ORIGINAL PAPER/PŮVODNÍ PRÁCE

Calcifying Aponeurotic Fibroma, a Rare Benign Entity to Consider: a Systematic Review of Literature

Kalcifikující aponeurotický fibrom, vzácný benigní útvar, kterému je třeba věnovat pozornost: systematický přehled literatury

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ABSTRACT

Purpose of the study

Calcifying aponeurotic Fibroma (CAF) is a benign neoplasm that most commonly onsets in the distal extremities during the childhood. It usually presents as a slow growing non-painful mass. The purpose of this study is to carry out a systematic literature review aimed to delineate the main clinical characteristics of this nosologically entity to define the therapeutic approach and outcome.

Material and methods

A systematic literature review was conducted from March to June 2022 using five major databases: PubMed, Scopus, Embase, MEDLINE, and the Cochrane Library. Studies published in English between 1953 and 2022 reporting clinical cases of Calcifying Aponeurotic Fibroma (CAF) were considered. Eligible studies included case reports and case series; non-English articles, animal studies, and papers lacking sufficient clinical detail were excluded. Two independent reviewers screened the studies following PRISMA guidelines. Extracted data included patient demographics, tumor characteristics, clinical presentation, diagnostic method, treatment strategy, histological findings, clinical outcome, and follow-up duration.

Results

74 papers were identified and 44 were considered relying on their title and content.

125 patients in total,49 females and 76 males have been included. The lesions were clinically presented as an indolent mass, sometimes associated with functional impairment and discomfort; the extremities were the most common localization. The diagnosis was made in 35 cases with a biopsy and in 60 cases it was obtained after the histological examination on the entire operating specimen without doing a preoperative biopsy. In the remaining 30 cases, there was no information about biopsy or histological examination. A total amount of 91 cases were surgically treated with wide excision and 68 of those had regular follow-up. The mean follow-up was 46.2 months, and local recurrence was observed in 20 cases of 68 (29.4%).

Discussion

Calcifying Aponeurotic Fibroma is a rare benign tumor, typically arising in the distal extremities of children and young adults. Although often indolent, it can exhibit locally aggressive behavior and recur after excision. Atypical sites and extensive forms suggest a broader clinical spectrum than previously recognized. Imaging aids diagnosis, but histological confirmation is essential due to overlap with other pediatric fibromatoses. The tumor shows myofibroblastic differentiation, frequent calcification, and occasional cartilage formation. While wide excision remains the preferred treatment to reduce recurrence, conservative surgery may be considered to preserve function in sensitive locations. Malignant transformation appears anecdotal and unconfirmed.

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Conclusions
CAF has been found to be a benign disease that affects both genders with similar frequency; it is rare even if it is probably underestimated. Surgical treatment should be as extensive as possible in order to reduce the risk of local recurrence. Further researches are however necessary to support the evidence provided by this first literature review.

Key words: benign tumor, excision surgery, foot tumor, hand tumor, soft tissue tumor.

INTRODUCTION

Calcifying aponeurotic fibroma (CAF), first described by Keasbey in 1953, is a rare, benign fibrous tumor belonging to the group of superficial musculoskeletal fibromatosis; it predominantly arises in the palms and soles (13, 18).

CAF typically occurs in individuals between 8 and 14 years of age, with a reported male-to-female ratio of approximately 2:1 and no evidence of hereditary predisposition (1, 4, 8, 12). Due to its rarity, comprehensive data on CAF are lacking, and current knowledge is derived primarily from case reports and small case series. The aim of this study is to provide a systematic review of the literature to better define the epidemiological and clinical features of CAF, as well as to outline appropriate diagnostic and therapeutic strategies.

MATERIAL AND METHODS

A comprehensive literature search was conducted between March and June 2022 using major scientific databases, including PubMed, Scopus, Embase, Medline, and the Cochrane Register. The keyword "Calcifying Aponeurotic Fibroma" was used to identify English-language publications reporting CAF cases, published between 1953 and 2022. Eligible studies included case reports and case series documenting the clinical history of patients diagnosed with CAF. Exclusion criteria were: non-English articles, animal studies, studies lacking sufficient clinical information, and unpublished research. No restrictions were placed on the number of patients included in the case series. Studies for which the full text was unavailable were excluded.

The primary objective of this review was to identify the epidemiological and clinical characteristics of CAF. The secondary objective was to determine the most appropriate treatment approach. Two researchers (SO and MB) independently screened the retrieved articles for eligibility. In cases of disagreement, consensus was achieved through direct discussion. The selection process adhered to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines.

The following patient parameters were extracted and analyzed: sex, age, tumor size at presentation, anatomical site, presence of symptoms, and general health status. Additional data included whether the case represented a primary diagnosis or a recurrence and, in the latter case, the time from initial surgery to recurrence, whether a preoperative biopsy was performed, the therapeutic strategy, type of surgery, wide or intralesional; type of treatment, conservative or surgical, or combined, and its timing, as well as tumor presentation, histological findings, clinical outcome, and status at last follow-up.

Descriptive statistics were used to summarize the data. All analyses were performed using Microsoft Excel (Microsoft, Redmond, Washington, United States). The study was conducted in accordance with the ethical principles outlined in the 1964 Declaration of Helsinki and its subsequent amendments or comparable ethical standards. Approval for the study was obtained from the local ethics committee. This research received no specific funding from public, commercial, or not-for-profit agencies. The authors declare no conflicts of interest.

RESULTS

Selected papers: The initial search identified 74 papers. Of these, 72 were selected based on title screening. Ten studies were subsequently excluded due to unavailability of the full text, and one was excluded due to language. Following full-text assessment, 44 articles met the inclusion criteria. An additional five studies were identified through reference screening. In total, 49 studies were included in the final review, comprising data on 125 patients. The selection process is summarized in Fig. 1.

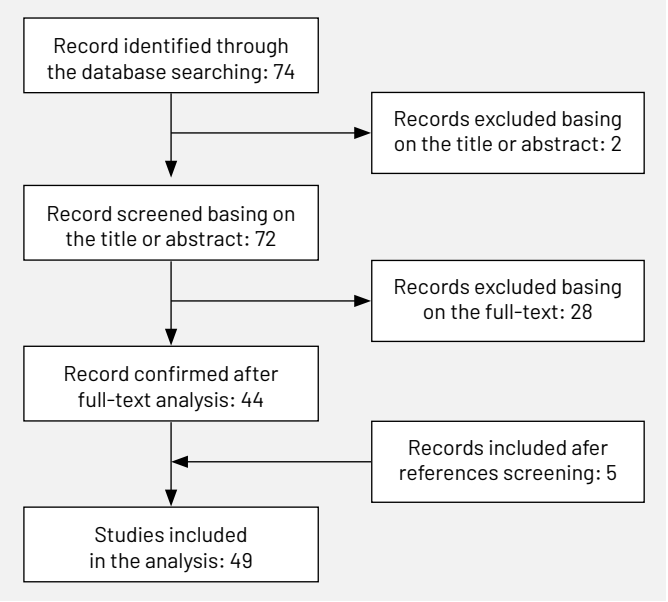

Fig. 1. **A flow-chart showing the selection process.**

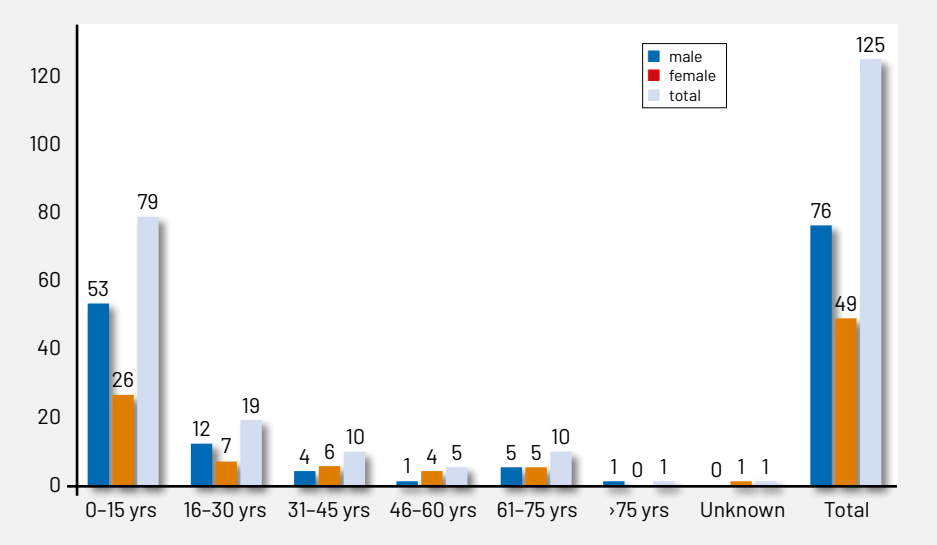

Fig. 2. **The age and sex distribution of the present series.**

Age and sex: The average age was 19.5 years, ranging from 2 months to 84 years, the median was 10.5 years, even if the age of one patient was unknown (Fig. 2). Patients were 49 females (39.2%) and 76 males (60.8%) (Table 1).

Sites: CAF was located in the upper limb in 63 patients and in the lower limb in 44 cases. Fifteen cases involved the trunk or the head and neck region. One patient presented with multiple lesions, while in three cases the anatomical site was not specified (Fig. 3) (Table 1).

Size: The average tumor size was 2.8 × 2.4 × 1.5 cm, based on the 10 studies that reported measurements along all three axes. Additionally, 16 studies did not report tumor size at all, while 21 provided only partial dimensional data without specifying measurements along all three axes (Table 1).

Symptoms: They were reported in 19 out of 125 cases; Discomfort was the most frequently described symptom (14 patients), followed by pain in 8 cases. In 11 patients, the mass was painless. One patient reported neurological symptoms due to median nerve compression, resulting in tingling and numbness, and another reported pruritus. The remaining 106 cases were described as asymptomatic (Table 1).

Diagnosis: The diagnosis was made in 35 cases with a biopsy and in 60 cases it was obtained after the histological examination on the entire operating specimen without doing a preoperative biopsy. In the remaining 30 cases, there was no information about biopsy or histological examination.

Treatment: Surgical treatment was performed in 91 cases, with detailed treatment information available for 86 of them. Complete excision was carried out in 77 cases, whereof 6 underwent wide excision, while 71 received marginal resection. Partial excision was performed in 9 cases. In three cases, surgery was not undertaken, and patients were managed with regular follow-up. For the remaining 31 cases, no information regarding the treatment was available (Table 1).

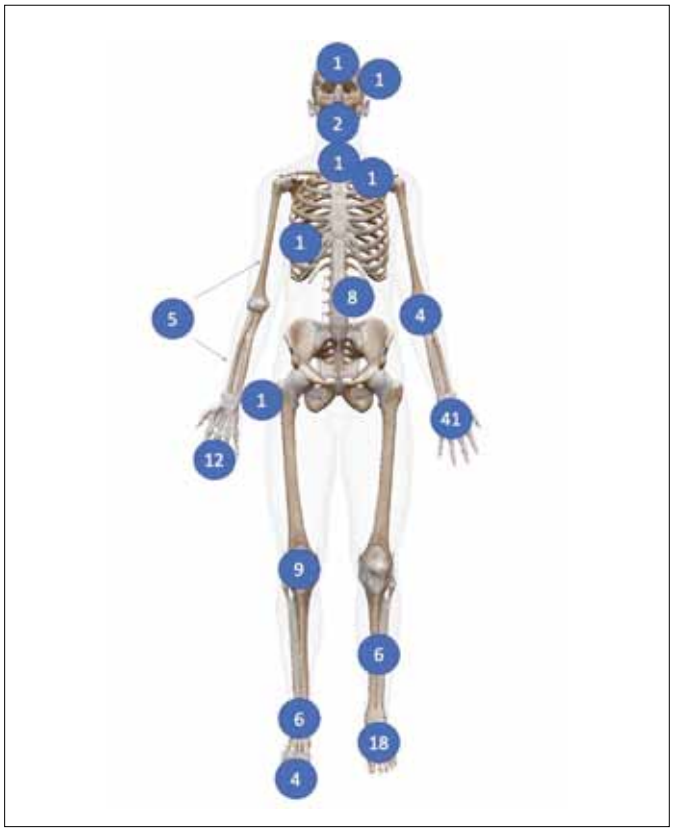

Fig. 3. **A picture showing the distribution of the disease; moreover, a case of multiple localizations has to be considered; in three cases the site of origin was not mentioned.**

Follow-up: The mean follow-up duration was 46.2 months (range: 4 to 168 months), reported for 68 of the 91 patients who underwent surgery. Of these, 58 were followed up after wide

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Table. **CAF epidemiological and clinical characteristics**

Age	Age: average 19.5 years (range 2 months–84 years)		
Sex	49 females (39.2%) and 76-male (60.8%)		
Sites	body region	anatomical sites	cases
	upper limb	hand and wrist	41
		fingers	12
		elbow	4
		arm and forearm	5
		clavicle	1
		total cases	63
	lower limb	foot	18
		toes	4
		ankle	4
		tight and gluteus maximus	7
		knee	9
		tendons	2
		total cases	44
	others	forehead	1
		scalp	1
		mandible	2
		back	8
		neck	1
		thorax	1
		generalized form	1
		total cases	15
	unknown	unknown	3
		total cases	3
Size	2.8 cm × 2.4.cm × 1.5.cm		
Symptoms (19 cases)	Discomfort: 14 Pain: 8 Hand tingling and numbness: 1 (median nerve compression) Itch: 1 Asymptomatic: 106		
Treatment (91 cases)	86 cases of 91 with treatment described in detail Complete excision: 77 (6 cases only received wide excision and 71 narrow margin resection) Partial excision: 9 Conservative treatment: 3 No information about treatment: 31		
Follow-up	46.2 months (min 4 months–max 168 months)		
Recurrence rate:	25.8% after wide marginal excision (15 out of 58 followed up after surgery) 71.4% after intralesional excision (5 out of 7 followed up after surgery)		

marginal excision, 7 after intralesional excision, and in the remaining 3 cases, no details regarding the type of surgical treatment were available (Table 1).

Recurrence: Fifteen patients (25.8%) experienced local recurrence following marginal excision. Among the 7 patients who underwent partial excision, 5 (71.4%) demonstrated tumor progression.

The recurrence-free survival was 31.5 months (range: 1 month–132 months) (Table 1).

DISCUSSION

CAF is a benign fibrous tumor that arises in soft tissues. The average age of onset of CAF was approximately 20 years, slightly higher than previously reported. The observed gender distribution did not confirm the commonly described male predominance, and no familial inheritance was identified.

Consistent with the literature, the most frequent sites of onset were the distal extremities of the upper and lower limbs; however, involvement of other anatomical regions is not uncommon. Actually, in 2010 Arora et al. reported an unusual case of CAF located in the gluteus maximus muscle, with an uncommon size of 10 × 9 × 5 cm (3). Additionally, Chaltsev et al., described a case of a 52-year-old man with seronegative rheumatoid arthritis, showing a generalized form of CAF characterized by multiple subcutaneous lesions at various sites (aponeuroses and fascia of the head, neck, trunk, upper and lower extremities) with a massive deposition of calcium salts (5).

The size of CAF is highly variable, and unfortunately, most studies do not provide detailed dimensional data, making it difficult to establish a reliable average size. Based on the studies that reported complete measurements, the mean tumor size in our review was 2.9 × 2.5 × 1.5 cm, consistent with existing literature indicating an average size of less than 3 cm.

The largest lesion was reported by Yuri et al., measuring 15 × 4 cm and located in the upper forehead, extending posteriorly to the anterior hairline. The patient, a 24-year-old woman, presented with a painless swelling that had been present for six months. The lesion was treated with excisional biopsy, and no recurrence was observed at the 12-month follow-up (21). Conversely, Corominas et al. described a particularly small case of CAF in a 4-year-old child, presenting with a firm, indolent, and poorly circumscribed mass in the palm of the left hand (6).

Histologically, CAF is characterized by a fibrous proliferation that extends into the surrounding tissues through multiple infiltrative processes, with centrally located foci of calcification and cartilage formation. Cellularity is variable and consists predominantly of plump fibroblasts with round or ovoid nuclei and indistinct cytoplasmic borders, embedded within a densely collagenous stroma and typically arranged in a fascicular pattern, particularly around areas of calcification.

Epithelioid mesenchymal cells are also commonly observed near chondroid foci (13). Nuclear atypia is absent, although occasional mitotic figures may be seen. Some authors have proposed a biphasic developmental pattern, consisting of an initial phase and a late phase (22). The initial phase, more commonly observed in younger patients, is characterized by diffuse tumor growth without prominent calcifications. In contrast, the late phase presents a more compact and nodular architecture, with more conspicuous calcification and cartilage formation. Immunohistochemically, tumor cells typically express smooth muscle actin (SMA) but not desmin, consistent with a myofibroblastic phenotype (22). In a review by Fetsch et al., all examined lesions (6 out of 6) demonstrated strong and diffuse positivity for vimentin. Additionally, three of the six cases showed positivity for CD99, which was also expressed in all five cases examined separately. CD99 expression was most evident in spindle cells and was also detected focally in epithelioid fibroblasts and a small number of chondrocytes. S100 protein (5 out of 6) and CD68 (5 out of 5) were expressed in the majority of cases. All tumors were negative for desmin and cytokeratins (10).

Diagnosis should be guided by clinical and radiological features but must always be confirmed histologically. Radiographically, CAF typically appears as a soft tissue mass without associated osseous lesions, often exhibiting fine stippling due to focal calcification. In some cases, cortical scalloping and bone thickening have been observed (19). Sonography can aid in detecting calcifications and excluding cystic lesions, while CT is useful for confirming calcified areas and their relation to adjacent bone structures. However, MRI is considered the most informative imaging modality for both diagnosis and preoperative planning. On MRI, CAF typically presents as an ill-defined subcutaneous mass with intermediate-to-low signal intensity on T1-weighted images and heterogeneous high signal intensity on T2-weighted sequences. Prominent globular areas of low signal intensity, corresponding to calcifications, may be present on all MRI sequences. Post-contrast images usually demonstrate intense heterogeneous enhancement following intravenous gadolinium administration (17).

Histological confirmation prior to surgery is essential. While primary wide excision may be acceptable for small lesions, larger tumors should only be resected after biopsy confirmation. CAF must be differentiated from other benign fibromatoses of infancy and childhood, including Giant Cell Tumor of the Tendon Sheath (GCTTS), Fibrous Hamartoma of Infancy (FHI), Infantile Digital Fibromatosis (IDF), infantile myofibromatosis, desmoid-type fibromatosis, and Hyaline Fibromatosis (HF).

GCTTS is the most common lesion affecting the fingers and toes. It is rare in children and typically lacks calcifications. Nonetheless, GCTTS and CAF share several clinical features, such as infiltrative growth, adherence to tendon sheaths, and a predilection for distal extremities. On MRI, GCTTS typically exhibits heterogeneous signal due to areas of low intensity on both T1- and T2-weighted images, and enhances after gadolinium administration (14, 18). Although these features overlap with those of CAF, MRI can aid in differentiating the two. CAF often displays speckled calcifications, ill-defined margins, and heterogeneous enhancement, whereas GCTTS usually presents with lobulated, well-defined margins, close association with the tendon sheath, and uniform enhancement (18). Two additional characteristics of GCTTS not commonly observed in CAF include its tendency to invade surrounding bone and, occasionally, to envelop it. In contrast, CAF may displace adjacent bone due to its slow, expansive growth (20).

IDF is a rare fibrous tumor affecting the fingers and toes of children. It is typically superficial, infiltrative, and prone to recurrence (9). Differences in age of onset and site predilection are useful for differential diagnosis: IDF usually presents within the first year of life and often involves the dorsal and lateral aspects of the distal and middle phalanges, while CAF more commonly affects the palms and soles (9).

FHI generally presents as a solitary, small, subcutaneous mass, most commonly in the axilla or upper arm. It is usually diagnosed within the first two years of life (9). MRI features helpful in distinguishing FHI from CAF include a lobular architecture with internal septa and areas showing fat-equivalent signal intensity (2, 7).

HF is a rare autosomal recessive disorder characterized by papulonodular skin lesions, typically ranging from 1 mm to 5 cm in size, and commonly affecting the nose, ears, scalp, back, and knees (2, 9). Although Kwak et al. reported that MRI does not reliably distinguish HF from CAF (15), clinical presentation and distribution may aid in differential diagnosis.

Malignant transformation of CAF is extremely rare. One case describes a 3-year-old girl with a CAF of the palm, resected with incomplete margins, who later developed disseminated fibrosarcoma. At age 9, a large mass occupying most of the right lung was identified, accompanied by multiple skeletal lesions. Histopathological analysis concluded that the metastatic disease originated from the previously resected tumor of the left hand (16). However, given the absence of additional cases, a misdiagnosis of fibrosarcoma at the initial presentation cannot be excluded, as CAF is generally considered a benign entity.

Surgical excision has been recommended and documented in nearly all reported cases. However, the extent of excision, whether conservative or radical, is inconsistently described, and opinions among authors remain divided. Some advocate for a conservative approach, even in cases of incomplete resection or local recurrence, citing the tumor's typically benign course and tendency to mature into a more nodular and less aggressive form over time (1, 13). Others caution against radical surgery unless functionally and cosmetically acceptable outcomes can be achieved. Wide excision should be considered when the expected postoperative morbidity is minimal.

In other cases, marginal excision combined with careful follow-up may be preferable.

An illustrative case reported by the American Society for Surgery of the Hand involved an aggressive, recurrent CAF of the thumb in an adult male. Due to extensive involvement of soft tissue and bone, amputation was necessary to achieve complete excision. Reconstruction with a trimmed great toe-to-thumb transfer yielded satisfactory functional and aesthetic results (11).

In our review of 47 studies with available follow-up data, the overall recurrence rate was approximately 29.4% (20 out of 68 patients), notably lower than the 50% recurrence rate previously reported in the literature. Recurrence was significantly more common after intralesional excision (71.4%) compared to wide marginal excision (25.8%).

Clinical recommendations summary: Based on our systematic review, CAF should be managed with tailored surgical treatment. Wide marginal excision is associated with a significantly lower recurrence rate (25.8%) compared to intralesional excision 71.4%). Therefore, wide excision is recommended whenever feasible without functional compromise. In cases where radical resection might lead to significant morbidity, a conservative approach with close follow-up is acceptable, especially considering the benign nature of the tumor. Preoperative biopsy remains crucial to confirm the diagnosis and plan the appropriate surgical strategy.

CONCLUSIONS

CAF is a rare, benign, soft tissue tumor that can present with various clinical patterns and may occur in several uncommon sites. It is important to make an accurate diagnosis through the use of the clinic and the imaging, in order to avoid misdiagnosis. The treatment is based on a meticulous excision in order to reduce recurrences. ■

References

1. Allen PW, Enzinger FM. Juvenile aponeurotic fibroma. Cancer. 1970;26:857–867.
2. Arioni C, Bellini C, Oddone M, Risso FM, Scopesi F, Nozza P, Serra G, Tomà P. Congenital fibrous hamartoma of the knee. Pediatr Radiol. 2006;36:453–455.
3. Arora S, Sabat D, Arora SK, Kumar V, Saran RK. Giant intramuscular calcifying aponeurotic fibroma of gluteus maximus: case report. Ann Trop Paediatr. 2010;30:259–263.
4. Carroll RE. Juvenile aponeurotic fibroma. Hand Clin. 1987;3:219–224.
5. Chaltsev BD, Vasilyev VI, Pavlovskaya AI, Palshina SG, Nikonorova NO. Multiple calcifying aponeurotic fibroma: case report and review of the literature. Ter Arkh. 2018;90:91–95.
6. Corominas L, Sanpera I Jr, Sanpera-Iglesias J, Ramos-Ansesio RF. Calcifying aponeurotic fibroma in children: our experience and a literature review. J Pediatr Orthop B. 2017;26:560–564.
7. Dickey GE, Sotelo-Avila C. Fibrous hamartoma of infancy: current review. Pediatr Dev Pathol. 1999;2:236–243.
8. Enzinger FM, Weiss SW. Calcifying aponeurotic fibroma in soft tissue tumors. In: Enzinger FM, Weiss SW (eds). Enzinger and Weiss's soft tissue tumors. 2nd ed. Mosby, St. Louis, 1988, pp. 190–195.
9. Enzinger FM, Weiss SW. Fibrous tumors of infancy and childhood. In: Enzinger FM, Weiss SW (eds). Enzinger and Weiss's soft tissue tumors. 3rd ed. Mosby, St. Louis, 1995, pp 231–268.
10. Fetsch JF, Miettinen M. Calcifying aponeurotic fibroma: a clinicopathologic study of 22 cases arising in uncommon sites. Hum Pathol. 1998;29:1504–1510.
11. Giuffre JL, Kovachevich R, Bishop AT, Shin AY. Recurrent calcifying aponeurotic fibroma of the thumb: case report. J Hand Surg Am. 2011;36:110–115.
12. Goldman RL. The cartilage analogue of fibromatosis (aponeurotic fibroma). Further observations based on 7 new cases. Cancer. 1970;26:1325–1331.
13. Keasbey LE. Juvenile aponeurotic fibroma (calcifying fibroma); A distinctive tumor arising in the palms and soles of young children. Cancer, 1953;6:338–346.
14. Kitagawa Y, Ito H, Amano Y, Sawaizumi T, Takeuchi T. MR imaging for preoperative diagnosis and assessment of local tumor extent on localized giant cell tumor of tendon sheath. Skeletal Radiol. 2003;32:633–638.
15. Kwak HS, Lee SY, Kim JR, Lee KB. MR imaging of calcifying aponeurotic fibroma of the thigh. Pediatr Radiol. 2004;34:43-–440.
16. Lafferty KA, Nelson EL, Demuth RJ, Miller SH, Harrison MW. Juvenile aponeurotic fibroma with disseminated fibrosarcoma. J Hand Surg Am. 1986;11:737–740.
17. Morii T, Yoshiyama A, Morioka H, Anazawa U, Mochizuki K, Yabe H. Clinical significance of magnetic resonance imaging in the preoperative differential diagnosis of calcifying aponeurotic fibroma. J Orthop Sci. 2008;13:180–186.
18. Parker WL, Beckenbaugh RR, Amrami KK. Calcifying aponeurotic fibroma of the hand: radiologic differentiation from giant cell tumors of the tendon sheath. J Hand Surg Am. 2006;31:1024–1028.
19. Robbin MR, Murphey MD, Temple HT, Kransdorf MJ, Choi JJ. Imaging of musculoskeletal fibromatosis. Radiographics. 2001;21:585–600.
20. Tai LH, Johnston JO, Klein HZ, Rowland J, Sudilovsky D. Calcifying aponeurotic fibroma features seen on fine-needle aspiration biopsy: case report and brief review of the literature. Diagn Cytopathol. 2001;24:336–339.
21. Thakur JS, Diwana VK, Sharma S, Thakur A. Calcifying (juvenile) aponeurotic fibroma of the scalp. Ear Nose Throat J. 2011;90:E14–16.
22. Weiss SW, Goldblum JR. Calcifying aponeurotic fibroma. In: Weiss SW, Goldblum JR (eds). Enzinger and Weiss's soft tissue tumors. 4th ed. Mosby, St. Louis, 2001, pp 388–395.