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Myxochondroid metaplasia of the plantar foot: a distinctive pseudoneoplastic lesion resembling nuchal fibrocartilaginous pseudotumor and the equine digital cushion

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Cartilaginous tumors of soft tissue are uncommon, with benign chondromas of soft parts greatly outnumbering rare soft-tissue chondrosarcomas. Over the past several years, we have seen in consultation a distinctive, benign-appearing chondroid soft-tissue lesion of the plantar foot that differs in a number of respects from chondroma of soft parts. Herein we report our experience with this distinctive lesion. A retrospective review of all cases from the foot in our soft-tissue consultation and institutional surgical pathology archives identified 9 similar cases, most often previously coded as 'fibroconnective tissue with chondroid metaplasia'. Six cases were submitted in consultation due to concern for a neoplastic process, in particular chondroma of soft parts or fibro-osseous pseudotumor of the digits. The patients were 4 young males (age range 8–16 years, mean 11.5 years) and 5 older patients, including 4 women and 1 man (age range 34–78 years, mean 56.4 years). All cases occurred in the subcutaneous plantar soft tissues of the feet, including four cases confined to the toes, and presented as non-specific, variably painful masses. Radiographic studies, available in six cases, did not show any evidence of bone involvement. Histologically, the lesions were characterized by a partially circumscribed, variably cellular proliferation of bland fibroblastic cells in a fibromyxoid background in areas showing distinct stromal basophilia and a chondroid appearance. Small foci of true cartilaginous metaplasia with lacuna formation were occasionally seen. Cartilaginous differentiation was confirmed in three cases with immunohistochemistry for S100 and ERG proteins. Intralesional cystic change was common, as were a variety of other reactive-appearing changes in the surrounding connective tissue. Characteristic morphological features of chondroma of soft parts and/or fibro-osseous pseudotumor of the digits were absent. Clinical follow-up (7 patients, 2–115 months, median 38 months) showed all patients to be without recurrent disease. We have identified a morphologically distinctive lesion of the foot that appears to represent a reactive, metaplastic process, presumably secondary to chronic mechanical stress. The morphological features of myxochondroid metaplasia of the plantar foot are reminiscent of those of nuchal fibrocartilaginous pseudotumor and the equine digital cushion, further suggesting a reactive/reparative etiology. Awareness of the unique features of this lesion should allow its ready distinction from other neoplastic and pseudoneoplastic (osteo) cartilaginous lesions of the feet.
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Chondroid matrix may be seen in benign and malignant soft-tissue tumors (eg, chondromas and chondrosarcomas), as well as in reactive, non-neoplastic processes, such as the variously named pseudosarcomatous osteocartilaginous proliferations of the digits[1–3] and tumoral calcinosis.[4] The clinical significance and treatment of these different chondroid lesions varies greatly, and their correct classification is important.

Over the past several years, we have seen in consultation several cases of a distinctive, benign-appearing, chondroid lesion of the plantar soft tissues of the foot, not clearly corresponding to a previously described entity. The present study was undertaken in order to more fully understand the

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clinicopathological features of these lesions and their proper place in the overall nosology of chondroid tumors of the soft tissues.

Materials and methods

The Mayo Clinic Institutional Review Board granted approval for this study. The consultation archives of one of the authors (ALF) were searched for cases previously coded as 'fibroconnective tissue with chondroid metaplasia', yielding six cases. Cases of myositis ossificans, subungual exostosis, and fibro-osseous pseudotumor of the digits were specifically excluded. Suggested diagnoses from the referring pathologists included chondroma of soft parts, fibroma of tendon sheath, calcifying aponeurotic fibroma, and fibro-osseous pseudotumor of the digits. Additionally, we reviewed all of our institutional archival cases from the feet for the period 1994–2012 (63 cases), yielding 3 similar cases. Clinical and follow-up information were obtained from the referring pathologists (see Acknowledgments) and our medical record system. All available hematoxylin and eosin-stained slides were re-reviewed. In order to confirm the presence of true cartilaginous metaplasia, formalin-fixed tissue sections from three selected cases were immunostained for S100 protein (polyclonal, 1:50–1:100, Dako) and the cartilage-associated nuclear regulatory protein ERG[5–7] (9FY, 1:50–1:100, BioCare) using heat-induced epitope retrieval. Appropriate controls were used.

Results

Table 1 summarizes the clinicopathologic features of the nine studied cases. The tumors occurred in 4 young males (age range 8–16 years, mean 11.5 years) and 5 adults, including 4 women and 1 man (age range 34–78 years, mean 56.4 years). All cases occurred in the plantar soft tissue of the feet, including four cases confined to the toes, and typically presented as variably painful soft-tissue masses. Clinically, the lesions were felt to represent non-specific soft-tissue masses (6 cases), a ganglion cyst (1 case), 'soft-tissue ossicle formation' (1 case), and 'non-union fracture fragments' (1 case). Radiographical studies, available for six cases, did not show evidence of bone or joint space involvement. All were interpreted as 'benign'. One patient had reportedly been previously involved in an automobile accident, with trauma to the foot. One patient, reportedly with Proteus syndrome, had macrodactyly and bilateral soft-tissue masses adjacent to both proximal third toes; these lesions showed identical histology to the others in this series (see below). No patient had a family history of plantar fibromatosis. None of the patients were known to be morbidly obese or to have an unusual sports or work history. Follow-up information was available for 7 patients with a follow-up duration of 2–115 months (median 38 months). No recurrences were observed. One case (case no. 9) was too recent for meaningful follow-up (<1 months).

Macroscopically, the excised tissue was typically described as showing an irregular, gray–white soft-tissue mass with a fibrous-to-myxoid consistency (Figure 1). Histologically, all cases had a similar appearance, with a partially circumscribed, subepidermal, variably cellular proliferation of bland fibroblastic cells in a fibromyxoid background (Figure 2a), sometimes with striking stromal basophilia (Figure 2b). An increased amount of irregularly distributed, wiry collagen was often present (Figure 2c). In areas the basophilic matrix 'coalesced', imparting an appearance that varied from vaguely to distinctly cartilaginous, sometimes resembling fibrocartilage with well-formed lacunae (Figures 2d–f). Intralesional cystic change was commonly present, as were a variety of other

Table 1 Clinicopathologic features and follow-up

Case no.	*Age (years)/ sex*	*Site*	*Clinical impression*	*Radiological finding*	*Therapy/follow-up (months)*
1	8/M	Right and left third toe	Soft-tissue ossicle formation	Soft-tissue ossification or calcification adjacent to the proximal third toe	Excision/NR (71)
2	11/M	Right foot	Soft-tissue mass	NA	Excision/NR (67)
3	11/M	Left fourth toe	Non-painful soft-tissue mass	2.0 × 1.5 cm soft-tissue mass, located on the lateral aspect of the left fourth toe	Excision/NR (44)
4	16/M	Right foot	Soft-tissue mass	Soft-tissue mass located near the great toe joint	Excision/NR (3)
5	34/F	Left hind foot	Non-union fracture fragments	Advanced soft-tissue degenerative changes	Excision/NR (115)
6	49/F	Right great toe	Painful soft-tissue mass	Soft-tissue prominence associated with deformity of the distal phalanx of the great toe	Excision/NR (18)
7	56/M	Right foot	Painful soft-tissue mass	Osseous fragments,?fracture fragments	Excision/NA
8	65/F	Right fifth toe	Well-circumscribed, subcutaneous soft-tissue mass	NA	Excision/NR (2)
9	78/F	Right heel	Soft-tissue mass	NA	Excision/NA

Abbreviations: NA, not available; NR, no recurrence.

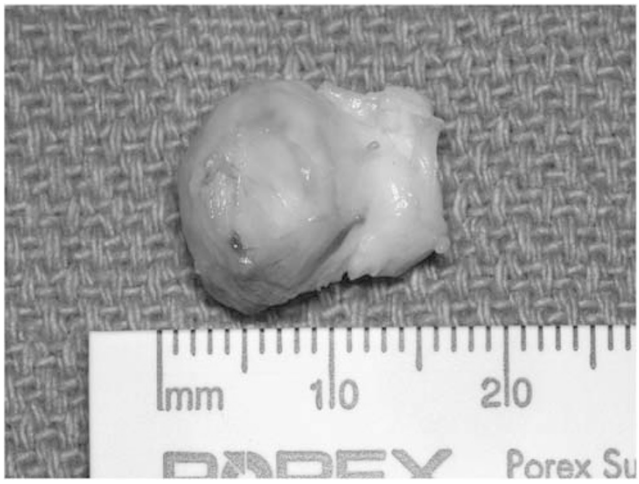


Figure 1 Grossly, myxochondroid metaplasia of the plantar foot presented as variably circumscribed, irregular, gray-white soft-tissue masses with a fibrous to myxoid consistency.

reactive connective tissue changes, including capillary proliferation, hemosiderin deposition, and fat necrosis (Figures 2g–i). Although relatively well-formed cartilage was occasionally present, other features of chondroma of soft parts, such as a lobular growth pattern, more abundant cartilage, and a giant cell-rich reaction were absent. Osteoid and/or woven bone production was absent in all the cases. By immunohistochemistry, variable expression of S100 protein and ERG was noted, both within basophilic zones lacking lacunae formation and in areas showing definite cartilaginous metaplasia (Figures 3a and b).

Discussion

Herein we have reported the clinical and pathological features of nine cases of a distinctive chondroid/cartilaginous soft-tissue lesion arising in the subepidermal soft tissues of the plantar foot, not clearly corresponding to one of the previously described cartilaginous or osteocartilaginous neoplasms or pseudoneoplasms of the feet. We strongly suspect that this represents a reactive/reparative process, based on its occurrence in a region subject to chronic mechanical stress, the presence of a variety of other reactive-appearing stromal changes, and its uniformly benign clinical course. The presence of true cartilaginous metaplasia in these lesions is supported by our finding of expression of both S100 protein and ERG protein expression within both basophilic zones that lacked lacunae and in areas with lacunae formation. ERG protein, more commonly associated by surgical pathologists with prostate cancer,[8] Ewing sarcoma,[9] endothelial neoplasms,[10] and myeloid leukemia,[11] has also been shown to have a critical role in the development and maturation of cartilage.[5–7] Although one case in our series occurred in a patient with Proteus syndrome, we suspect this is a chance occurrence, as lesions with these features have not been previously reported as part of this very rare syndrome.[12] Conceivably the bilateral, symmetrical presentation in this patient was secondary to a gait disturbance caused by other aspects of the Proteus syndrome.

The morphological features of myxochondroid metaplasia of the foot are, in many respects, similar to those of nuchal fibrocartilaginous pseudotumor, a distinctive pseudotumor of the neck. First described in detail by O'Connell *et al*[13] in 1996, nuchal fibrocartilaginous pseudotumor presents as a soft-tissue mass in the posterior aspect of the neck and is microscopically composed of a poorly delineated, nodular fibrocartilaginous proliferation at the junction of the ligamentum nuchae and the deep cervical fascia, with surrounding degenerative changes of the ligamentous tissue. Other reactive-appearing changes, such as capillary proliferation and stromal myxoid change, are frequently present.[14] Local trauma and/or chronic mechanical stress are felt to underlie the pathogenesis of nuchal fibrocartilaginous pseudotumor and fibrocartilaginous metaplasia of tendons and ligaments in other anatomical locations.[13–15] Lesions showing morphological features of nuchal fibrocartilaginous pseudotumor have not, to the best of our knowledge, previously been described in non-nuchal locations. Indeed, given the similar clinicopathological features of the lesion that we are reporting, an argument could be made that these be termed 'extra-nuchal, nuchal-type fibrocartilaginous pseudotumors'.

Interestingly, the histopathological features of myxochondroid metaplasia of the human foot are also reminiscent of those of the so-called 'digital cushion' of the horse.[16] The equine digital cushion comprises a thick connective tissue layer in the deep dermis of the digital pad and frog, the portion of the hoof that normally touches the ground on soft footing.[17] These distinctive equine hoof structures consist of an admixture of coarse connective tissue, fibrocartilage, myxoid tissue, and fat, functionally combined together to absorb mechanical shock (Figures 4a–d).[16] Importantly, the equine digital cushion is an *acquired* structure, not present in poorly exercised horses, and it has been hypothesized that it develops as a reaction to constant mechanical stress.[16] It is thus tempting to speculate that myxochondroid metaplasia of the human foot develops by a similar mechanism. Interestingly, somewhat similar changes, including chondroid metaplasia, have been reported in human runners with chronic plantar fasciitis.[18]

A variety of soft-tissue tumors may contain a component of cartilage-forming tissue, and these should be distinguished from myxochondroid metaplasia of the plantar foot. Although chondromas of soft parts frequently involve the feet, they are composed of well-defined cellular lobules of

moderately cellular hyaline cartilage, often showing degenerative calcification and an osteoclast-like giant cell-rich reaction.[19] Fibro-osseous pseudotumors of the digits not only frequently contain cellular cartilaginous tissue but also exhibit a nodular fasciitis-like myofibroblastic component and woven bone production in various stages of maturation.[1–3] Tumoral calcinosis, which may on occasion involve

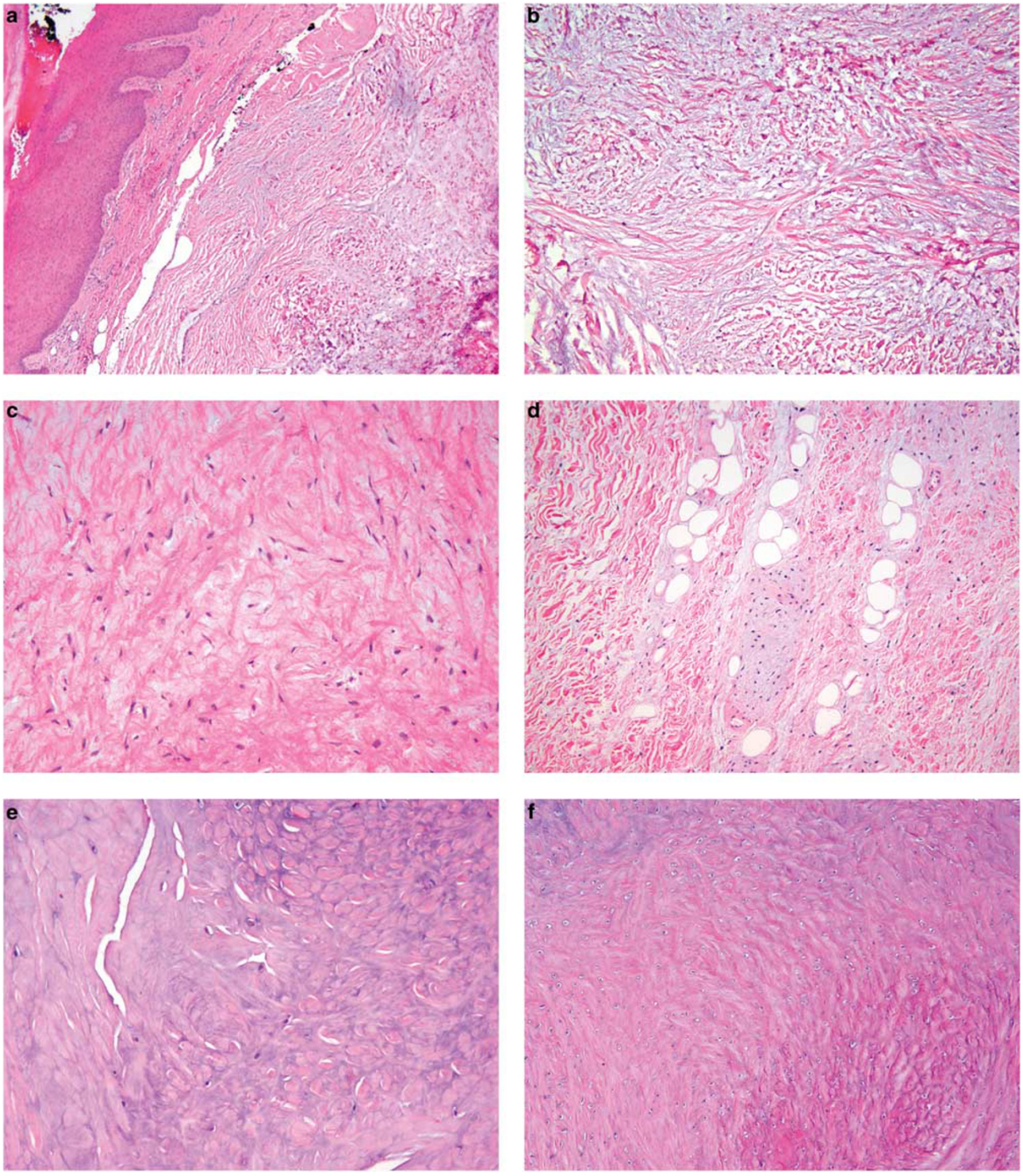
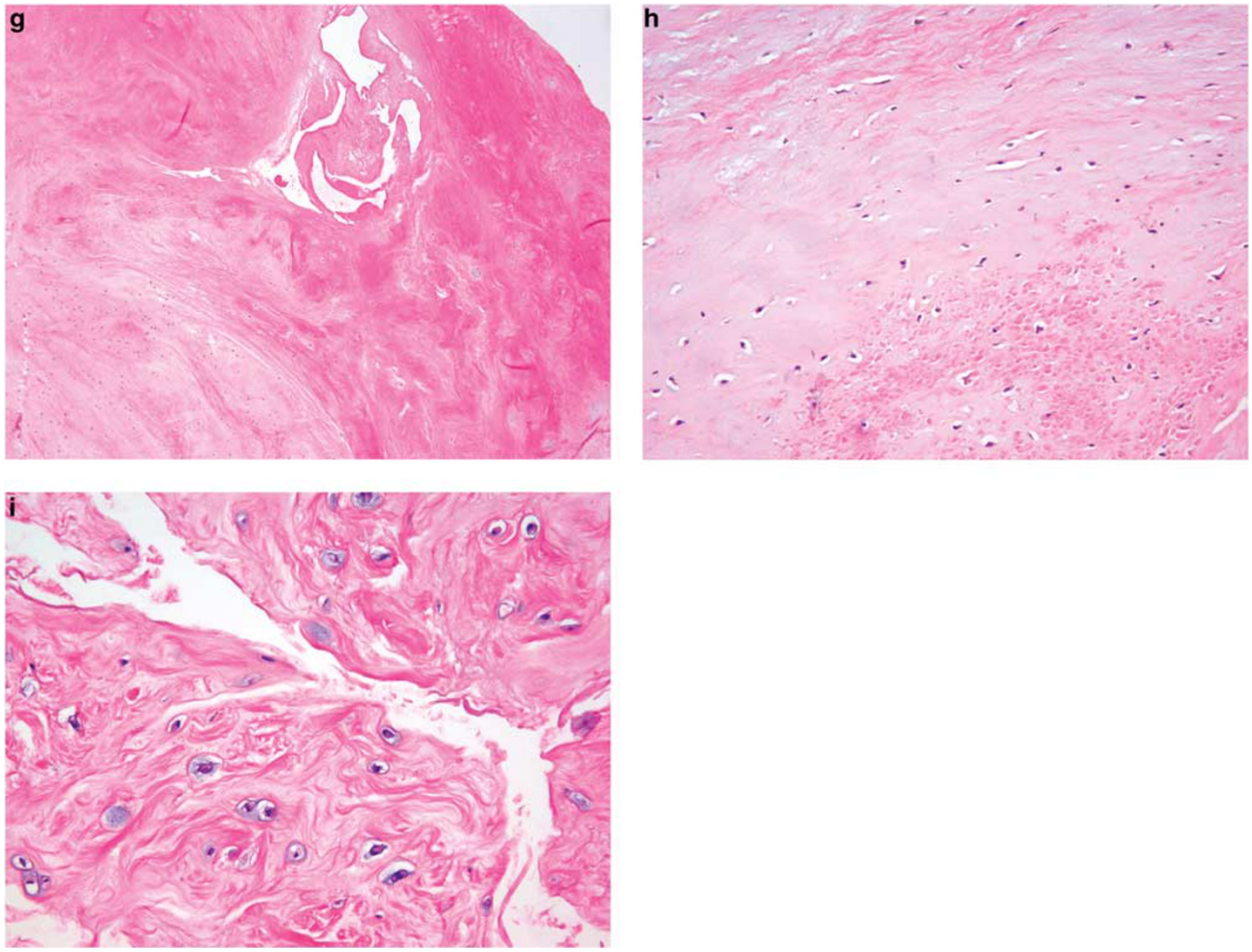


Figure 2 The lesions typically arose in a subepidermal location (**a**) and showed a deep dermal/subcutaneous accumulation of basophilic ground substance with increased amount of wiry collagen (**b**). More heavily collagenized areas contained an increased number of bland fibroblastic cells (**c**). In areas this basophilic matrix 'coalesced', creating a vaguely (**d**) or distinctly (**e**) chondroid appearance. Relatively well-formed cartilaginous tissue with lacunae formation was occasionally present (**f**). A variety of reactive and degenerative changes were frequently present, including cystic change (**g**), eosinophilic cartilaginous degeneration (**h**), and fissuring of the cartilaginous matrix (**i**).



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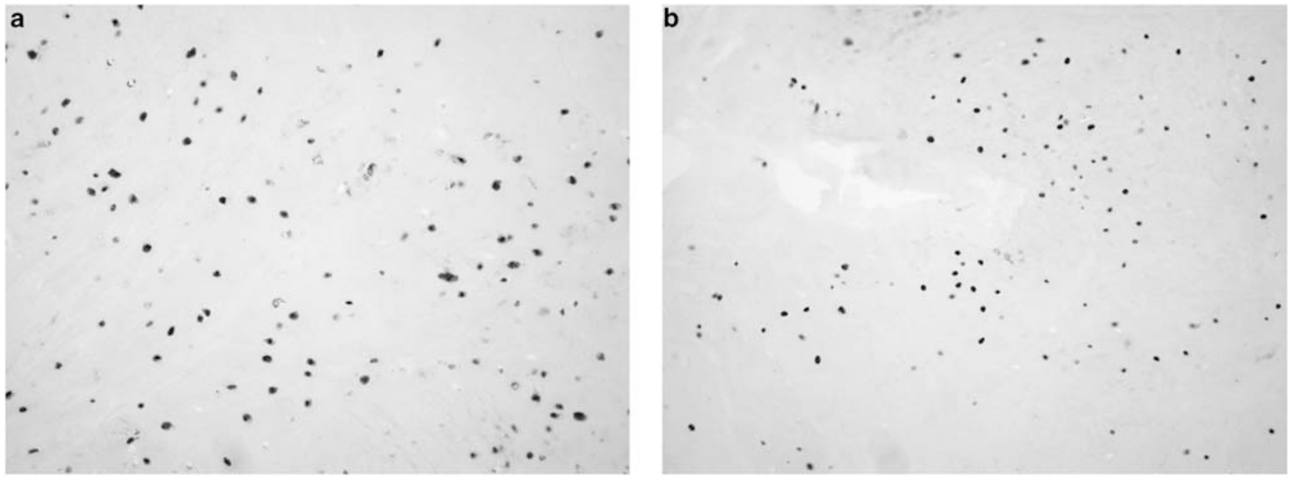

Figure 3 Expression of S100 protein (**a**) and ERG protein (**b**) in myxochondroid pseudotumor, confirming cartilaginous differentiation.

the hands and feet, consists of aggregates of deeply basophilic, amorphous calcification, often surrounded by an exuberant histiocytic reaction.[4] Calcifying aponeurotic fibroma, which often occurs in young males, contains an infiltrative, cellular fibroblastic component in addition to islands of variable calcified, chondroid matrix.[20] Synovial chondromatosis may, in neglected instances, present as a soft-tissue mass,

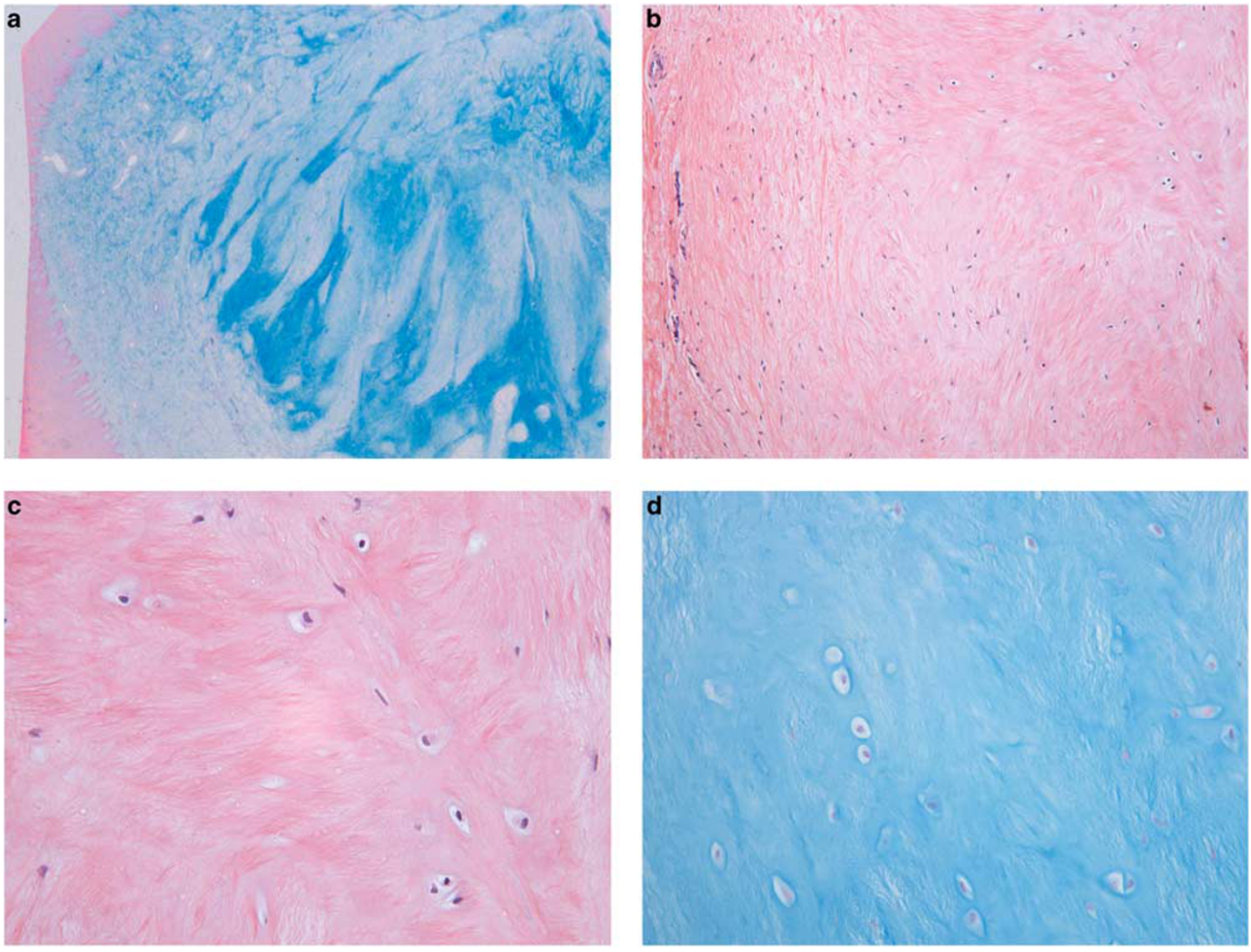

Figure 4 Representative images of the equine digital cushion (courtesy of Dr Monika Egerbacher, University of Veterinary Medicine, Vienna, Austria). Similar to myxochondroid metaplasia of the human foot, the equine digital cushion consists of a subepidermal accumulation of Alcian blue positive, hyaluronidase-resistant chondroid matrix (**a** and **c**), in association with abundant collagen (**b**) and cartilaginous tissue, including lacunae (**d**).

but arises from the synovium of a joint, tendon, or bursa, and consists of nodules of cellular hyaline cartilage lined peripherally by synovium.[21] Fibromas of tendon sheath typically lack myxochondroid stromal changes.

In summary, we have described the clinicopathological features of myxochondroid metaplasia of the plantar foot, a distinctive pseudoneoplastic lesion resembling nuchal fibrocartilaginous pseudotumor and the equine digital cushion and most likely representing a peculiar connective tissue response to chronic mechanical stress. Aware of the distinctive features of this distinctive lesion should allow for its ready distinction from other neoplastic and non-neoplastic chondroid lesions of the feet.

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Disclosure/conflict of interest

The authors declare no conflict of interest.

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