Autopsy Case Reports

Article / Clinical Case Report

Calcified fibrous pseudotumor with Castleman disease

Ísmail Harmankaya[a], Nevzat Serdar Ugras[a], Tamer Sekmenli[b], Fatih Demir[a], Yavuz Köksal[c]

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ABSTRACT

Simultaneous calcified fibrous pseudotumor (CFT) and Castleman disease (CD) is an extremely rare association. CD is an uncommon lymphoproliferative disease that can arise in various sites of the body, while CFT is a rare type of benign fibrous lesion that frequently affects children and young adults, occurring as solitary or multiple lesions throughout the human body. Both entities are rare and exhibit typical and diverse histomorphological features. We report the case of a 15-year-old female patient, who, at the age of 13 had a biopsy performed at an external medical center; however, after 4 months the lesion had regrown. This lesion was removed with a surgical operation; however, it regrew 2 years later and was removed a third time. The results of the latter two biopsies were the same: CFT accompanying CD. The histologic examination of the excised lymph node and the surrounding tissue showed hyalinized fibrous tissue containing dystrophic and psammomatous calcification. In this case, the hyaline vascular type of CD was found to be intertwined with a CFT, which hampered the differentiation of whether both entities emerged within the lymph node or if the CFT developed from the soft tissue and then involved the lymph node. Future studies involving larger case series will provide a more precise insight, which should serve to resolve the current uncertainty.

Keywords
Castleman Disease; Pathology; Tumor.

INTRODUCTION

Calcified fibrous pseudotumor (CFT) is rare type of benign fibrous lesion, which was first described in 1988 by Rosenthal and Abdul-Karim.[1] CFT has been diagnosed in different age groups and in various localizations.[2]

The term "Castleman disease" has its origins in a case report published in 1954 by the pathologist Dr. Benjamin Castleman. It is a rare, benign disease of unknown etiology. This initial case report was soon followed by more detailed analysis of patients having isolated mediastinal lymphadenopathy.[3] Keller et al.[4] defined two distinct clinicopathological variants of CD, namely the hyaline vascular type (HV) and the plasma cell type (PC). The disease presents clinically as unicentric or multicentric in nature.[3]

In this report, a case of CFT accompanied by CD is presented. To the best of our knowledge, our case is only the fifth report in the English literature to describe an association between these two entities.[5]

[a] Selçuk University, Faculty of Medicine, Department of Pathology. Konya, Turkey.
[b] Selçuk University, Faculty of Medicine, Department of Pediatric Surgery. Konya, Turkey.
[c] Selçuk University, Faculty of Medicine, Department of Pediatric Hematology and Oncology. Konya, Turkey.

CASE REPORT

A 15-year-old girl sought the Pediatric Surgery Clinic complaining of a non-tender, slow-growing mass on her right supraclavicular fossa, which, on the physical examination revealed to be enlarged lymph nodes, which were hard and immobile (Figure 1).

Her past medical history included an adenoidectomy at the age of 13 years due to a cleft palate and a nasopharyngeal stricture. A supraclavicular lymph node lesion was diagnosed, and a biopsy was performed at the external center; however, the patient revisited the center 4 months later with a regrowth of the lesion. This was surgically removed, but 2 years later the lesion had regrown and was surgically removed for the third time.

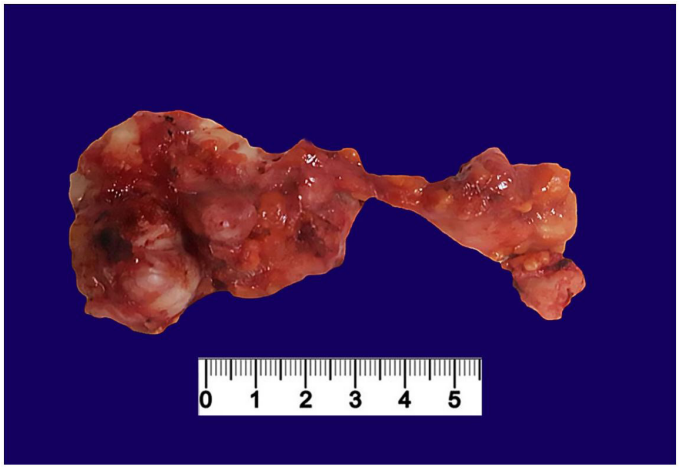

Figure 1. Gross view of the surgical specimen.

Histology results revealed the diagnosis of CD associated with CFT. The patient's physical examination was normal except for the bulging mass over the supraclavicular fossa. Considering her past history, the working diagnosis was a relapse of the CD. Therefore, another surgical procedure was undertaken to remove the new tumor, which measured 5 × 5 × 2.5 cm. At this time, the histopathological findings of the lymph node sections showed increased lymphoid follicles and atretic germinal centers, as well as a proliferation of the internal and external vessels inside and outside the follicles. A concentric mantle zone consisting of small lymphocytes was observed around the follicles (Figures 2 and 3).

The histochemical and immunohistochemical examination showed the tumor cells of the CFT component staining focally with SMA and CD34, while the collagen fibers were stained diffusively with Masson's trichrome (Figure 4). The tumor cells diffusively expressed vimentin, the plasma cells CD38, the histiocytes CD68, the endothelium CD31, the mast cells stained with Toluidine Blue, and the connective tissue with PAS. EMA, ALK, Elastic stain, and Congo red were negative. The morphological, histochemical, and immunohistochemical findings altogether supported the diagnosis of CFT associated with CD.

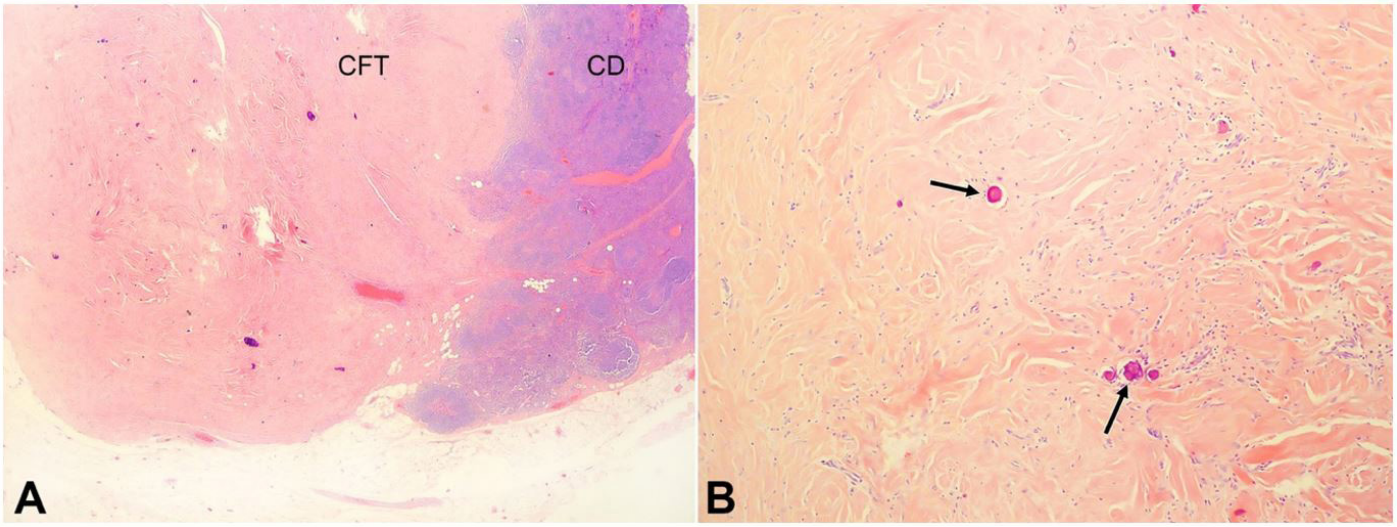

Figure 2. Photomicrography of the lymph node. **A –** Castleman disease (CD) intertwined with calcified fibrous pseudotumor (CFT) (H&E, 20X); **B –** CFT with collagen fibers, lymphoid cells, and calcifications can be seen (arrows) (H&E, 100X).

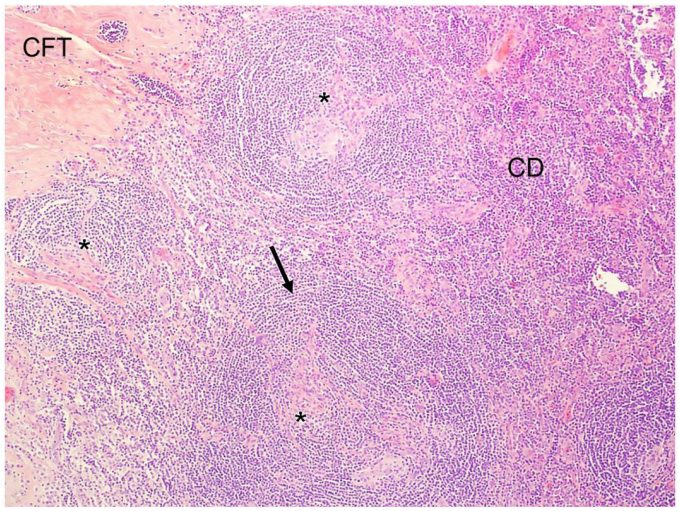

Figure 3. Photomicrography of the lymph node showing the Castleman disease with the vessels at the germinal centers (asterisk), concentric lymphoid zone around the follicle (arrow), accompanied by a calcified fibrous pseudotumor focus (H&E, 100X, CFT; Calcified fibrous tumors, CD; Castleman Disease).

DISCUSSION

CD, also known as angiofollicular lymph node hyperplasia, is an uncommon lymphoproliferative disorder, which may involve the salivary glands, lung, pancreas, larynx, parotid gland, meninges, and even the limb muscles.[6]

Clinical variants of CD are unicentric, multicentric, human herpes virus 8 (HHV8)-positive CD and thrombocytopenia, ascites/anasarca, myelofibrosis/fever, renal dysfunction/reticulin fibrosis, and organomegaly (TAFRO) syndrome. In unicentric CD, the lymph nodes are significantly enlarged and have histopathologic features of the hyaline-vascular variant (90%). Marked plasmacytosis is rarely seen (10%). In multicentric CD, patients typically present with diffuse lymphadenopathy. There are two common histologic patterns identified: Hypervascular and

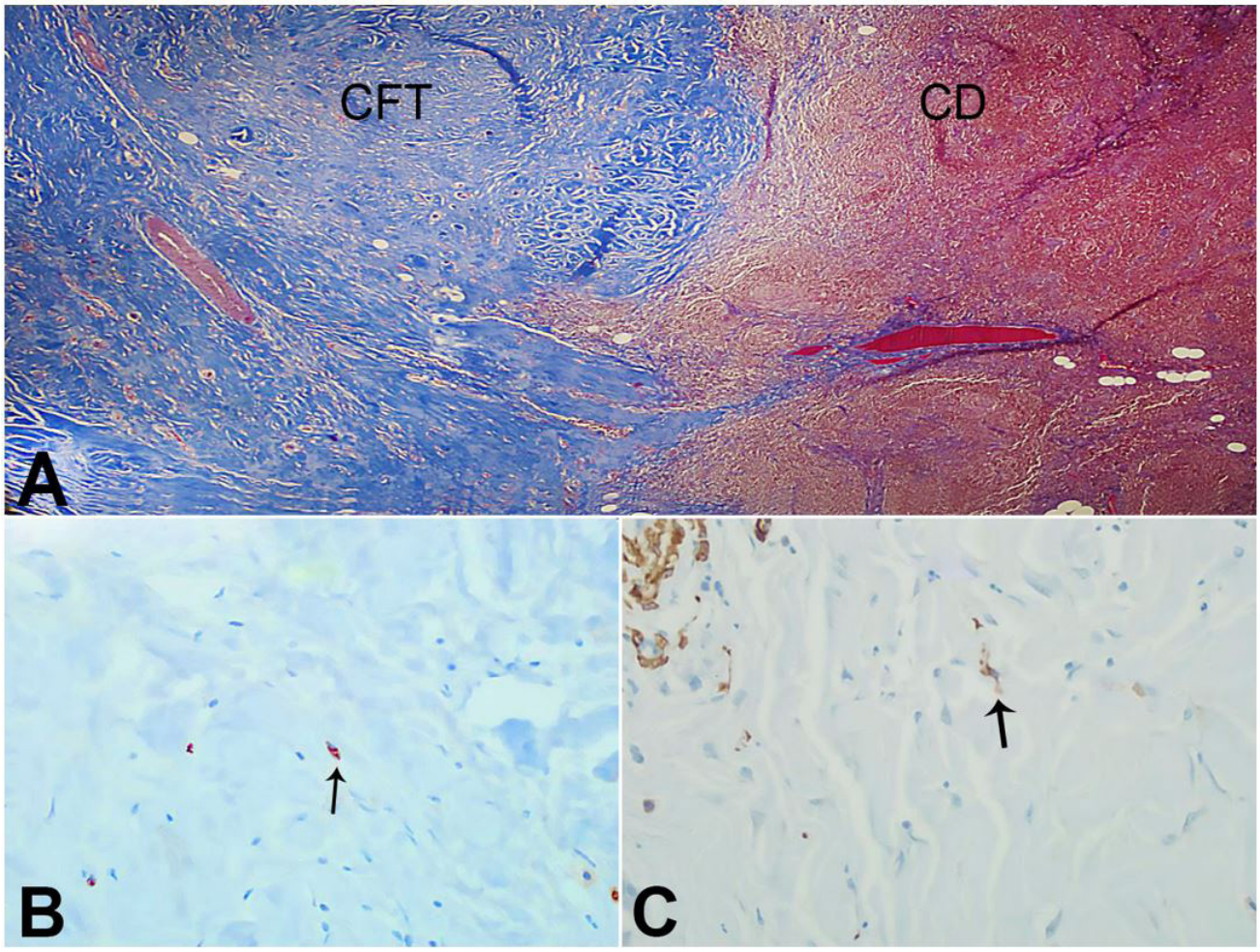

Figure 4. Photomicrography of the lymph node. **A –** Calcifying fibrous tumor (CFT) and Castleman disease (CD) (Masson Trichrome, 400X); **B –** Arrow, focal staining in the CD tumor cells (CD34 staining, 200X); **C –** Arrow, focal staining in the CFT tumor cells (SMA stain, 400X).

plasmacytic variant. The plasmacytic variant is most commonly seen in multicentric CD and is characterized by the prominence of interfollicular plasma cells within the lymph node. By immunohistochemistry, the plasma cells in multicentric Castleman disease are typically polytypic with respect to immunoglobulin light chain expression. Multicentric CD is seen in the dysregulation of interleukin (IL)-6 (increased) or other cytokines, such as vascular endothelial growth factor, IL-1, tumor necrosis factor-α. The syndrome of TAFRO is a recently described variant of idiopathic HHV8-negative multicentric Castleman disease. In this variant, there are similar clinicopathologic features to that of idiopathic multicentric Castleman disease. TAFRO typically performed to evaluate thrombocytopenia show megakaryocytic hyperplasia with clustering in a background of diffuse reticulin fibrosis. HHV8-positive CD is similar to multicentric CD in clinicopathologic features. In contrast, in HHV8-positive CD the lambda light chain restricted plasmablasts present within mantle zones.[3]

The characteristic finding of hyaline vascular type CD is the abnormal proliferation of dendritic cells in the follicles. The plasma cell type of CD may be accompanied by fever, anemia, and a decrease in hypergammaglobulinemia following the excision of the lesions. In addition, polyclonal plasma cells are found in the lymph nodes.[7]

CFT is a rare type of benign fibrous lesion that typically affects children and young adults, and involves the gastrointestinal tract, pleura, peritoneum, and mesentery, together with the deep and superficial soft tissues of the body.[8]

In 1988, Rosenthal and Abdul-Karim[1] first described CFT as a "childhood fibrous tumor with psammoma bodies."

In 1993, Fetch et al.[2] named it as CFT. This entity emerges as a slow-growing, painless, subcutaneous or deeply located mass that is microscopically seen as a benign fibrous tumor with well-defined borders and unencapsulated, hyalinized, and fibrosclerotic tissue, including lymphocytes and plasma cells at various ratios. Characteristically, focal or diffuse dystrophic and frequently psammomatous calcifications are seen.[9]

There are few studies that report the association of CD and CFT. A stroma-rich variant of hyaline-vascular CD is described, which shows the over growth of a variety of stromal cells with predominantly vascular components and fibrosis in more than 50% of the lesion. These morphological features presented by this variant can be a differential diagnosis with CFT.[10] A rare case of HV-CD with angiomatous lymphoid hyperplasia, collagenization, and focal calcification was previously described.[5] However, our case was typical of both lesions.

The HV-CD type also has been found to be a localized lesion supporting CFT characteristics. Although some CFT cases have shown CD modifications, which suggests lymphoid tissue involvement, CFT formation in the HV-CD type is extremely rare.[11] Valladolid et al.[12] reported a case in which a mass had to be surgically removed because of an ileocolic intussusception with associated mesenteric lymphadenopathy. The mass was found to be a poor-cell CFT including lymph nodes with significant vascularity, atretic follicles, and histomorphological CD-specific findings.

The number of articles describing the association of CD and CFT is very low.[5] Dargent et al.[11] reported a HV-CD type associated with CFT in an inguinal lymphadenopathy case.

Although CD primarily involves the lymphatic system, it can also involve the extra lymphatic organs. However, CFT is not seen in the lymphatic system, but rather involves the soft tissues. Both of these rare diseases have typical histomorphological findings. In the present case, the HV type of CD involving the lymph node was found to be interwoven with the soft tissue, which rendered uncertainty as to whether the CFT first developed in the soft tissue and then invaded the lymph node, or vice versa.

The causes of both diseases remain unclear. Although there have been no findings in isolated CD indicating the presence of CFT, in advanced cases the stromal overreaction may display a CFT-like histomorphological appearance. In isolated CFT cases, along with the mild inflammation of the surrounding tissue, there has been no follicle hyperplasia or hyalinization of the follicle veins indicating CD. These diseases are hence considered to be two different entities.

In conclusion, although there have been very few reports on the coexistence of CD and CFT, the HV type of CD with stromal overreaction has been reported by

some researchers to be a different variant.[5] Further studies involving larger case series will provide a clearer insight, which should serve to resolve the current uncertainty in this regard.

REFERENCES

1. Rosenthal NS, Abdul-Karim FW. Childhood fibrous tumor with psammoma bodies. Clinicopathologic features in two cases. Arch Pathol Lab Med. 1988;112(8):798-800. PMid:3395217.
2. Fetsch JF, Montgomery EA, Meis JM. Calcifying fibrous pseudotumor. Am J Surg Pathol. 1993;17(5):502-8. http://dx.doi.org/10.1097/00000478-199305000-00010. PMid:8470765.
3. Wu D, Lim MS, Jaffe ES. Pathology of Castleman disease. Hematol Oncol Clin North Am. 2018;32(1):37-52. http://dx.doi.org/10.1016/j.hoc.2017.09.004. PMid:29157618.
4. Keller AR, Hochholzer L, Castleman B. Hyaline-vascular and plasma-cell types of giant lymph node hyperplasia of the mediastinum and other locations. Cancer. 1972;29(3):670-83. http://dx.doi.org/10.1002/1097-0142(197203)29:3<670::AID-CNCR2820290321>3.0.CO;2-#. PMid:4551306.
5. Ma H, Jiang M, Xiao W. A rare stroma-rich variant of hyaline-vascular Castleman's disease associated with calcifying fibrous pseudotumor. Int J Clin Exp Pathol. 2015;8(3):3362-4. PMid:26045869.
6. Gündüz E. Nadir bir lenfoproliferatif hastalık: Castleman hastalığı. Osmangazi J Med. 2016;38:6-16.
7. Büyükbeşe MA, Özdemir S, Hilal A, et al. Hepatosplenomegali ile başvuran bir hbsag taşıyıcısında castleman hastalığı. Cerrahpaşa Tıp Dergisi. 1999;30(3):228-32.
8. Gamsızkan M, Yıldırım C, Daş K, Günhan Ö. Calcifying fibrous tumor: A case report/kalsifiye fibröz tümör: Olgu sunumu. Turkish J Pathol. 2015;31(2):141-4.
9. Dervişoğlu S. Yumusak doku tümörleri. 1. Baskı. Ankara: Kongre Kitabevi. 2016.
10. Danon AD, Krishnan J, Frizzera G. Morpho-immunophenotypic diversity of Castleman's disease, hyaline-vascular type: with emphasis on a stroma-rich variant and a new pathogenetic hypothesis. Virchows Arch A Pathol Anat Histopathol. 1993;423(5):369-82. http://dx.doi.org/10.1007/BF01607150. PMid:8116226.
11. Dargent J-L, Delplace J, Roufosse C, Laget JP, Lespagnard L. Development of a calcifying fibrous pseudotumour within a lesion of Castleman disease, hyaline-vascular subtype. J Clin Pathol. 1999;52(7):547-9. http://dx.doi.org/10.1136/jcp.52.7.547. PMid:10605414.
12. Valladolid G, Weisenberg E, Sundaresan R, Maker AV. Calcifying fibrous tumor of the small intestine associated with Castleman-like lymphadenopathy. J Gastrointest Surg. 2014;18(6):1205-8. http://dx.doi.org/10.1007/s11605-014-2458-8. PMid:24452381.

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The authors retain an informed consent signed by the patient, and the manuscript is in accordance with the Institutional Ethics Committee requirements.

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Correspondence
Tamer Sekmenli
Selcuk University Medical Faculty, Department of Pediatric Surgery
Alaeddin Keykubat Campus, 42131 – Selçuklu/Konya, Turkey
Phone: +(90) 332 241 21 81
dr_sekmenli@hotmail.com