Calcifying aponeurotic fibroma (CAF) is a very rare tumor of the extremities, which can be difficult to diagnose due to its wide cyto-architectural pattern. We herein report the clinicopathologic features of a case of CAF localized on the dorsal face of the foot in a 5-year-old male child, diagnosed by needle core biopsy. Differential diagnostic problems are discussed. The present case emphasizes that the diagnosis of CAF can be confidently rendered on core needle biopsy if the main morphological components of this tumor are concurrently present; however, before making the diagnosis of CAF, the clinical and radiological context should be considered.

**Key words**
Calcifying aponeurotic fibroma • Needle core-biopsy • Histological diagnosis • Immunohistochemistry

**Summary**
Calcifying aponeurotic fibroma (CAF) is a very rare tumor of the extremities, which can be difficult to diagnose due to its wide cyto-architectural pattern. We herein report the clinicopathologic features of a case of CAF localized on the dorsal face of the foot in a 5-year-old male child, diagnosed by needle core biopsy. Differential diagnostic problems are discussed. The present case emphasizes that the diagnosis of CAF can be confidently rendered on core needle biopsy if the main morphological components of this tumor are concurrently present; however, before making the diagnosis of CAF, the clinical and radiological context should be considered.

**Introduction**
In 1953 Keasbey described a tumor characteristically occurring in the palms and soles of young children, for which the term “juvenile aponeurotic fibroma” was proposed. Subsequent studies revealed that this tumor can occur, not only at any age, but also in various sites including wrist, forearm, elbow, upper arm, neck, abdominal wall, lumbar paravertebral area, leg, ankle, and thigh. On clinical examination CAF presents as a single, firm, painless, slowly growing mass occurring more frequently in males. Multiple lesions have also been reported in the literature. Given its tendency to local invasion, typically into the surrounding fascia or muscle, a high local recurrence rate (up to 50%) can be documented after surgical excision. Malignant transformation into fibrosarcoma has also been rarely reported. Gross examination reveals a whitish mass with irregular borders, usually attached to fascia or tendons. The cut section shows a fibrous surface with gritty foci of calcifications. Histologically, two distinct components can be identified: i) fibromatosis-like proliferation of bland-looking spindle shaped cells set in a fibrous stroma; ii) nodules, some of them with chondroid metaplasia, variably calcified, and usually rimmed by plump round to epithelioid cells, as well as multinucleated osteoclast-like giant cells.

Some authors suggested the existence of different phases of tumor growth. The early phase is characterized by high cellularity, with neoplastic cells mainly arranged in fascicles; chondroid or immature cartilaginous foci are present but calcifications are lacking or only focally detectable. Mitoses may be present. Later, the deposition of granular calcifications in the nodular tumor component predominates. During this phase, the calcified areas are surrounded by plump round/epithelioid fibroblasts and osteoclast-like multinucleated giant cells. In the last phase, tumor is predominantly hypocellular with a diffusely fibrotic and calcified stroma. These different histological phases explain the heterogeneous appearance on radiological imaging, which is variable according to the patient’s age, presence of calcifications and osseous involvement. On radiography, CAF appears as a soft tissue mass, with or without fine stippled calcification. Signs of bone involvement, such as scalloping of the cortex and adjacent bone erosion, may be seen. Computed Tomography (CT) scan is helpful to detect the calcified areas. Although magnetic resonance (MRI) is the most accurate tool in the evaluation of soft tissue tumors, MR imaging could not detect the calcified areas.
features of CAF are not available in the literature, with rare exceptions. Kwak et al. 12 reported a case of radiologically “non-calcified” CAF in a young child, and described the MRI findings as an intensity signal lower than that of muscle on T1WI and T2WI. Hasegawa et al. 13 demonstrated subcutaneous distribution, tendency to local infiltration, close location to fascia or tendon, and heterogeneous enhancement after gadolinium contrast injection. They stated that the low signal intensity on T2WI was attributed to the fibrous component and little cellularity of the mass and this finding is more commonly seen during the initial phase.

We herein report the clinicopathologic features of a case of CAF localized on the dorsal face of the foot in a 5-year-old male child, emphasizing the possibility of needle core biopsy-based diagnosis. Although in one case the diagnosis of CAF was suspected by fine needle aspiration biopsy (FNAC) 14, to the best of our knowledge, this is the first case of CAF diagnosed pre-operatively by needle core biopsy.

Case report

A 5-year-old male child presented with a firm, palpable and painless mass on his left forefoot. CT scans revealed a swelling mass, about 17 x 17 mm in size, with elastic consistency and separated from adjacent skeletal segments. The deep component of the lesion was sited between the shaft of the II and III metatarsal bones. Multiple inert calcifications were seen. RMI imaging showed an expansile, oval-shaped subfascial mass, measuring approximately 22 mm in its greatest dimension, hypointense on T1-weighted images, hyperintense on the T2-weighted images, with regular margins delimited by a hypointense rim. The heterogeneous contrast enhancement is due to the simultaneous presence of both hypointense and hyperintense areas likely due to calcifications. No signal abnormalities of bone structures was appreciable (Fig. 1). Clinically and radiographically the mass was interpreted to be suspicious for sarcoma. Fine needle core biopsy was performed.

Materials and methods

Biopitic and the relative surgical specimens were fixed in 10% buffered formalin, routinely processed and embedded in paraffin. Two sections were stained with haematoxylin and eosin while additional sections were cut for immunohistochemical procedures. Immunohistochemical studies were performed with the labeled streptavidin-biotin peroxidase detection system using the DAKO automated immunostainer (Glostrup, Denmark). The following antibodies were tested: vimentin (dilution 1:100), α-smooth muscle actin (dilution 1:200), desmin (dilution 1:100), myogenin (dilution 1:100), S-100 protein (dilution 1:500), CD34 (dilution 1:50), pancytokeratins (dilution 1:50), β-catenin (dilution 1:100), EMA (dilution 1:100); INI-1 (dilution 1:100 ) all from DakoCytomation, Glostrup, Denmark.

Pathologic findings

Core biopsy specimen revealed a proliferation of spindle to stellate cells intermingling with multinucleated osteoclastic-like giant cells and set in a fibrous stroma (Fig. 2a-d). The cells showed only a mild nuclear atypia, while mitoses and necrosis were absent. Notably microcalcifications were scattered throughout the fibrous stroma (Fig. 2d). Immunohistochemical analyses showed a diffuse staining only for vimentin. No immunostaining was obtained with α-smooth muscle actin, desmin, myogenin, S-100 protein, CD34, pancytokeratins and EMA. The proliferation of spindle- to stellate-shaped cells with a fibroblastic profile, intermingling with osteoclastic-like cells, set in a fibrous stroma was consistent with the diagnosis of CAF. This suspicion was also supported by the age and the site of the tumor mass. However it was recommended to clinicians of evaluating histologically the entire tumor mass after complete surgical excision. Grossly the surgically-resected tumor presented as a well-circumscribed, 3 cm nodule, firm in consistency and whit-
ish in color. The cut surface showed a fibrous mass with gritty foci of calcifications. Histologically, at low magnification, tumor had a multinodular appearance with hypercellular areas alternating with more hypocellular fibrous areas (Fig. 3a-c). Notably some nodular areas were extensively calcified (Fig. 3c). The neoplastic proliferation was focally present at the resection margins (Fig. 3d). Higher magnification showed highly cellular areas composed of bland-looking spindle cells arranged in long, variably intersecting, fascicles closely reminiscent of desmoid-type fibromatosis (Fig. 4a). These areas were variably blending with hypocellular fibrous areas in which the cells adopted a stellate shape (Fig. 4b-d). Notably a significant number of multinucleated osteoclastic-like giant cells were variably intermingling with the neoplastic cells (Fig. 4b). Mitotic count was low (up 2 mitoses x 10 high power field). Osteoid and/or cartilaginous matrix was absent. Nuclear pleomorphism, atypical mitoses and necrosis were absent. Immunohistochemically neoplastic cells were diffusely stained with vimentin and focally with alpha-smooth muscle actin and WT1 (cytoplasmic staining alone) (Fig. 5). Based on morphological and immunohistochemical features, the diagnosis of CAF was rendered.

Discussion

Recently young-type fibromatoses have been interpreted as an unique group of benign or intermediate, non-metastasizing fibroblastic- myofibroblastic proliferations. Their clinical behavior ranges from a self-limiting mass to locally recurrent tumor. Fibroblasts and myofibroblasts are present in variable proportions and arranged in a wide variety of growth patterns in each single entity and they are usually interspersed in a predominantly fibrous stroma. Their morphological heterogeneity likely reflects their phenotypic plasticity. The following clinicopathologic entities are currently included in the category of young-type fibromatoses: infantile myofibroma (myofibromatosis), fibromatosis colli, infantile digital fibromatosis (fibroma), fibrous hamartoma of infancy, calcifying aponeurotic fibroma, lipofibromatosis, juvenile nasopharyngeal fibroma, hyaline fibromatosis (juvenile and infantile types). The immunohistochemical expression of vimentin, alpha-smooth muscle actin and WT1 is helpful in revealing the fibroblastic/myofibroblastic profile shared by all these entity. CAF is a very rare tumor which can be difficult to diagnose due to its wide morphological spectrum. Accordingly differential diagnostic problems may arise with a variety of benign and malignant soft tissue tumors. Unfortunately, radiologic features of CAF, including those of the present case, are not specific, and thus the correct diagnosis is still based on the histological examination. Although the diagnosis of CAF is usually straightforward in surgically-resected specimen if all the diagnostic clues are present, it may be challenging when evaluating needle core biopsies. This is mainly due to
Fig. 3. Surgical specimen. (A) Low magnification showing a tumor with a multinodular appearance, attached to tendon fascia (arrows). (B) Tumor showing hypercellular areas alternating with more hypocellular fibrous areas. (C) Notably some tumor nodules were extensively calcified. (D) The neoplastic proliferation was focally present at the resection margins (tendon fascia).

Fig. 4. Surgical specimen. (A) Higher magnification showing highly cellular areas composed of bland-looking spindle cells arranged in a fibromatosis-like pattern. (B) Hypercellular areas blending with hypocellular areas containing multinucleated osteoclastic-like giant cells. (C) This area shows the different morphological phases of CAF: hypercellular areas blending into hypocellular and more extensively fibrotic areas with microcalcifications. (D) Tumor area in which spindle-, stellate-shaped cells and multinucleated giant cells coexist.
the fact that CAF often shows a wide variety of cellular composition and growth patterns. Apart from morphology, the patient’s age, tumor site, and radiological features are very helpful for a correct pre-operative diagnostic approach.

We herein report the first case of CAF occurring in the foot of a 5-year-old male child and diagnosed pre-operatively by needle core biopsy. Differential diagnosis on needle core biopsy mainly included desmoid-type fibromatosis, tenosynovial giant cell tumor (localized type), and epithelioid sarcoma. Differentiating CAF from desmoid-type fibromatosis can be difficult as the latter can arise in the soft tissues of the proximal extremities. In addition CAF usually contains hypercellular areas which look like desmoid-type fibromatoses. In our case the majority of the cells had a spindle shape but they were not arranged in distinct fascicular pattern as they do in desmoid-type fibromatosis. In addition the presence of osteoclast-like multinucleated giant cells and calcifications, along with the absence of immunostaining for β-catenin, argued against the diagnosis desmoid-type fibromatosis. Tenosynovial giant cell tumor, localized type, shares some clinical features with CAF in that both lesions present as asymptomatic, slowly-growing masses attached to the tendon sheath and/or joint capsule. Magnetic resonance imaging is helpful in the differential diagnosis as CAF shows speckled calcifications and ill-defined margins, whereas the former has lobulated and well-defined margins. In addition erosions of the adjacent bone can be observed in tenosynovial giant cell tumor. Although the presence of multinucleated giant cells in the needle core biopsy of our case was reminiscent of tenosynovial giant cell tumor, it was ruled out as the characteristic mononuclear cells, foamy histiocytes and siderophages were lacking. The spindle cell component seen in our case is not a feature of tenosynovial giant cell tumor. In the present case the identification on needle core biopsy of spindle cells set in a fibrous stroma containing microcalcifications may arise diagnostic problems with epithelioid sarcoma, spindle cell variant. However this malignant tumor was ruled out by immunohistochemistry that showed INI1 expression, as well as no immunostaining with both cytokeratins and EMA. The present case emphasizes that the diagnosis of CAF can be confidentially rendered on core needle biopsy if the main morphological components of this tumor are concurrently present: proliferation of spindle to stellate cells set in a fibrous stroma, osteoclast-like giant cells and microcalcifications. Immunohistochemistry is helpful in revealing the fibroblastic/myofibroblastic profile of the neoplastic cells. Before making the diagnosis of CAF, the clinical and radiological context should be taken in consideration by pathologists. However we suggest that the final diagnosis of CAF should be rendered on the surgically-excised nodule.

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**Fig. 5.** Immunohistochemical findings in surgical specimen. (A) Neoplastic cells were diffusely stained with vimentin and only focally with alpha-smooth muscle actin (B). (C) WT1 immunostaining was restricted to cytoplasm of neoplastic cells. (D) INI1 was diffusely expressed in the nuclei of neoplastic cells, ruling out the diagnosis of epithelioid sarcoma.
References


