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# Calcifying Fibrous Tumor

Review of 157 Patients Reported in International Literature

Angeliki Chorti, Theodossis S. Papavramidis, and Antonios Michalopoulos

**Abstract:** Calcifying fibrous tumor (CFT) is a benign lesion characterized by its specific histological findings and is found as solitary or multiple lesions in several locations of the human body. The aim of the present systematic review is to give a detailed account of all reported cases of CFT in the literature and to analyze the available data, to completely characterize the entity from epidemiological, medical, and surgical aspects.

A bibliographic research was performed from 1988 until 2015. A database with the patients' characteristics was made, including sex, age, location of the tumor, symptoms, symptoms duration, size of the tumor, diagnostic methods, treatment, metastasis, and follow-up.

A total of 104 articles were identified, reporting 157 cases of CFT. Mean age of patients was 33.58 years and the ratio between men and women was 1:1.27. The most common locations of CFT were stomach (18%), small intestine (8.7%), pleura (9.9%), mesentery (5%), and peritoneum (6.8%). Mean diameter of the tumor was estimated 4.6 cm. The correlations proceeded showed that as age increases, size decreases (P = 0.001) and that the tumor is larger in females (P = 0.027). Kruskal-Wallis test showed that the larger tumors appear in the neck and adrenal gland (P = 0.001). The percentage of asymptomatic patients was 30.57%. Computed tomography and biopsy were the most common tests for the diagnosis of CFT. Open surgical procedure was performed in the majority of cases. The median hospitalization was 6.06 days and the mean follow-up period was 29.97 months. Recurrences were mentioned in 10 of 96 patients with available data. No deaths owing to CFT were mentioned in the literature.

CFT should be included in the differential diagnosis of enlarging mass revealed by clinical or imaging examination either incidentally or after specific acute or chronic symptomatology.

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**Abbreviations**: AE1/AE3 = cytokeratin, ALK-1 = anaplastic lymphoma kinase-1, CFT = calcifying fibrous tumor, CT = computed tomography, EMA = epithelial membrane antigen, GIST = gastrointestinal stromal tumor, IMT = inflammatory myofibroblastic tumor, MOC = myositis ossificans circumscripta, MRI = magnetic resonance imaging, MSA = muscle-specific actin, SFT = solitary fibrous tumor, SMA = smooth muscle actin.

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# INTRODUCTION

C alcifying fibrous tumor (CFT) is a rare benign lesion that is composed of abundant dense well-circumscribed hyalinized collagen with lymphoplasmatic infiltrate, spindle cells, lymphoid aggregates, and psammomatous or dystrophic calcifications. This tumor was first described in the deep soft tissue in children by Rosenthal and Abdul-Karim,<sup>1</sup> but subsequent reports revealed the occurrence of this lesion also in adults.<sup>2–8</sup> Common sites that CFT arises from are pleura, abdominal cavity, mediastinum, heart, lung, neck, mandible, oral, inguinal, paratesticular, intrascrotal, spine, back, arm, and thigh. The etiology and pathogenesis of the tumor are controversial.

The aim of the present systematic review is to give a detailed account of all reported cases of CFT in the literature and to analyze the available data, to completely characterize the entity from epidemiological, medical, and surgical aspects.

#### METHODS

A bibliographic research was performed using PubMed, Scopus, and Embase. The search terms employed were "calcifying fibrous tumor" and "calcifying fibrous pseudotumor." Since 1988, when the first description of CFT was made, until 2015, 104 articles were found in total (Figure 1). Among these, we spotted 157 well-documented cases of CFT. Ninety-nine articles were in English, 3 articles were in French, and 1 article was in Chinese. These articles were carefully studied and a database with the patients' characteristics was made. The database included sex, age, location of the tumor, symptoms, symptoms duration, size of the tumor, diagnostic methods, treatment, metastasis, and follow-up. The cases that fulfilled at least 8 of these 10 criteria have been included in the statistical analysis. Table 1 displays the number of cases presenting the criteria. An ethical approval is not required because this study is a review of the existing international literature.

To express results, descriptive statistics were used appropriately. Means, medians, and standard deviations were used for continuous variables and frequencies for categorical variables. Spearman test has been calculated for the correlation between size and age. Independent samples *t* test has been calculated for the distribution of age among males and females. We compared the size of the tumor of male versus female subjects, using Mann–Whitney *U* test. Mann–Whitney *U* test was also calculated for the distribution of size across categories of symptoms duration. As far as size and localization of CFT are concerned, Kruskall–Wallis test has been calculated for this correlation. In this test, locations of the tumor with a frequency <5 cases have been excepted, so that the statistical error is minimized. Statistical significant levels were those with P < 0.05.<sup>9</sup> The statistical analysis was performed in SPSS version 23 (SPSS Inc, Chicago, IL).

## RESULTS

Characteristics of CFTs were determined concerning sex, age, localization, size of the tumor, symptoms duration,

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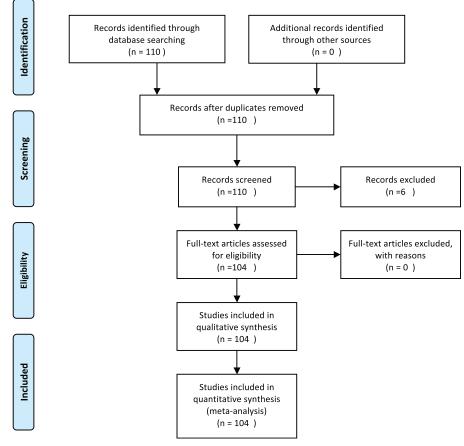


FIGURE 1. Flow Diagram according to PRISMA Statement 2009.

diagnostic methods, histopathological and immunohistochemical examination, treatment, follow-up, recurrences, and metastasis.

Concerning sex, 43.94% of the patients were male (69 patients), whereas 56.05% were female (88 patients).

TABLE 1. Cases of	of Calcifying	Fibrous Tumor	Fulfilling Criteria
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Criteria	Number of Cases	%
Sex	157	100
Age	157	100
Localization*	161	100
Size	140	89.17
Symptoms duration	135	85.98
Diagnostic tests	146	92.99
Histopathological and immunohistochemical examinations	115	73.24
Treatment	134	85.35
Hospitalization	16	10.19
Follow-up	90	57.32

\*Considering the multiple lesions in some cases.

The ratio between men and women was 1:1.27, suggesting a female predominance in the reported CFT population.

The age distribution is shown in Figure 2, from which it is concluded that CFT most frequently appeared in age ranges from 0 to 4, 25 to 29, and 30 to 34 years. Mean age of the 157 patients (100%) was 33.58 years, ranging from 5 weeks to 84 years. We compared the distribution of age among male and female patients and we found that the age at which tumor appeared does not differ statistically between males and females ( $35.11 \pm 21.52$  and  $31.93 \pm 18.76$  years respectively, P = 0.321).

As far as the localization of the tumor is concerned, CFT can be found as solitary or multiple lesions. In our database, 9 of 157 patients (5.73%) had multiple lesions, which means that the total amount of cases calculated in the location section was 161. The most common locations of CFT are stomach (29 patients, 18%), small intestine (14 patients, 8.7%), pleura (16 patients, 9.9%), neck (10 patients, 6.2%), mesentery (8 patients, 5%), mediastinum (8 patients, 5%), and peritoneum (11 patients, 6.8%). Frequent sites that this tumor arises from are omentum (4 patients, 2.5%), thigh (5 patients, 3.1%), adrenal gland (5 patients, 3.1%), back (5 patients, 3.1%), lung (3 patients, 1.9%), and pericardium (3 patients, 1.9%), whereas rare locations are mandible (2 patients, 1.2%), spleen (2 patients, 1.2%), liver (2 patients, 1.2%), axilla (2 patients, 1.2%), rectum (2 patients, 1.2%), abdomen (2 patients, 1.2%), abdominal wall (2 patients, 1.2%), forearm (2 patients, 1.2%), lower leg

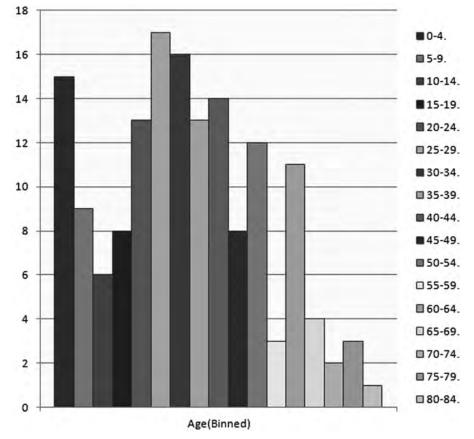


FIGURE 2. Age (Binned).

(2 patients, 1.2%), intrascrotal (2 patients, 1.2%), and colon (2 patients, 1.2%). There are also cases reported in the literature, in which CFT occurred at some sites only once such as esophagus, spine, heart, retroperitoneal, breast, gallbladder, subscapular, upper arm, spermatic cord, mesocolon, tongue, oral, shoulder/ wrist, paratesticular, lower leg, groin, fallopian tube, and nuchal. Figure 3 displays the localization of CFTs.

Furthermore, 140 of 157 cases (89.17%) provided information about the size of the tumor. Mean diameter of the tumor was estimated 4.6 cm, ranging from 0.1 to 25 cm. Figure 4 displays graphically the tumors' size. The statistical analysis showed a statistically significant correlation between size and age (P = 0.001, r = -0.285). As seen in Figure 5, the association between these 2 variables is negative; as age increases, size decreases. The comparison of the size of the tumor of male and female subjects proved that the tumor is larger in females (U = 1875.5, P = 0.027). Figure 6 shows the distribution of size across males and females. Moreover, the distribution of size across categories of symptoms' duration has been proved to be the same (P = 0.485). As far as the localization of CFT is concerned, Kruskall-Wallis test has proved that the larger tumors appear in neck and adrenal gland, as shown in Figure 7 (P = 0.001).

Symptomatology of the tumor could not be evaluated because of heterogeneity of the localization of CFT. However, we distinguished symptomatic from asymptomatic (48 patients, 30.57%) cases. The symptoms are characterized as nonspecific, including lack of appetite, fever, weight loss, fatigue, progressive weakness, chest or back pain, fever, dyspnea, shortness of breath or ecchymosis, and erythema, and as specific ones, referring to each organ system. The symptoms' duration was estimated and separated into 2 main categories: acute and chronic. Among 135 (85.98%) cases with data on this section, 24 (17.77%) patients presented with acute symptoms and 111 (82.22%) had chronic symptomatology.

As far as the diagnostic tests required for the diagnosis of CFT are concerned, computed tomography (CT), laboratory test, and biopsy seemed to be the most common ways to diagnose CFT or to exclude other similar conditions. Data were available for 146 (92.99%) patients, from whom 63 (43.15%) got a CT scan, 35 (23.97%) laboratory test, and 44 (30.13%) underwent a biopsy. Helpful imaging examinations proved to be echo (28 patients, 19.17%), endoscopy (31 patients, 21.23%), magnetic resonance imaging (MRI) (25 patients, 17.12%), and radiographs (25 patients, 17.12%) according to the localization of the tumor. All preoperative imaging tests revealed the tumor, its size, and localization, but the final diagnosis was made with the histopathological examination.

For the histopathological and immunohistochemical examination of CFT, among 115 (73.24%) cases with available data, only 9 (7.82%) had positive lymph nodes. Calcifications-psammoma bodies, inflammatory cells, and dense hyalinized collagen were found at a rate of 100%, as expected by definition. Various markers are used to characterize CFTs. Figure 8 shows the distribution of positive and negative expression of immunohistochemical markers.

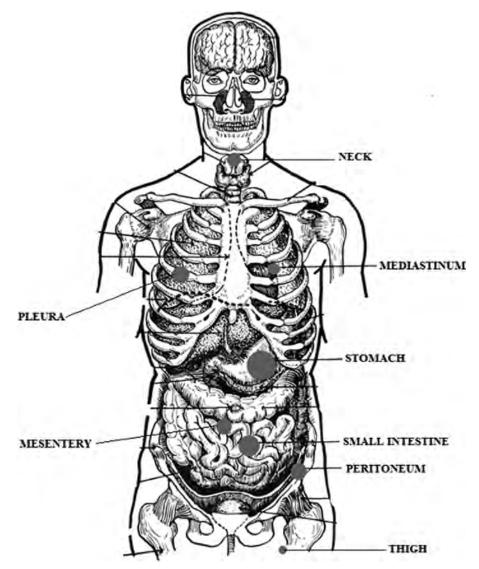


FIGURE 3. Schematic localization of most frequent sites of calcifying fibrous tumors. The diameter of the dot is proportional to the frequency of appearance.

Surgical excision is the main treatment for patients with CFT. In our database, open surgical procedure and endoscopic procedure are used for the excision of the tumor. Open surgical excision was performed in 116 of 134 (86.56%) cases with information provided, whereas the endoscopic one was performed in 18 (13.43%) cases.

Duration of hospitalization was provided only for 16 cases (10.19%), giving this analysis low credibility. However, the median hospitalization was 6.06 days, ranging from 1 to 18 days, depending on the location of the tumor.

Follow-up period was mentioned for 90 (57.32%) patients. The mean period was 29.97 months, ranging from 1 to 228 months. It was <60 months for 80 (88.88%), 60 to 120 months for 5 (5.55%), and >120 months for 5 (5.55%) patients. During the follow-up period, recurrence of the tumor was developed in 10 patients. Eight patients (8.33%) had 1 recurrence and 2 patients (2.08%) had 2 recurrences. Special note has to be made to 1 patient that had 1 possible recurrence that has not been confirmed because of discontinuance of follow-up.<sup>10</sup> Only

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1 patient with tumor recurrence had also positive lymph nodes detected in operation, but there are not so much data as needed to establish a correlation between recurrences and positive lymph nodes or inappropriate surgical technique.

No deaths owing to CFT were reported in the literature and as a result long-term survival was estimated at a rate of 100%.

# DISCUSSION

#### History

CFTs are rare, benign lesions, which show a predilection for soft tissue. They are characterized by the presence of hypocellular, densely hyalinized collagen with psammomatous or dystrophic calcification and mononuclear inflammatory infiltrate. They were first described in 1988 by Rosenthal and Abdul Karim<sup>1</sup> as a "childhood fibrous tumor with psammoma bodies" in 2- and 11-year-old girls in peripheral axial soft tissue. Fetch et al<sup>2</sup> reported 10 cases of a distinctive benign fibrous lesion and first used the term "calcifying fibrous

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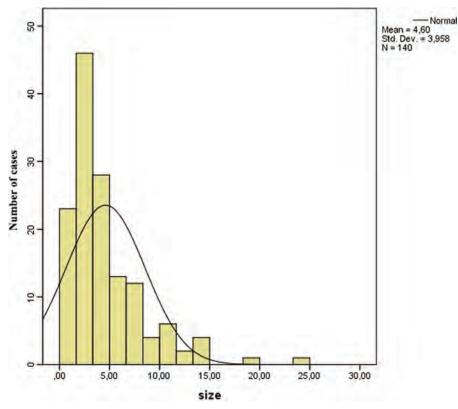
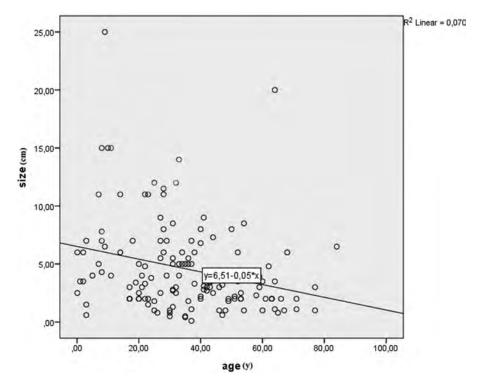


FIGURE 4. Distribution of diameter of calcifying fibrous tumor.



**FIGURE 5.** Correlation between size and age (P = 0.001, r = -0.285).

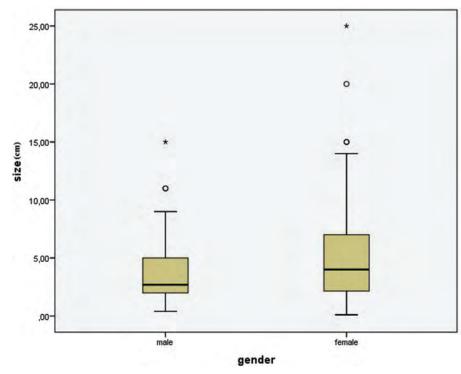


FIGURE 6. Box-plot demonstrating the size distribution among males and females (P = 0.027).

pseudotumor." "Pseudotumor" was used to reflect the belief that the underlying process was most likely inflammatory.<sup>2</sup> However, Nascimento et al<sup>11</sup> suggested a true neoplasm with a tendency for local recurrence. The World Health Organization (WHO) established the name for this lesion in 2002 as "Calcifying Fibrous Tumors" in the newly published classification of tumors of soft tissue and bone.<sup>12</sup> Furthermore, WHO classified the pseudotumor as a tumor of the soft tissue in 1999.<sup>13</sup> In

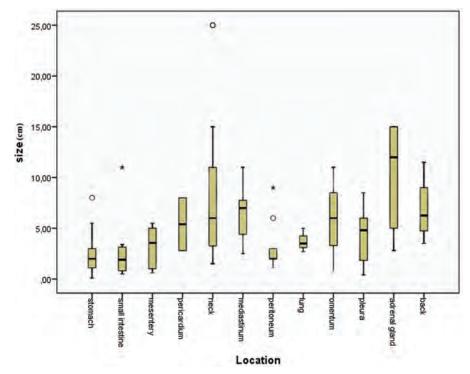


FIGURE 7. Box-plot demonstrating the size distribution among calcifying fibrous tumor locations (P=0.001).

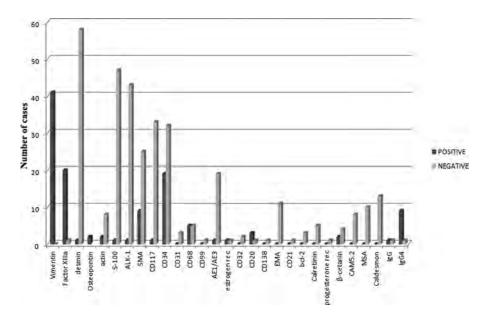


FIGURE 8. Distribution of expression of immunohistochemical markers.

addition, CFT of the pleura is included in the neoplasms of the pleura by Hammar et al in 2008.<sup>14</sup>

Many scientists tried to sum up CFTs in large series. The first attempt was made by Jeong et al<sup>4</sup> in 1996 who summarized 16 cases. Some years later, Hoffman et al<sup>15</sup> reviewed 20 patients between 1988 and 1997, whereas Ben Izhak et al<sup>16</sup> calculated 7 cases of CFTs in the abdominal cavity. Moreover, Elpek et al<sup>17</sup> mentioned 34 cases of intra-abdominal CFTs that were referred in the literature until then. As far as CFT of the pleura is concerned, Shibata et al<sup>18</sup> mentioned only 6 cases, and Ishida et al<sup>19</sup> compiled only 7 cases of the tumor in this specific location. Last but not least, Im et al<sup>20</sup> found 6 cases of intestinal CFT between 2008 and 2014. Searching carefully the English literature from 1993 to 2015, we found a total of 157 well-documented cases.

# **Epidemiology and Pathogenesis**

Calcifying fibrous tumor seems to have a female predilection (ratio 1:1.27). Age distribution seems to be trimodal with one pick at 0 to 4 years, a second one in the mid-20s, and a third one in the mid-30s. This trimodal distribution may reflect different pathogenesis in the 3 different groups. Concerning the third spike (around thirties), there are many indications that CFT results as a late sclerosing stage of myofibroblastic tumor.<sup>5,21–23</sup> Trauma may also be the basis of pathogenesis of this second spike.<sup>8,24</sup> Concerning the early first spike, one can blame genetic and/or embryologic factors for CFT. Notably, Fukunaga et al<sup>7</sup> found a diploid DNA content into CFT. Moreover, one cannot exclude embryonic ectopic remnants leading in the early years of life to CFTs.

CFTs are located in several organ systems, but mainly in the gastrointestinal track. Considering that the lumen of the gastrointestinal tract is actually external environment, the traumatic etiopathology of CFTs seems realistic. In those cases, the trauma results possibly by aggressive factors included "by accident" in food.

The frequency of the abdominal CFT was estimated to be 1 case per year worldwide based on histopathological archives, but a frequency for CFT as a whole does not exist yet. One retrospective study by Ogasawara et al<sup>25</sup> has suggested that the incidence of gastric submucosal lesions is 0.36%, whereas Agaimy et al<sup>26</sup> confirmed this suggested rarity of CFT of gastrointestinal track. Most lesions are generally solitary, but multiple CFTs are also described in the literature.<sup>5,21,27–29</sup> In 9 cases, there were multiple foci of CFTs.

## **Clinical Features**

The majority of the cases are asymptomatic and the tumor has been found incidentally on a routine imaging examination. When symptomatology is present, the clinical features of CFT are variable and could be categorized into 2 groups: acute or chronic findings. As a chronic condition, it can be seen as a visible, enlarging painless mass or as a facial growth, as far as the extremities are concerned.<sup>1,7,30-36</sup> In a case report, the patient complained about a foreign body sensation in throat, whereas in another case of CFT of the spine, the patient noticed a flank pain in spine with worsening intensity.<sup>37,38</sup> In the thoracic cavity, CFT may cause chest or back pain, fever, dyspnea, systolic heart murmur, shortness of breath or ecchy-mosis, and erythema.<sup>3,6,18,39-49</sup> Intrabdominal CFTs present with a great variety of symptoms, both general and more specific.<sup>10,11,16,20,21,23,27,44,50–75</sup> Lack of appetite, fever, weight loss, fatigue, and progressive weakness are examples of general symptoms. More specific ones are dyspepsia, flatulence, halitosis, nausea, vomiting, red blood per rectum, and altered bowel habits. The predominant symptom of intrabdominal CFT is pain. It is characterized as dull, intermittent, progressive, acute, sharp, crampy or not, episodic, local, radiating or not, notrelated with the intake of food or epigastric pain after eating with early satiety. Moreover, 7 cases of gastric CFT with an ulcer on its surface have been reported.  $^{26,53,65,73,76-78}$  As an acute condition, it usually causes acute peritonitis or there are several case reports that state CFT in the intestine causes intussusception.  $^{8,23,54,79}$ 

# **Differential Diagnosis**

The differential diagnosis of CFT depends on its localization. The major diagnostic problem is to determine the

character of the tumor, which means that it is difficult to distinguish malignant from benign tumors in the preoperative stage. As far as the neck, the pleura, and the thoracic cavity are concerned, the differential diagnosis includes fibromatosis, solitary fibrous tumor (SFT), calcified granulomas, calcified pleural plaques, chronic fibrous pleuritis, intrapulmonary tumors, inflammatory myofibroblastic tumor (IMT), intermediate fibrous histiocytoma, rare dendrocytoma, desmoplastic mesothelioma, and amyloid tumor.<sup>4,13,15,28,42,80-85</sup> Kawahara et al<sup>86</sup> mentioned another tumor that should be taken in consideration in differential diagnosis: the monophasic synovial sarcoma. This type of tumor consists of spindle cells in dense cellular sheets or vague fascicles; hyalinization and calcifications can occasionally be seen and the cells are positive for cytokeratin and epithelial membrane antigen (EMA), which distinguish this tumor from CFT. Calcified granulomas contain residual histiocytes and multinuclear giant cells, whereas calcified pleural plaques and chronic fibrous pleuritis are characterized by diffuse pleural thickening. The cells in chronic fibrous pleuritis are more adjacent to the pleura and the capillaries are vertically aligned. Rare dendrocytoma stains for XIIIa factor consists of dermal dendrocytes and is characterized by a "donation." Intrapulmonary tumors are most commonly childhood lung tumors and there is no specific method (laboratory check or imaging) in order that these tumors are distinguished from CFT. Malignant mesothelioma has got sarcomatous areas and a weak positive staining for osteopontin, but is strongly positive for cytokeratin.

Leiomyoma, desmoid fibromatosis, calcifying aponeurotic fibroma, and myositis ossificans circumscripta (MOC) must be considered in the differential diagnosis of tumors in the musculoskeletal system.<sup>31,39</sup> MOC can be distinguished from CFT only by MRI or scintigraphy. Leiomyoma has undergone degenerative changes, has calcifications and ossifications, and its cells are positive or smooth muscle actin (SMA), desmin, caldesmon, and XIIIa factor.<sup>17</sup> Calcifying aponeurotic fibroma belongs to the same category of tumors as CFT, but occurs typically in hand and feet, it is less circumscribed, and has metaplastic cartilage and multinuclear giant cells. Desmoid fibromatosis is a locally aggressive fibrogenic neoplasm, characterized by lack of psammoma bodies and by the positive expression of  $\beta$ -catanin.

Mangat et al<sup>43</sup> mentioned 2 diseases that must be considered in the diagnosis of CFT of the breast. The first one is the idiopathic benign calcifications, which follow different patterns of calcium layering, and the second one refers to the diabetes mastopathy, caused by type I diabetes mellitus and characterized by a palpable mass with sclerosing lymphocytic lobulitis and no calcifications, which has mammographically increased density, and in the ultrasound scan has different acoustic shadowing.

As far as adrenal gland is concerned, Lau et al<sup>55</sup> have included IMT, SFT, and peripheral nerve sheath tumors such as schwannoma and neurofibroma into the differential diagnosis of CFT of this anatomical site.

The principle consideration in differential diagnosis of intrabdominal CFT is gastrointestinal tumors (GISTs).<sup>20,51,54,71,81,87–89</sup> GIST is much more cellular than CFT and does not consist of hyalinized collagen and calcifications and is not characterized by chronic inflammation. The mesenteric one has got a malignant behavior. GISTs are described as solid masses in CT scan.<sup>90</sup> The cells of GIST are strongly positive for CD117 and CD34 and there are also some references in which it is mentioned that GIST is also

positive for platelet-derived growth factor receptor.<sup>16,54</sup> Other tumors that must be included in the differential diagnosis of intrabdominal CFT are solitary fibrous tumors, IMTs, carcinoid tumors, lipomas, reactive nodular fibrous tumors, leiomyoma, schwannoma, inflammatory fibrous polyps (IFPs), desmoid-type fibromatosis, retroperitoneal fibrosis, associated fibrous-inflammatory screlotizing infiltrations, calcifying aponeurotic fibroma, neuroendocrine tumors, myomas, cystic lesions, neurofibromas, small bowel desmoids, plexiform fibromyxoma, mesenteric fibromatosis, sclerosing mesenteritis, and adrenal neuroblastoma.91-97 Furthermore, heterotopic pancreas and enlarged lymph nodes should also be included.<sup>16,17,20,25,51,54,69,71,81,98</sup> Plexiform fibromyxoma, mentioned by Jang et al,<sup>81</sup> is larger (>5 cm) than CFT, is commonly a tumor of the antrum with capillary network, fibromyxoid stroma, hypercellularity, and positive staining for SMA. Sclerosing mesenteritis is characterized by inflammatory tissue and fat necrosis, which distinguish it from CFT. Mesenteric fibromatosis can infiltrate growth patterns and as far as desmoid type fibromatosis Im et al<sup>20</sup> reported that except for the other above mentioned characteristics, it has also a negative staining for XIIIa factor and Farah et al<sup>69</sup> added that it has also not got inflammatory aggregates, calcifications and has got thin-walled vessels. Schwannoma has peritumoral and intratumoral lymphoid, which is a common characteristic with CFT, but this one has no schwannoma tissue and a negative expression for S-100. Reactive nodular fibrous pseudotumor is characterized by overlying inflammatory process, such as an ulcer, a diverticula, a strangulated hernia, or a fistula, by the infiltration of small bowel, lack of calcifications, and by the positive staining for vimentin and cytokeratin. Amyloid tumors have got a giant cell response. IFPs consist of whorl-like arrangement of spindle cells around blood vessels and glands, eosinophilic infiltration, and CD34-positive staining. Solitary fibrous tumor has got hypercellular areas, patternless arrangement of spindle cells, and is positive for CD34, CD99, and bcl-2. In the case of gallbladder CFT, stromal tumors, IMT, and SFT must be considered.<sup>71</sup> In the case of spleen CFT, hamartoma, littoral cell angioma, inflammatory pseudotumor, and follicular dendritic cell tumor must be included in the differential diagnosis.<sup>52</sup> Littoral cell angioma is characterized by positive staining for XIIIa factor, CD31, CD34, CD68, KP-1, CD8, whereas follicular dendritic cell tumor is positive for CD21, CD35, and S-100. Hamartoma is an overgrowth of structures of red pulp of the spleen and is positive only for CD8, which is a pathognomonic sign of this tumor.

Nevertheless, the main consideration on the differential diagnosis of CFT is IMTs.<sup>11,15,20,25,28,51,54,55,70,71,79,81,89,99–102</sup> IMTs tend to affect younger patients than CFT, they have symptoms and signs such as fever, pain, weight loss, malaise, anemia, thrombocytosis, increased sedimentation rate, and hypergammaglobulinemia, and can have multiple lesions, in contrast with CFT that can be asymptomatic and is rarely multifocal. Coffin et al,<sup>100</sup> on the basis of 84 IMTs, found 3 basic histological patterns, in which there are similarities with CFT but in IMTs include acute inflammatory cells, plasma cells, lymphocytes, inflammatory infiltrate and proliferation leading to granulation tissue and fibromatosis.<sup>5,11,99</sup> Immuno-histochemically, IMT is strongly positive for SMA, actin, desmin, and anaplastic lymphoma kinase (ALK-1). The last one is a pathgnomonic sign of IMT. In addition to this, it has a focal staining for XIIIa factor. IMT may recur locally, but it rarely metastizes.<sup>11</sup> Its prognostic significance is unclear, but it can progress and lead to death.<sup>99</sup>

# Diagnosis

The diagnosis of CFT is based on the imaging findings and the pathological findings (histological appearance and immunohistochemical studies) owing to heterogeneity of symptoms. A variety of imaging techniques can be used to examine CFT. The radiographic appearance of CFT reflects its histological composition. Plain radiograph provides with the basic information needed to determine the exact anatomical site of the tumor.<sup>31</sup> In a conventional radiograph, calcifications could also not be seen. Ultrasonographically, tumors are well-circumscribed masses with various echogenicity because of scattered calcifications. Furthermore, acoustic shadowing may also be noticed.<sup>31,38,103</sup> CT scan is much more sensitive at detecting early mineralization.<sup>104</sup> Calcifications demarcate the tumor from the surrounding tissue. The histological composition and the calcium layering create the pattern on CT scan. In the literature, there are variable descriptions of this pattern. Typical examples are "irregular," "scattered," "punctate," "Thick and Band-like," "clustered," "amorphous." Contrastenhanced CT can also be used to achieve a better imaging result. Fan et al<sup>65</sup> mentioned that CFT on a CT scan may be a round hyper- or hypodense mass. MRI has similar findings with CFT, but could also provide additional and important anatomical information about the tumor. CFT is a hypointense signal ass on T1-weighted and T2-weighted MRI and an isointense signal in gadolinium T1-weighted imaging.<sup>17,56,57,59,68,105</sup> In the literature, it is also referred that on 3-dimensional reconstruction, CFT can be shown similar to fibromatosis.<sup>2,32</sup> Endoscopic imaging may also be used to acquire more precise information about the nature of the tumor according to the anatomical site at which it is located. For example, on endoscopic ultrasound in a case of gastric CFT, the tumor was a hypoechoic mass with hyperechoic foci owing to calcifications.<sup>17,68</sup> Laboratory examination proved not to be so useful in CFT diagnosis. The essential tool for certain diagnosis of CFT remains biopsy.

# Pathology

## **Histological Appearance**

CFT originates from the subcutaneous and the deep soft tissue and, macroscopically, it is a well-circumscribed, nonencapsulated mass, which has got a wide range of size and diameter (0.1-25 cm) and can infiltrate the surrounding tissues. Microscopically, it is characterized by the presence of hypocellular, densely hyalinized collagen with psammomatous or dystrophic calcifications, a proliferation of (myo)fibroblastic spindle cells, mononuclear inflammatory infiltrate, and lymphoid aggregates such as focal plasmocytes, eosinophils, neutrophils, and mast cell infiltrations. Sometimes, lymph nodes can be found enlarged and positive for CFT.

# Immunohistochemical Studies

Immunohistochemical studies are of great significance for the differential diagnosis of CFT. Most scientists agree that fibroblasts in CFT do express vimentin and factor XIIIa, whereas, on the contrary, they do not express desmin, actin, S100, ALK-1, SMA, CD117, CD31, CD99, AE1/AE3, CD32, CD20, CD130, EMA, CD21, bcl-2, estrogen receptor, progesterone receptor, calretinin,  $\beta$ -catanin, CAM5.2, caldesmon, and osteopontin. Furthermore, there are several articles in the English medical literature in which it is reported that CD34, CD68, IgG, and IgG4 can be occasionally focally expressed in mast cells of CFT.<sup>99,106</sup> Larson et al<sup>66</sup> mentioned that CFT shares certainly some morphologic features with an IgG4related disease, as they found increased IgG4 in serum of a patient with CFT. Based on the sex predominance of these tumors, we believe that further study should be done on sex hormone receptors.

#### Treatment

All scientists agree that CFT should be excised when diagnosed. Local excision is the preferred therapeutic approach in CFT. There are 2 types of excision that are recommended in the literature: the open surgical excision and the endoscopic one. It is found that the majority of cases are treated with the classic surgical excision, leading to the conclusion that open surgical excision has a predominant role in treating CFT until today. There are 2 references in the literature presenting endoscopic excision of CFT, including 5 cases of CFT of the stomach.<sup>25,71</sup> Moreover, laparoscopic and minimally invasive surgery (video-assisted thoracoscopic surgery) are used in several cases for the excision of the tumor.<sup>13,57,59,67,80,86,107–109</sup>

#### Prognosis

In general, the prognosis is excellent in CFTs. No recurrences or metastasis are observed, except for 6 cases of patients who appeared with a recurrence within their follow-up period, including 2 cases of neck CFT in an infant, 2 cases of neck CFT in 3-year-old children, 1 case of small intestine CFT in 43-yearold man, who also had a metastasis, and 1 case of upper extremities CFT in an 1-year-old child.<sup>2,10,11,21,28,33,66,81</sup> More than 88% of the patients are cured by the local surgical excision of the tumor. No deaths have been noted owing to CFT and long-term survival of patient seems to be certain.

# CONCLUSION

In summary, we conclude that CFT is a benign lesion that is characterized by its wide variety of localizations and should be taken into consideration in the differential diagnosis of an enlarging mass revealed by clinical or imaging examinations either incidentally or after specific acute or chronic symptomatology. The final diagnosis of CFT is made among several similar entities only with histological and immunohistochemical studies, as the tumor is characterized by its specific unique findings in these examinations. Further dedicated studies should be performed for the identification of the exact pathogenesis of the tumor and the evaluation of the age distribution and female predominance of the tumor.

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