

## LETTER - CLINICAL

### A case of atrophic dermatofibroma: a possible role of matrix metalloproteinase-2<sup>☆</sup>



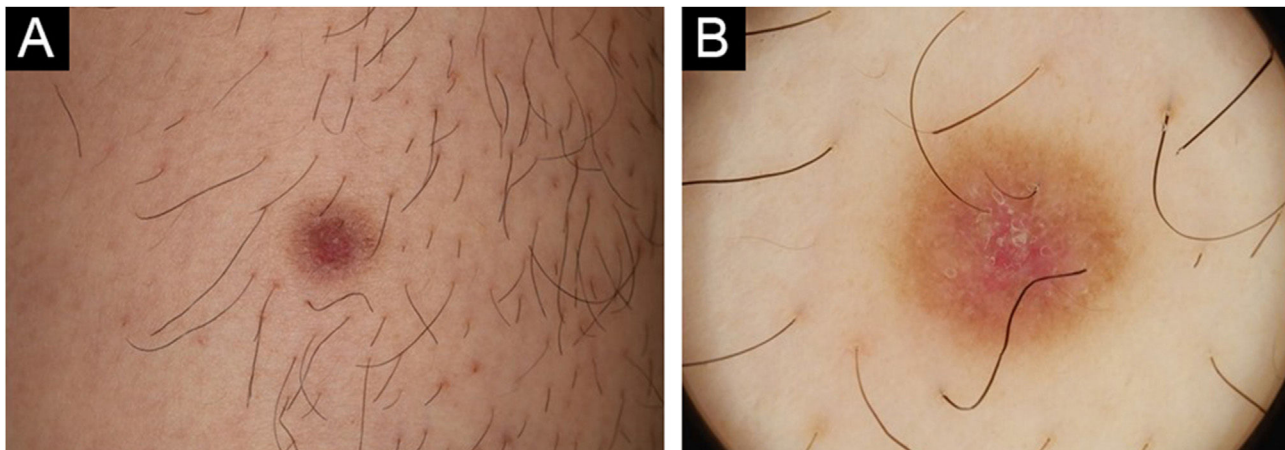
Dear Editor,

A 47-year-old male visited our department complaining of an asymptomatic nodule on the lower extremity, which appeared 5 years previously. He was otherwise healthy and did not recognize any triggering events such as insect bite or minor trauma. Physical examination showed a 5-mm-sized brownish dermal nodule with a central depression on the left thigh (Fig. 1A). Dermoscopy showed a central, reddish-colored area with scales surrounded by a brownish pigment network (Fig. 1B). The nodule was surgically removed with a 2-mm margin under local anesthesia. Histopathological examination showed a central depressed area and dermal atrophy (Fig. 2A). Higher magnification revealed the proliferation of fibroblastic tumor cells in the dermis and hyperplasia of the overlying epidermis (Fig. 2B). Factor XIIIa was positively stained, but CD34 was negatively stained. Elastica van Gieson stain revealed decreased elastic fibers in the dermis (Fig. 2C). Immunohistochemistry was performed

using antibodies against Matrix Metalloproteinase-2 (MMP-2), MMP-7, MMP-9 and MMP-12, and intense expression of MMP-2 was observed in the fibroblastic tumor cells (Fig. 2D).

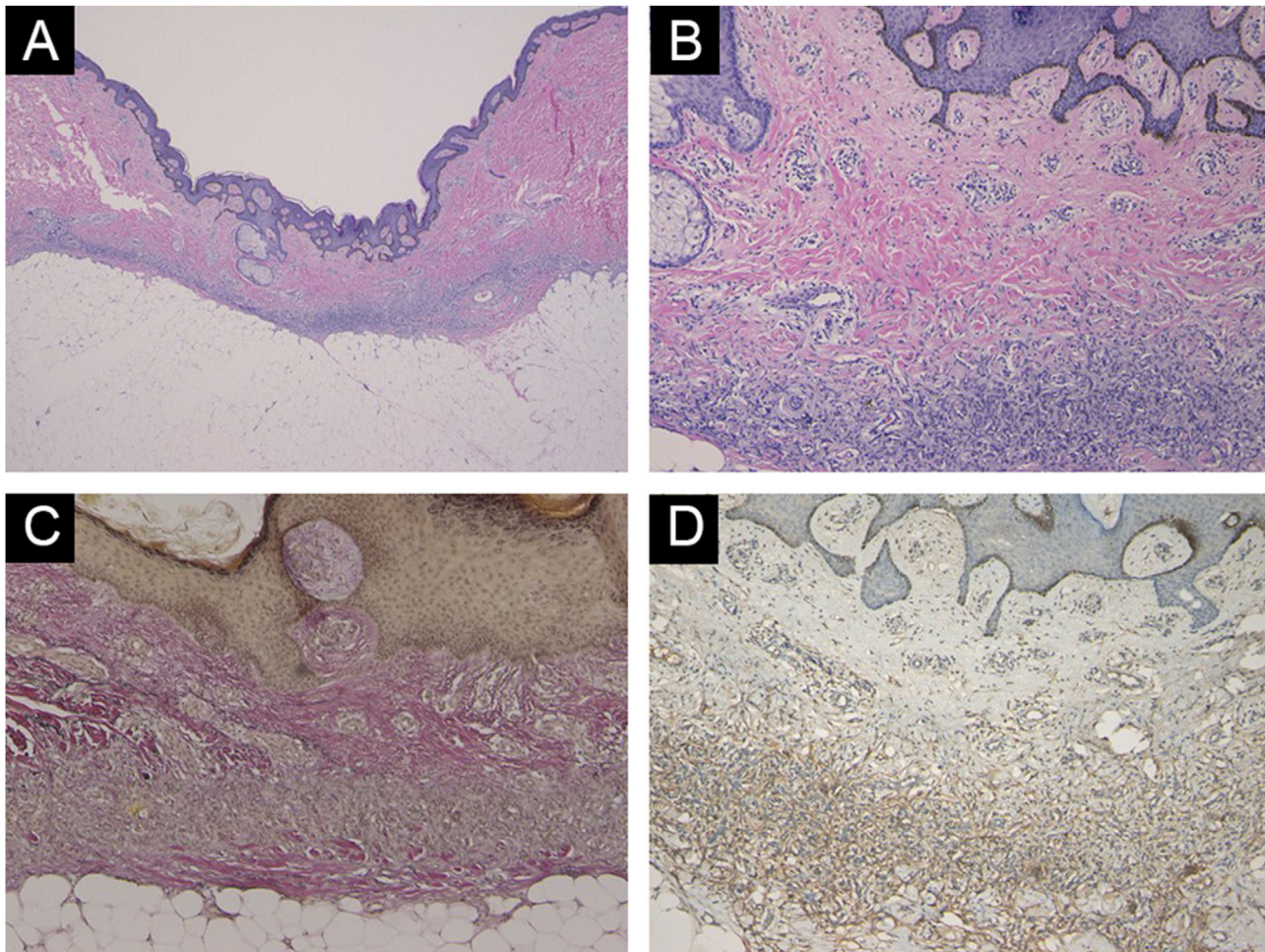
Atrophic dermatofibroma is a rare form of dermatofibroma and is clinically characterized by a solitary brownish nodule or plaque with a central umbilication.<sup>1,2</sup> Its dermal thickness is usually half of the thickness of the adjacent dermal tissue. In a recent review of atrophic dermatofibroma in 64 patients, the most common locations were shoulder (25%), lower extremity (23.4%), and back (17.2%).<sup>1</sup> Because of the characteristic clinical features such as brownish nodules or plaque with central depression, the clinical diagnosis is not so difficult. Dermoscopic examination shows a patchy pigment network multiple scar-like white patches, and pink-reddish coloration,<sup>3,4</sup> which may be of some help for the clinical diagnosis of atrophic dermatofibroma.

The pathomechanism of dermal atrophy in atrophic dermatofibroma is unknown. Previous studies revealed that elastic fibers are either decreased or absent in atrophic dermatofibromas. Recently, overexpression of MMP-1 by tumor cells has been reported in atrophic dermatofibroma.<sup>5</sup> In addition, in the present study, we have found that MMP-2 was strongly expressed in the fibroblastic cells, whereas



**Figure 1** (A) Clinical appearance of the brownish nodule with a central depression. (B) Dermoscopy showing a central reddish patch with white-yellow scales surrounded by a brownish pigment network.

<sup>☆</sup> Study conducted at the Department of Dermatology, Fukushima Medical University, Fukushima, Japan.



**Figure 2** Light Microscopy -(A) Lesion with a central depression showing dermal atrophy (Hematoxylin & eosin,  $\times 40$ ). (B) Higher magnification showing proliferation of fibroblastic tumor cells in the dermis and hyperplasia of the overlying epidermis (Hematoxylin & eosin,  $\times 200$ ). (C) Decreased elastic fibers in the atrophic dermis (Elastica van Gieson,  $\times 200$ ). (D) Intense expression of MMP-2 in the fibroblastic tumor cells, magnification  $\times 200$ .

expression of other MMPs such as MMP-7, MMP-9, and MMP-12 was not observed. The limitation is that we did not examine MMPs expression in ordinary dermatofibromas without atrophy. Therefore, we cannot conclude that enhanced expression of MMP-2 is the main cause of such a characteristic feature of atrophic dermatofibromas. Nevertheless, MMP-1 and MMP-2 may play an important role in the degradation of connective tissues in atrophic dermatofibromas, and further studies are necessary.

### Financial support

None declared.

### Author's contributions

Misaki Kusano: Data collection, analysis, and interpretation; Preparation and writing of the manuscript.

Toshiyuki Yamamoto: Manuscript critical review; Approval of the final version of the manuscript.

### Conflicts of interest

None declared.

### References

1. Cohen PR, Erickson CP, Calame A. Atrophic dermatofibroma: a comprehensive literature review. *Dermatol Ther (Heidelb)*. 2019;9:449–68.
2. Gutierrez N, Calame A, Erickson C, Cohen PR. Atrophic dermatofibroma: a unique dermatofibroma variant. *Cureus*. 2021;13:e14570.
3. Kelati A, Aqil N, Baybay H, Gallouj S, Mernissi FZ. Beyond classic dermoscopic patterns of dermatofibromas: a prospective research study. *J Med Case Rep*. 2017;11:266.
4. Karabay EA, Demir D, Gürsoy F, Zindanci I. A rare case of atrophic dermatofibroma with dermoscopic findings. *J Cosmet Dermatol*. 2021;20:2598–601.
5. Yano-Takamori A, Tsuji G, Nakahara T, Kido-Nakara M, Furuie M. A case of atrophic dermatofibroma overexpressing matrix metalloproteinase-1. *Case Rep Dermatol*. 2019;11:264–7.

Misaki Kusano , Toshiyuki Yamamoto \**Department of Dermatology, Fukushima Medical University, Fukushima, Japan*

\* Corresponding author.

E-mail: [toyamade@fmu.ac.jp](mailto:toyamade@fmu.ac.jp) (T. Yamamoto).

Received 11 May 2022; accepted 11 June 2022

Available online 27 November 2023

<https://doi.org/10.1016/j.abd.2022.06.011>

0365-0596/ © 2023 Sociedade Brasileira de Dermatologia.

Published by Elsevier España, S.L.U. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

## Amelanotic malignant melanoma in a child<sup>☆</sup>

*Dear Editor,*

A 3-year-old girl presented with a 7-month history of a pinkish nodule on the left leg. The lesion was firstly about 2 mm papule, then it enlarged in size within 7 months, and erosion and exudation of the nodule appeared under frequent scratching. The girl had no systemic symptoms, and her family history was unremarkable. The ulcerated nodule had no response to oral antibiotics. Physical examination showed a pinkish nodule 2.5 × 2.5 cm in diameter on the inner of the left leg, with a hard texture, irregular border, and ulcerated surface, closely surrounded by two scattered small papules (Fig. 1A). Blood tests including routine blood tests, liver and kidney functions, and coagulation results were normal. According to the clinical manifestations, dermatofibrosarcoma protuberans, sporotrichosis, and atypical mycobacterial infections were considered clinically. The nodule was completely excised under an operation and a histopathological examination of the total lesion was consequently performed. Histopathologic findings (Fig. 1B–D, Fig. 2A–B) demonstrated pseudoepitheliomatous hyperplasia and ulcerated lesion, melanocyte proliferation with angulated nuclei in a lentiginous pattern in dermal-epidermal junction, a few atypical melanocytes with pagetoid scatter in the epidermis and epithelioid melanocytes partially in nests in the upper dermal component. In the lower bottom field of the lesion, poor circumscription, dense cellularity, lack of maturation, and infiltrative growth were detected. High magnification exhibited hyperchromatic nuclei, large irregular nuclei with prominent atypia and poor differentiation, nuclear molding in the dermal component, and tumor cells extended invasively into the deep tissues. Immunohistochemical staining (IHC) (Fig. 2C–D, Fig. 3A–D) showed Melan A (+), S-100 (+), HMB-45 (–), P16 (–), Cyclin D1 (+), Ki-67 (about 20%, +) suggesting elevated proliferation. The diagnosis of amelanotic malignant melanoma (AMM) was confirmed based on the ulcerated irregular nodular, microscopic finding, and IHC results. Investigations, including computed tomography of the head and chest, and ultrasonography of superficial lymph nodes, liver, spleen, and kidney were normal. These results did not indicate any lesioned metastasis. The patient is care-

fully being followed-up, for up to 2-years, and she is still luckily alive and in healthy condition with normal growth and development.

AMM is a rare type of melanoma and is challenging to diagnose for lacking the classic clinical and pathological features of malignant melanoma (MM), especially for children.<sup>1</sup> The common locations of AMM for younger children are the head, neck, and extremities, while there are very few literature available indicating that AMM in childhood involves unusual areas, such as iris, vola, and intra-cranium, and may be a complication of oculocutaneous albinism and neurocutaneous melanosis.<sup>2–4</sup> Although pathological result directly ruled out the infectious disease, AMM can clinically or pathologically present as spitzoid lesion, which is easily misdiagnosed as Spitz nevus and leads to inappropriate or delayed treatment. The key to distinguishing the AMM and Spitz nevus is based on the comprehensive analysis of clinical presentations and histopathologic changes. Clinically, the lesion is often no bigger than 1 cm in diameter and vanishingly ulcerates. Under microscopy, melanocyte maturation, clear demarcation, good symmetry, clefts, and Kamino bodies are detected in Spitz nevus. Absent these changes of Spitz nevus, lack of maturation, poor differentiation, large irregular nuclei with prominent atypia, high proliferation index and mitoses in the bottom of the tumor, are identified in AMM. In most cases, histopathology can give the correct diagnosis, but in some cases, it may be misleading or hard to make a different diagnosis, immunohistochemical markers can help us better understand the nature of lesions. In our case, the negativity for P16 and positivity for CyclinD1 are consistent with the diagnosis of melanoma, reversibly in Spitz nevus. In this fact, we propose that physicians keep vigilant for amelanotic nodules in children. Molecule testing for melanoma emerges to help convey the diagnosis, such as BRAF V600E, NRAS, ROS, TERT-p, and NTRK by pyrosequencing.<sup>5</sup> Surgery is the most effective way for MM. Adjuvant therapy such as TNF- $\alpha$  injection in children remains unclear.

### Financial support

None declared.

### Authors' contributions

Anwei Chen: Wrote the manuscript.

Faliang Ren: Wrote the manuscript, provided the case and revised the manuscript.

<sup>☆</sup> Study conducted at the Department of Dermatology, Chongqing Medical University Affiliated Children's Hospital. Chongqing, China.