



## Case report

## Castleman's disease: A rare case report and review of literature

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## ABSTRACT

Castleman's disease – also known as giant lymph node hyperplasia – is a rare pathology, poorly understood. Described for the first time in 1954, it is considered a lymphoproliferative disorder that manifests without any other obvious symptoms and may be confused with other causes of lymph nodal enlargement. We are reporting in this paper the case of a 30-year-old Maldivian female who presented to our surgical OPD with a right cervical large solitary soft tissue lesion. All the investigations were negative except for a large highly vascularized unicentric soft tissue mass measuring around 4 cm in the anterior triangle of the neck seen by the ultrasound separable from all other surroundings. An excisional biopsy & complete resection was done under general anesthesia in the operation theater of a Maldivian Regional hospital. Unicentric Castleman's disease as a diagnosis was confirmed based on the final histopathological study of the specimen, and the absence of other cervical and extra-cervical lymphadenopathy. The patient doesn't have recurrence or newly developed lymph nodes at the time of reporting this article.

## 1. Introduction

Castleman's disease (CD) is a rare, often poorly understood lymphoproliferative disorder that shares common lymph node histological features. The disease was first described by Dr. Benjamin Castleman in a single case in 1954 [1], followed by a small cases series in 1956 [2]. There were two clinical entities described: Unicentric with a confined disease to a single anatomic lymph node and multicentric which is characterized by generalized lymphadenopathy and more aggressive & progressive clinical course [3]. It has three histological subtypes: hyaline vascular, plasma cellular and a mixed type. The clinical characteristics and survival differ significantly between the three subtypes. The majority of the previously reported cases of CD in the neck were of the hyaline vascular type and the most common sign was an asymptomatic neck mass same as our case report [4]. The aim of this case reporting is to describe a spotted case of cervical unicentric CD, its diagnostic tools, the perioperative management after 12 months of close monitoring.

This case report has been reported in line with SCARE 2020 criteria [5].

## 2. Presentation of case

A 30-year-old Maldivian female patient medically & surgically free presented with an isolated right sided painless mass of the neck slowly

evolving over the past 4 years. On physical examination a solitary firm and non-fixed right lateral neck mass was found measuring around four centimeters. Ultrasound echography showed a 4 centimeter well-defined hypoechoic oval mass with central and peripheral vascularization of the right anterior aspect of the lower neck (Fig. 1). Excisional biopsy was done under general anesthesia by The Surgical Team of a General Surgery Specialist (the author) & OT nurses in the operation theater of a Maldivian Regional hospital and the mass was completely excised then sent for histopathological assessment (Fig. 2). The patient's postoperative stay went uneventful. The diagnosis of hyaline Castleman's disease was made based on final histological findings (Fig. 3). The postoperative imaging did not show any other systemic lymph nodal enlargement. We did not observe recurrence, newly developed neck masses, or new systemic lymphadenopathy appearance 12 months after surgery during regular clinic monthly follow-ups and systemic workup.

## 3. Discussion

CD is a rare lymphoproliferative disorder, described for the first time by Castleman et al. [1,2] in 1954 in a single case then in 1956 in a group of 13 patients with localized benign lymphadenopathy. This rare disease is also termed as localized nodal hyperplasia, angiomatous lymphoid hamartoma, or giant lymph node hyperplasia [1]. Williams and Kaude both reported that lymph nodes in the mediastinum were the most

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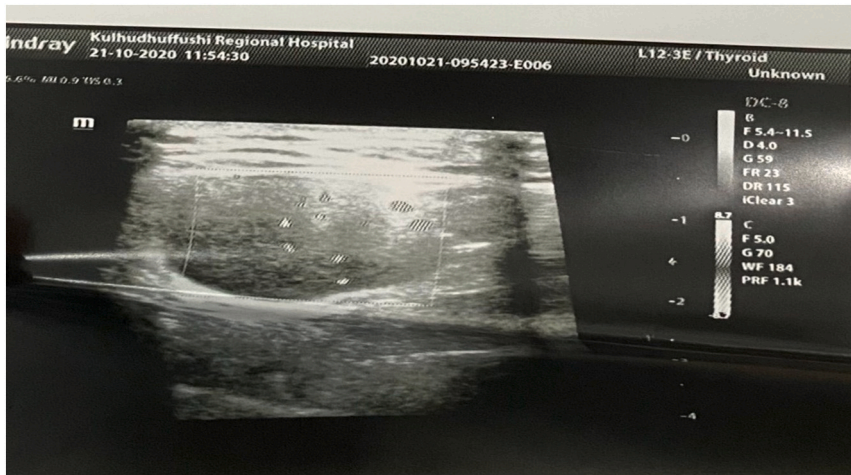


Fig. 1. Ultrasound images of the oval right sided neck mass.



Fig. 2. Intraoperative view of the solitary lymph node from the anterior triangle of the neck.

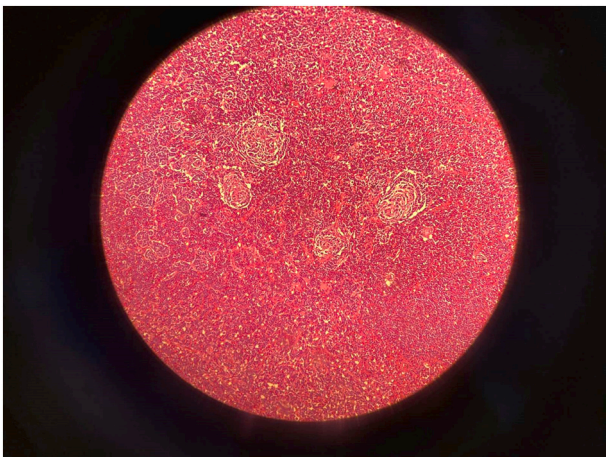


Fig. 3. Histology slides: the follicle is surrounded by a broad mantle zone consisting of a concentric layering of lymphocytes resulting in an “onion-skin” appearance.

common presentation (70 %) and that the neck and abdomen were the least common (15 %) sites for CD [6]. Even though the exact pathogenesis of CD is vague, studies have indicated that the occurrence of CD may be related to the infection of human herpes virus-8 (HHV-8) or human immunodeficiency virus (HIV), immune dysfunction, and excessive production of interleukin-6 (IL-6). Asao et al. was the first one to prove that IL-6 transgenic mice showed similar disorders related to CD, which supported the contribution of IL-6 to CD [7]. The final conclusive diagnosis of CD is based on histopathological assessment. There are three different types of CD: hyaline-vascular type, plasma cell type and mixed variant type [4,8]. Hyaline-vascular type is the most common clinical finding (90 %) characterized by follicular hyperplasia with regressed germinal centers and important vascular proliferation. Plasma cell type is characterized by Russell bodies and exhibits larger lymphoreticular nodules and fewer hyalinized blood vessels compared with the hyaline-vascular type. Mixed variant type is a rare variant and exhibits features of hyaline-vascular and plasma cell type [4].

The incidence of CD is unknown and can occur at any age, however it is mainly reported in adults in the literature with a slight feminine predominance (60 %). There are two different clinical types: the unicentric and the multicentric type. The localized form of the disease like the case that we are reporting is mostly asymptomatic with a single site lymph node enlargement. Although localized CD most often occurs in the mediastinum, it may occur in any other areas of the body where

lymph nodes are found such as the lung, neck, axilla, mesentery, pelvis, or retroperitoneum [6]. It is often discovered incidentally during routine examination, chest X rays, or due to discomfort secondary to local compression. Diagnosis is confirmed by histopathological assessment of the lymph node biopsy sent postoperative [8,9]. The multicentric form, however, presents with systemic symptoms along with multiple lymph nodes hyperplasia. The systemic symptoms are thought to be initially a consequence of elevated Interleukin-6 (IL-6) production. They present as asthenia, weight loss, fever, polyadenopathy with a mean of four-site involvement and are often associated with hepatosplenomegaly [9]. Some other forms of multicentric CD are associated with Kaposi's sarcoma, which develops in the clinical course of most HIV-positive multicentric CD cases. Such cases show an increased prevalence of pulmonary symptoms and can be differentiated from other types of HIV-associated systemic lymphoproliferative disorders [10,11]. It was noticed that HIV-negative Kaposi's sarcoma is associated with CD to a much lesser extent [10]. CD often shows well-defined, mildly hypodense or isodense, homogeneous nodules or masses on different imaging modalities (CT/MR), and intermediate and marked enhancement on contrast-enhanced CT/MR images. The hypertrophy of blood vessels is also considered as valuable features [12]. The calcification in affected lesions is common and is more commonly observed in hyaline vascular variant unicentric CD [13].

In our case, ultrasound was enough as an indicator for the solitary well-defined lymph node that was clear and separable from other surroundings. Fine needle aspiration cytology (FNAC) findings may not always be conclusive. CT and MRI are usually of great value in the case prognosis. Surgical resection is considered the cornerstone of radical treatment for unicentric CD and is the most widely accepted therapy in the literature therefore the upfront excision decision was taken in our case for diagnostic and radical concerns. A systematic review by Talat et al. [14] of 278 unicentric patients found that surgical resection resulted in 95 % disease-free survival at 3 years. In case the surgical resection was not applicable, or the lymph node is not accessible, radiation therapy could be an effective way to destroy the affected tissue. Radiation doses of ranges 30–45 Gy appear to be effective, although tumor responses have been documented at lower doses [8]. Multicentric CD however tends to have a variable prognosis with no documented treatment consensus. A variety of combination treatments have been tried with surgical excision, chemotherapy and steroids [12]. In patients with associated Kaposi's sarcoma monthly polychemotherapy (e.g.: cyclophosphamide, vincristine, doxorubicin and prednisone) has been tried with limited success [9]. Anti-IL 6 antibodies have shown success with systemic symptoms, as have steroids. Most treatment modalities involve immunosuppression, increasing the chances of opportunistic infections [12]. Recent suggestions are that treatment with the anti-herpes virus drug ganciclovir or the anti-CD20 B cell monoclonal antibody, rituximab, may markedly improve outcome [9].

#### 4. Conclusion

This case report is presented for the purpose of its rare incidence. Mediastinal lymph nodes are involved by CD and may be confused with other common causes of neck lymphadenopathy like tuberculosis, lymphoma and nodal secondaries. Surgical resection of the tumors in the unicentric localized type of CD is the Diagnostic & Therapeutic Procedure of choice. We should never miss the fact that all patients diagnosed with CD should receive a systemic survey to exclude the possibility of ignored lesions or double pathologies and the importance of regular follow ups to monitor the possibility of recurrence.

#### Provenance and peer review

Not commissioned, externally peer-reviewed.

#### Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editor of this journal.

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#### Credit authorship contribution statement

Mohamed Saadallah was responsible for collecting information of the current case, performing a literature review, and writing the manuscript.

#### Declaration of competing interest

None declared.

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