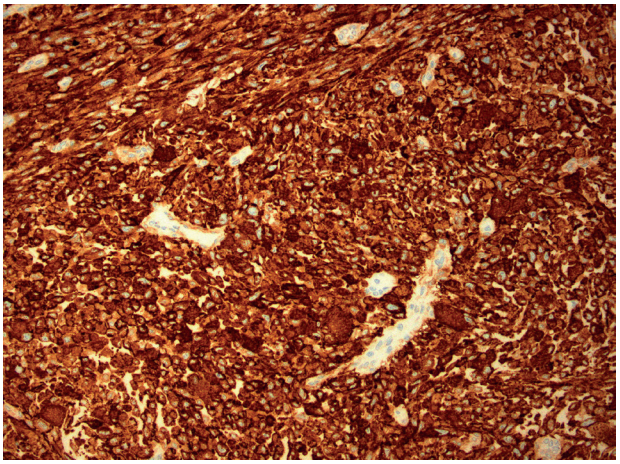


Figure 6. *CD10 positivity (20×).*

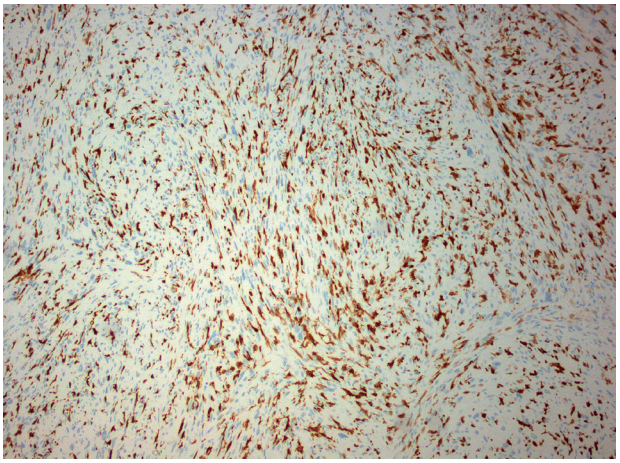


Figure 7. *FXIIIa positivity (20×).*

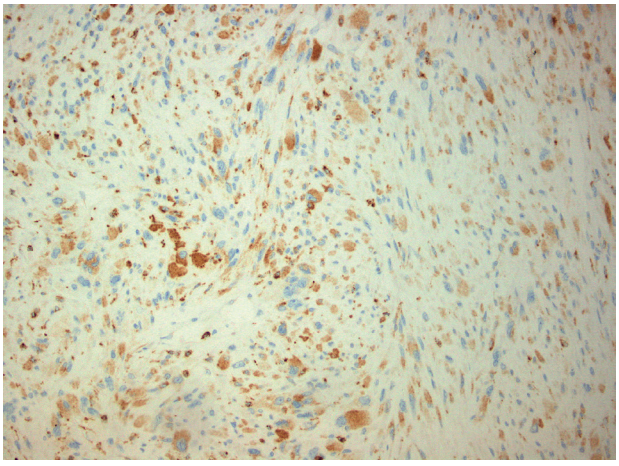


Figure 8. *CD68 positivity (20×).*

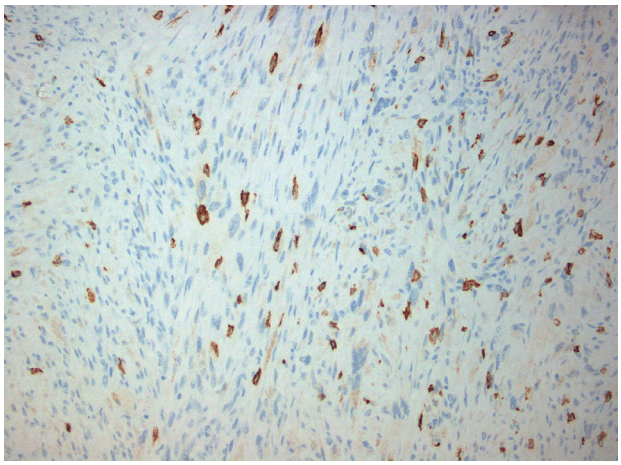


Figure 9. *CD117 focal positivity (20×)*

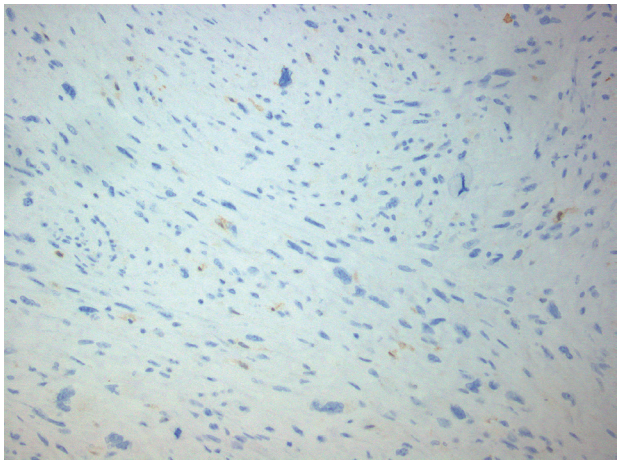


Figure 10. *S-100 negativity (20×).*

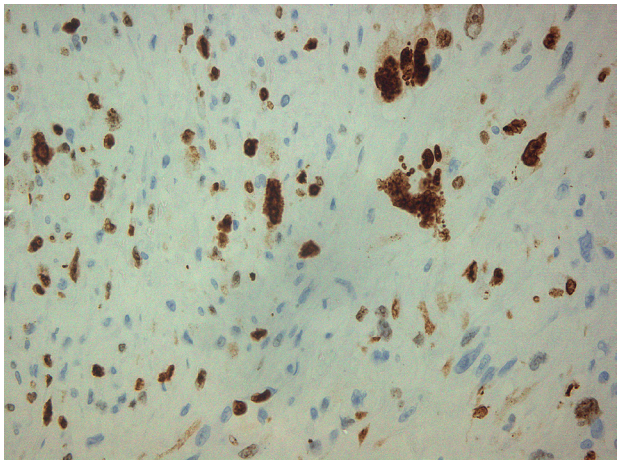


Figure 11. *Cell proliferation rate Ki-67 (20×).*

Discussion

Atypical fibroxanthoma is a cutaneous benign tumor of uncertain origin, measuring usually < 2 cm. It appears mainly sun-exposed or irradiated skin, with the latent period between the exposure to radiation and the appearance of lesion being more than 10 years [2]. The incidence is higher in elder people, affecting more males. Its superficial location (it rarely infiltrates the superficial subcutaneous fat, without deeper extension) is linked to its good prognosis. Histologically, the diagnosis of atypical fibroxanthoma is an "exclusion diagnosis." Tumor cells are usually arranged in fascicles or sheets in the dermis. Cases of atypical fibroxanthoma extending into the superficial adipose subcutaneous tissue with an expansile growth have been also described [3], which otherwise met the diagnostic criteria. Tumor cell population is generally pleiomorphic, showing generally epithelioid, spindle and multinucleated morphology and they may be mixed with chronic inflammatory cells. There is marked nuclear pleomorphism with vesicular and hyperchromatic chromatin, with visible multiple nucleoli. Mitotic activity may be high and atypical. The presence of intratumoral hemosiderin deposition and hemorrhage may be observed. Considering the polymorphism of the tumor cells and their proportion within the tumor as well as the morphological variation that the stroma may present, several variants of atypical fibroxanthoma have been described, such as spindle cell [4], clear cell [5], osteoclastic [6], osteoid [7] and chondroid [8] formation, pigmented [9], and granular cell [10]. Additionally, to all these, atypical fibroxanthoma with myxoid degeneration should be included, resulting from accumulation of hyaluronic acid in the stroma.

In our case, the microscopic evaluation of the lesion revealed a well-circumscribed lesion composed of an epithelioid and spindle-shaped cell population, with moderate mitotic activity and presence of few atypical mitoses not extending beyond the dermis. The differential diagnosis included some malignant, easily metastasizing neoplasms such as poorly differentiated squamous cell carcinoma, melanoma, leiomyosarcoma, epithelioid angiosarcoma, pleomorphic dermal sarcoma with myxoid degeneration, and also some lower grade tumors with locally aggressive behavior such as dermatofibrosarcoma protuberance, solidary fibrous tumor, and cellular/atypical dermatofibroma. Given the fact that there is not any specific marker for this tumor and the large spectrum of the differential diagnosis, including neoplasms with myxoid degeneration [11], an extensive immunohistochemical work-up was carried out. p40 and CK5/6 were negative and poorly differentiated squamous cell carcinoma was excluded. S-100 was negative, removing the possibility of a myxoid liposarcoma. This finding, combined with the negativity for SOX-10 and Melan-A, ruled out the possibility of a melanoma. Although SMA was focally positive, the negativity to Desmin [12] and Caldesmon [13] made the diagnosis of a leiomyosarcoma very unlikely. Angiosarcoma was excluded because of lack of CD31, CD34, and ERG expression. Negativity for CD34 was also conclusive for the exclusion of dermatofibrosarcoma protuberans. Finally, the diffuse and strong positivity of CD10, the focal positivity of CD68, FXIIIa, CD99 [14], CD117 [15], and D2-40 stains and the heterogenous stain of cell proliferation rare Ki-67 reaching 20%, gave us a step forward to the histiocytic nature of the neoplasm.

The exclusion of pleomorphic dermal sarcoma was the most challenging and critical, given that this type of tumors have a higher rate of local recurrence and metastasis, showing overlapping morphological and immunohistochemical features with atypical fibroxanthoma. In our case, despite the sizes (> 2 cm) and the presence of areas of myxoid degeneration, the good circumscription of the lesion, the absence of necrosis, absence of perineural and lymphovascular invasion, combined with the lack of extension into the excised subcutaneous adipose tissue, helped us exclude the possibility of a pleomorphic dermal sarcoma and led us to the diagnosis of atypical fibroxanthoma [16].

Conclusion

Atypical fibroxanthoma is a benign lesion, the diagnosis of which may be proved difficult and challenging. Moreover, when we deal with a histologic variant, such as the atypical fibroxanthoma with myxoid change, the strict application of histological criteria, and the immunohistochemical findings can lead us to the correct diagnosis, excluding malignant, easily recurring and metastasizing neoplasms, such as in the differential diagnosis pleomorphic dermal sarcoma.

What is new?

Myxoid atypical fibroxanthoma is a rare variant that present similar features with dermal sarcomas. Only the strict application of histological criteria supported by the proper immunohistochemical findings can lead us to the correct diagnosis.

List of Abbreviations

CD	Cluster Differentiation
CK	Cytokeratin
DFSP	Dermatofibrosarcoma protuberans
SMA	Smooth muscle actin

Consent for publication

Written informed consent was taken from the patient.

Ethical approval

Ethical approval is not required at our institution for publishing an anonymous case report.

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References

1. Fletcher CDM, Bridge JA, Hogendoorn PCW, Mertens F. WHO Classification of tumours of the soft tissue and bone. 4th ed. Lyon, France: IARC Press; 2013. pp 202–3.
2. Goldblum J, Weiss S, Folpe AL. Enzinger and Weiss's soft tissue tumors. 7th ed. Amsterdam, The Netherlands: Elsevier; 2019. pp 453–6.
3. Luzar B, Calonje E. Morphological and immunohistochemical characteristics of atypical fibroxanthoma with a special emphasis on potential diagnostic pitfalls: a review. J Cutan Pathol. 2010;37:301–9. https://doi.org/10.1111/j.1600-0560.2009.01425.x
4. Harding-Jackson N, Sangueza M, Mackinnon A, Suster S, Plaza JA. Spindle cell atypical fibroxanthoma: myofibroblastic differentiation represents a diagnostic pitfall in this variant of AFX. Am J Dermatopathol. 2015;37(7):509-14; quiz 515-6. https://doi.org/10.1097/DAD.0000000000000313
5. Bedir R, Agirbas S, Sehitoglu I, Yurdakul C, Elmas O. Clear cell atypical fibroxantoma: a rare variant of atypical fibroxanthoma and review of the literature. J Clin Diagn Res. 2014;8(6):FD09–11. https://doi.org/10.7860/JCDR/2014/8798.4466
6. Tomaszewski M-M, Lupton G. Atypical fibroxanthoma: an unusual variant with osteoclast-like giant cells. Am J Surg Pathol. 1997;21:213. https://doi.org/10.1097/00000478-199702000-00012
7. Chen KT. Atypical fibroxanthoma of the skin with osteoid production. Arch Dermatol. 1980;116:113. https://doi.org/10.1001/archderm.1980.01640250115030
8. Wilson PR, Strutton GM, Stewart MR. Atypical fibroxanthoma: two unusual variants. J Cutan Pathol. 1989;16:93. https://doi.org/10.1111/j.1600-0560.1989.tb00017.x
9. Diaz-Cascajo C, Weyers W, Borghi S. Pigmented atypical fibroxanthoma. A tumor that may be easily mistaken for malignant melanoma. Am J Dermatopathol. 2003;25:1. https://doi.org/10.1097/00000372-200302000-00001
10. Sarah N Rudisaile, Mark A Hurt, Daniel J Santa Cruz. Granular cell atypical fibroxanthoma. J Cutan Pathol. 2005;32(4):314–7. https://doi.org/10.1111/j.0303-6987.2005.00326.x
11. Patton A, Page R, Googe PB, King R. Myxoid atypical fibroxanthoma: a previously undescribed variant. J Cutan Pathol. 2009;36(11):1177–84. https://doi.org/10.1111/j.1600-0560.2009.01255.x
12. Bruecks AK, Medlicott SA, Trotter MJ. Atypical fibroxanthoma with prominent sclerosis. J Cutan Pathol. 2003;30:336. https://doi.org/10.1034/j.1600-0560.2003.00077.x
13. Sakamoto A, Oda Y, Yamamoto H, Oshiro Y, Miyajima K, Itakura E, et al. Calponin and h-caldesmon expression in atypical fibroxanthoma and superficial leiomyosarcoma. Virchows Arch. 2002;440(4):404–9. https://doi.org/10.1007/s004280100521
14. Hartel PH, Jackson J, Ducatman BS, Zhang P. CD99 immunoreactivity in atypical fibroxanthoma and pleomorphic malignant fibrous histiocytoma: a useful diagnostic marker. J Cutan Pathol. 2006;33(Suppl 2):24. https://doi.org/10.1111/j.1600-0560.2006.00492.x
15. Mathew RA, Schlauder SM, Calder KB, Morgan MB. CD117 immunoreactivity in atypical fibroxanthoma. Am J Dermatopathol. 2008;30(1):34. https://doi.org/10.1097/DAD.0b013e31815b8ed5
16. Graadt van Roggen JF, Hogendoorn PC, Fletcher CD. Myxoid tumours of soft tissue. Histopathology. 1999;35(4):291. https://doi.org/10.1046/j.1365-2559.1999.00835.x

Summary of the case

1	**Patient (gender, age)**	73-year-old male
2	**Final diagnosis**	Atypical fibroxanthoma with myxoid change
3	**Symptoms**	Cutaneous nodule growing slowly during the last years
4	**Medications**	-
5	**Clinical procedure**	Total surgical excision
6	**Specialty**	Pathology, Plastic Surgery, Dermatology