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Reminder of important clinical lesson

# Multifocal peritoneal calcifying fibrous tumour: incidental finding at cholecystectomy

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## Summary

Calcifying fibrous tumour (CFT) is a benign tumour of elusive aetiology and a potential for local recurrence. Despite its peculiar histological characteristics it can still be confused with interrelated differential diagnosis like inflammatory myofibroblastic tumour (IMT) or solitary fibrous tumours. The clinical differential diagnosis is however much wider. To date seven cases of multiple peritoneal CFTs are on record. The authors present a case discovered incidentally during laparoscopic cholecystectomy, with no previous history and no radiological diagnosis achieved despite having undergone magnetic resonance cholangiopancreatography (MRCP) and normal routine perioperative investigation. The patient is disease-free 12 months after diagnosis. The case report is followed by a detailed literature review.

## BACKGROUND

The recognition of calcifying fibrous tumour (CFT) first occurred in 1988 under the name of 'childhood fibrous tumour with psammoma bodies', by Rosenthal and Abdul Karim.[1] A series of 10 cases by Fetsch *et al* in 1993 defined the lesion as 'calcifying fibrous pseudotumour', as some of the cases had dystrophic calcification, and the age range was no longer confined to childhood.[2] The WHO[3] since 2004 recognised its potential for local recurrence, as shown in six cases published to date,[2 4–6] and renamed the entity CFT.

We present an unsuspected case of multifocal peritoneal CFT presenting incidentally during laparoscopic surgery. This case illustrates how rarely, what initially perioperatively looks like omental metastatic disease can be a benign soft tissue tumour with good outcome and also how this lesion can escape detection by routine pre-operative screening.

## CASE PRESENTATION

A 32-year-old gentleman was being investigated for recurrent bouts of symptomatic cholelithiasis and deranged liver biochemistry compatible with non-alcoholic steatohepatitis, the latter attributed to a significantly raised body mass index. There was no history of previous surgery in the abdomen.

## INVESTIGATIONS

A MRCP revealed only cholelithiasis. During elective laparoscopic cholecystectomy, multiple (21) omental solid deposits, as well as nodules adherent to the cystic duct, mesentery of the terminal ileum, tail of pancreas and splenic hilum were noted. The operation was converted to a laparotomy. There were no signs of bowel obstruction or ischaemia. The common bile duct was not compressed by these lesions. Local excision of all lesions was performed.

On gross examination all 21 lesions were of solid consistency, somewhat glistening white cut surface and some possessing a gritty texture on sectioning. The size of these lesions did not exceed 3 cm. Adherence to omental fat could easily be noted, despite the circumscribed nature of these lesions. No haemorrhagic, necrotic or cavitary foci were noted (figure 1A,B). None of the lesions had an identifiable capsule.


**Figure 1** (A,B) Multiple solid omental nodules with white glistening cut surface.

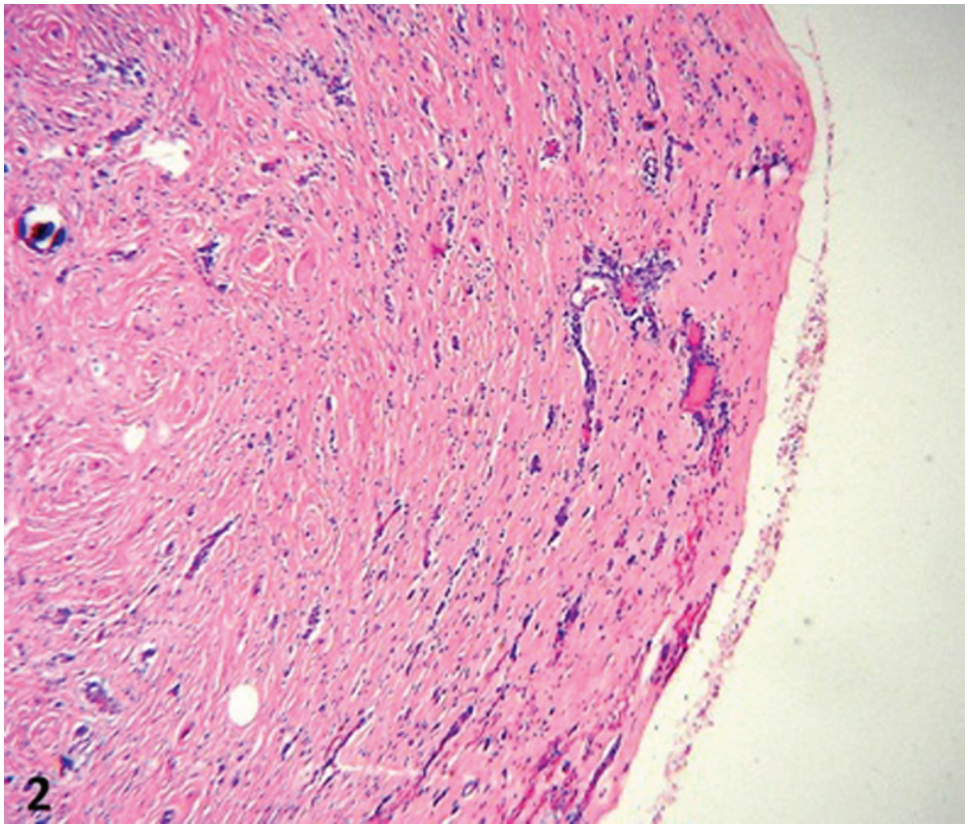


**Figure 2** Unencapsulated circumscribed nodule with densely hyaline fibrosclerotic stroma, low power.

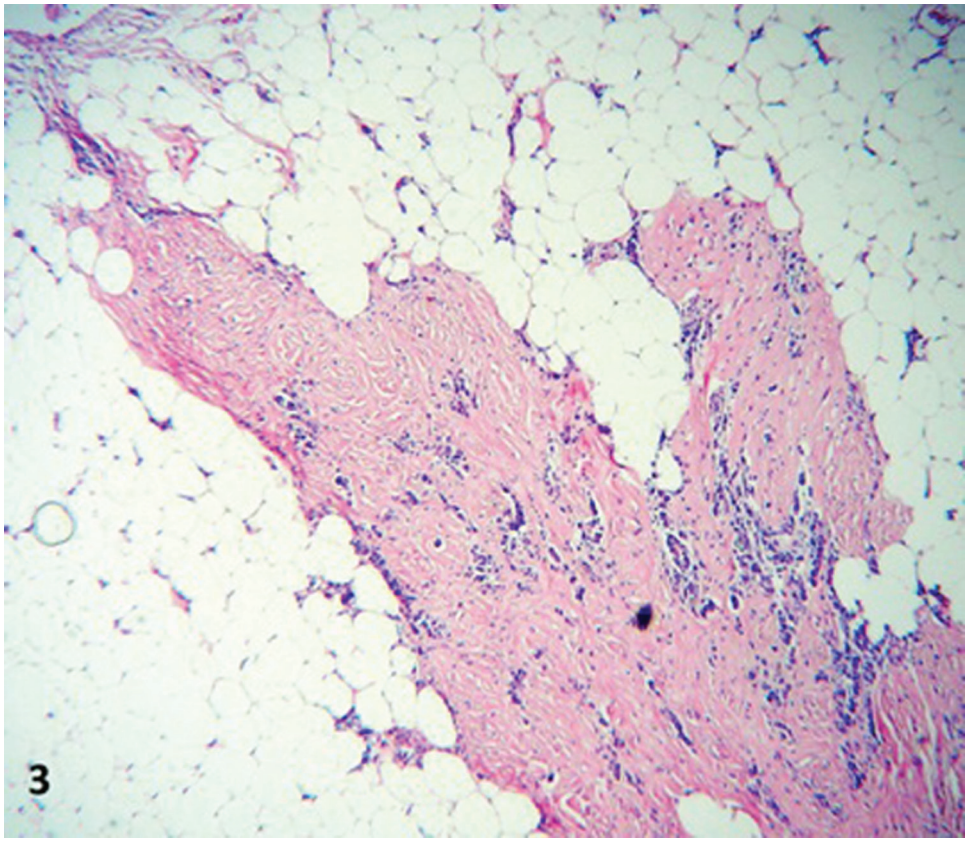


**Figure 3** Lymphoplasmacytic infiltrates within stroma and infiltration into adipose tissue, high power.


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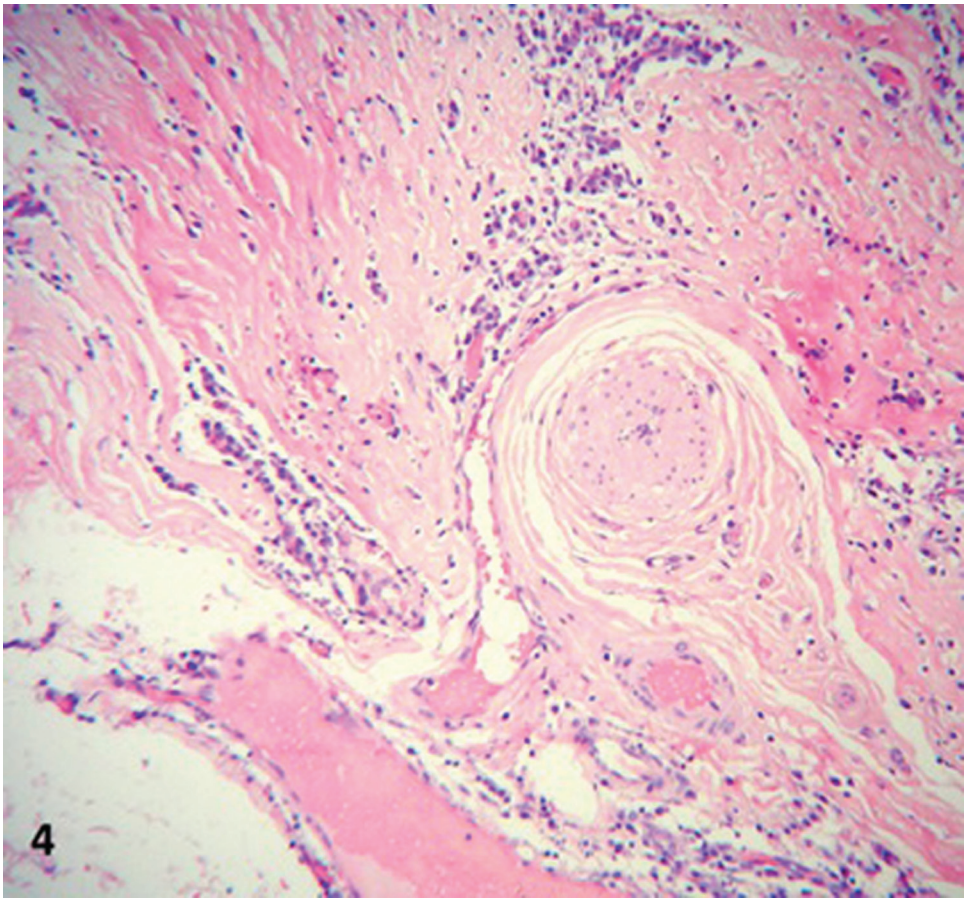


**Figure 4** Entrapment of neurovascular bundle, high power.

The excised peritoneal nodules were fixed in 10% neutral buffered formalin. The paraffin-embedded tissue sections were stained with H&E. Immunohistochemical staining was performed using the avidin-biotin/horse radish peroxidise complex. The antibodies tested were vimentin (CloneV9 1/350; DAKO – Glostrup, Denmark), factor XIIIa (Clone AC-1A1 1/50; Abcam – Cambridge, UK), CD34 (Clone QBEnd10 1/50; DAKO), CD117 (rabbit polyclonal 1/450; DAKO), smooth muscle actin (SMA) (Clone 1A4 1/70; DAKO), Desmin (Clone D33 1/80; DAKO) and anaplastic lymphoma kinase (Clone ALK-1 1/50; Monosan). Appropriate positive control samples were run concurrently with the above.

On microscopy, all lesions had similar histology, consisting of unencapsulated nodules with a densely hyalinised fibrosclerotic stroma. (figure 2). Benign slender spindle fibroblast-like cells are embedded within this matrix, with thick collagen bundles sometimes forming whorled arrangements. Most areas were paucicellular, only to be interrupted by haphazardly spaced lymphoplasmacytic infiltrates, mostly perivascular, without germinal centre formation. Other features of note were Russell bodies, entrapped omental adipose tissue and neurovascular bundles (figures 3 and 4), a high microvessel density (MVD), mostly at the periphery of the nodules, focal haemosiderin deposits and numerous CD117 positive mast cells. Also distinctive calcifications, largest measuring 80 µm in diameter were irregularly scattered in the stroma. Most of the calcifications had a typical lamellated psammomatous appearance but minor areas of dystrophic calcification were also seen (figure 5).

Mitotic figures were not seen. MVD was calculated by strictly counting CD34 positive vessels in 10 random high power fields (HPF), that is, magnification ×400, total area 3 $mm^2$ and ranged from 77 to 90 vessels per 5 HPF.

Strong and moderate cytoplasmic staining of the spindle cells was seen with vimentin and factor XIIIa, respectively (figure 6). SMA, CD34, CD117, ALK and desmin were negative. CD34 stained the endothelial cells of the blood vessels and CD117 stained the mast cells. These findings, together with the typical histological features described above led to the diagnosis of CFT, of which a concise discussion about its properties and pathogenesis will ensue.

## OUTCOME AND FOLLOW-UP

Postoperative recovery was uneventful and the patient is disease-free 12 months following the intervention.

## DISCUSSION

Since its establishment as a benign soft tissue tumour, numerous reports have expanded the range of clinical presentations and properties of this tumour. A total of 109 cases have been reported so far, with almost any organ being affected.[2 4–50] Fourteen cases have a multifocal presentation,[5 7 10 14–18 20 21 29 50] seven of which are peritoneal.[5 10 14 15 21 29]

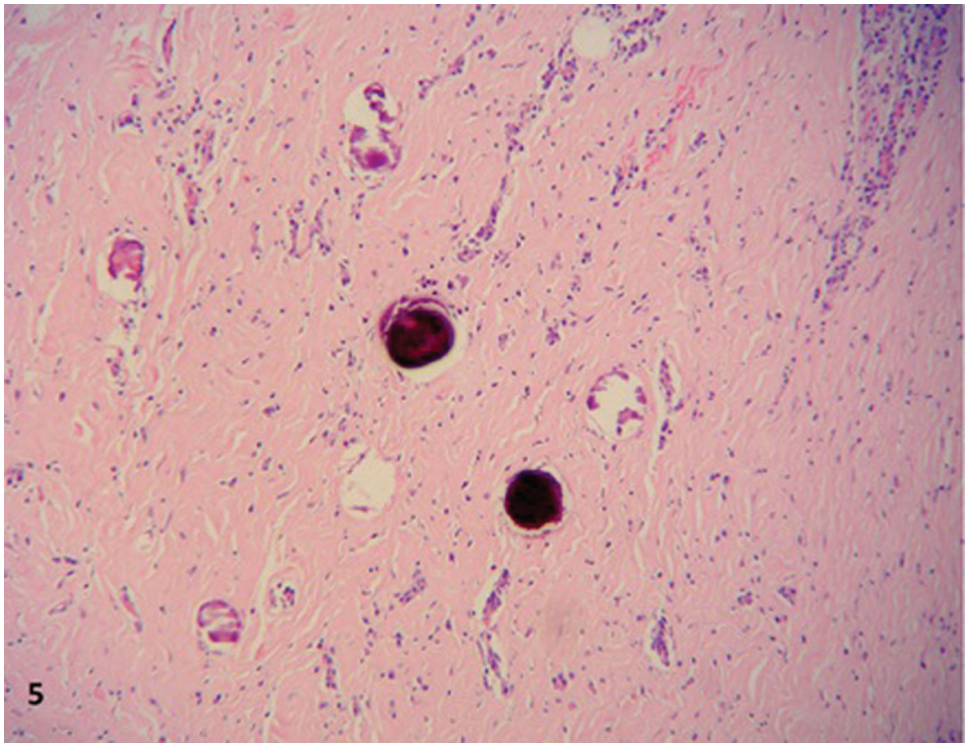


**Figure 5** Psammomatous and dystrophic calcifications, high power.

The histological features, when present are now recognised as typical and most of the times the diagnosis is clinched on H&E. These lesions are circumscribed unencapsulated masses composed of a paucicellular population of spindle-shaped fibroblasts in a densely hyalinised, often lamellated collagenous stroma.[2 3] Collagen deposition is also noted around small vessels.[7] Most contain lymphoplasmacytic infiltrates often in a perivascular location.[10] The cellularity of the spindle cells tends to be less in the periphery of the lesions.[7] Both psammomatous and dystrophic calcifications are present[3] ranging in size from 10 to 110 μm.[7] Rare foci of ossification are also described.[4] Entrapment of neighbouring structures is a common sight in these tumours.

Less common features are Russell bodies, mast cells, eosinophils, polymorphonuclear leucocytes, xanthoma cells and multinucleated giant cells, often surrounding calcifications.[2 9] Some lesions, like in this case, show focal haemosiderin deposition.[9] Occasionally the stroma can have a myxoid consistency.[10]

The lymphoid aggregates can be seen in the stroma or more often perivascular, with or without germinal centre formation.[10] When present around hyalinised capillaries, it may be confused with the hyaline vascular variant of Castleman's disease,[9] and to complicate matters a unique CFT was also reported as arising within a node with the hyaline vascular variant of Castleman's disease.[46]

Microvascular density in CFT is distributed equally centrally and peripherally, a feature which can also help to distinguish it from (IMT).[4] The technique used above is similar to the method described by Weidner *et al*,[51] and results correlate well with published data.[4]

CFT are now known to have a wide age range, from 1 year of age to 65 years,[5] with no gender predilection, although multifocal lesions tend to be commoner in women.[15] The size of the lesions is variable, tending to be greater in soft tissues with the largest on record measuring 25 cm.[5] Peritoneal nodules tend to be smaller, the largest not exceeding 3.5 cm.[21] Most CFT are sessile and broad-based, but pedunculated lesions are also on record.[8] Not uncommonly, macroscopic haemorrhage, necrosis and cavitation can be encountered,[3] but usually the cut surface is homogenous but in different shades of white, grey or tan-pink.[7]

MRI imaging shows sharp circumscription of the lesions, especially in the soft tissue, with a signal intensity closer to muscle than to fat.[2] MRCP is not sensitive, as evidenced by our case. Contrast enhanced CT scans can show calcifications as areas with higher attenuation than the enhancing vessels.[7] On electron microscopy, the spindle cells are shown to be fibroblasts, surrounded by abundant collagen fibrils, where the initial event in intracytoplasmic calcification is organelle degeneration.[1 7] Calcification in CFT can be both intracellular and extracellular.

Immunohistochemical staining properties of the fibroblasts do not vary according to region of the body, with the slight exception of CD34. CFT typically shows cytoplasmic positivity for vimentin and factor XIIIa, and are negative for skeletal muscle actin, desmin, ALK and cytokeratins.[3 10] SMA is usually negative but is rarely reportedly positive.[10] CD34 fibrocyte positivity in CFT was first described in the peritoneum,[8] and its expression is now thought to represent early submesothelial fibroblast properties, where the reactive fibroblast can then differentiate into myofibroblasts, myxoid fibroblasts and collagenous fibroblasts.[13] Most CD34-positive CFT occur in the peritoneum.[13]

The aetiological factors behind CFT are unknown, although previous trauma has been reported in some


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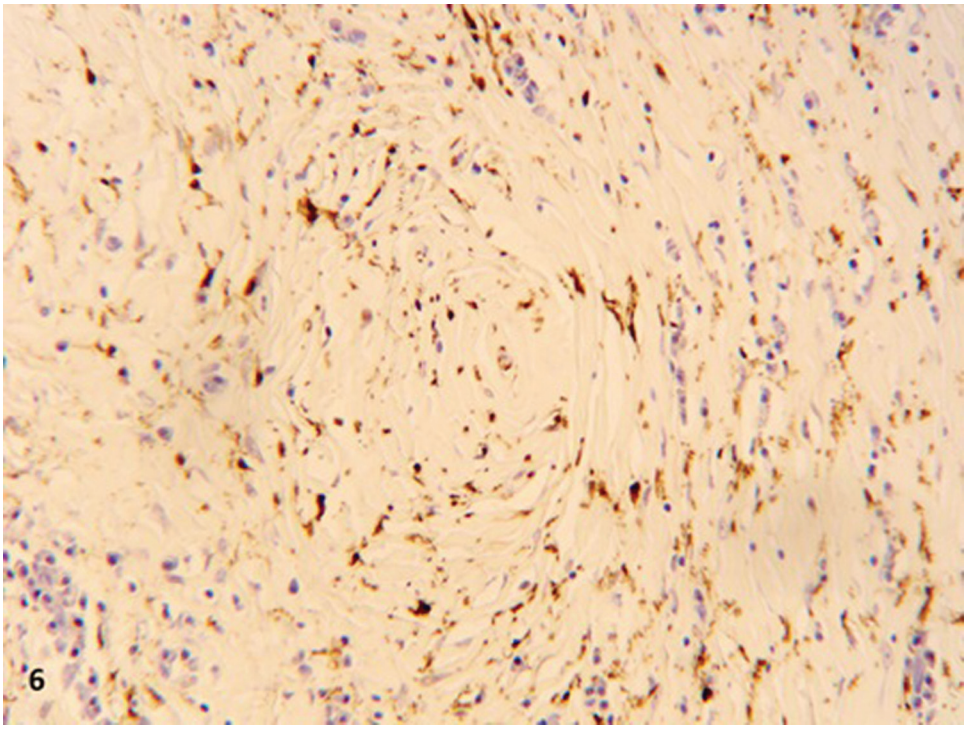


**Figure 6** Diffuse moderate intensity cytoplasmic positivity of spindle fibre cells for factor XIIIa, high power.

cases.[1 7 8] To date, only a single occurrence of familial CFT is described, between two sisters, each presenting at 17 years of age with multiple peritoneal lesions.[10]

The differential diagnosis of CFT in the abdomen includes pelvic or mesenteric fibromatoses, elastofibroma of the omentum, retractile mesenteritis, smooth muscle tumours, solitary fibrous tumour of the peritoneum, IMT and hyalinising granuloma. These are usually easily distinguished on H&E, except for cases of early IMT and localised solitary fibrous tumour of the peritoneum.[8] An inter-relationship and pathological continuum between CFT and IMT was previously proposed, due to the occurrence of these two entities in the same lesion.[7 10 12 21] However, large series published in the last decade demonstrate notable differences in immunohistochemical staining properties between the two. IMT almost always stains positive for ALK-1 antibody (a product of its peculiar 2:5 chromosomal translocation) and skeletal muscle actin but only focally for factor XIIIa (less than 10% of area examined), while CFT never stained positive for ALK-1 and skeletal actin but shows diffuse positivity for factor XIIIa.[4 5] Thus it is unlikely that there is a pathologic continuum from IMT to CFT, but rather a common earlier, short-lived precursor lesion, as discussed earlier.

So far no mortality has been attributed to CFT. An asymptomatic multifocal peritoneal presentation during elective surgery is uncommon. In most cases, after local excision, a short-term follow-up programme and reassurance are all that is needed. The caring physician should keep in mind the possibility of its benign nature, and the pathologist should not forget other more common differential diagnoses.

## Learning points

- Single or multiple omental deposits can rarely be inflammatory or low grade benign tumours.
- In this respect one should look for history of trauma, metabolic disease and concomitant soft tissue lesions after having explored the common sites of origin of a primary carcinoma.
- CFT is a benign soft tissue tumour which can rarely present as multiple omental solid deposits. No mortalities have been attributed to this entity so far.

**Competing interests** None.

**Patient consent** Obtained.

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