

## CASTLEMAN'S DISEASE – CASE REPORT

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We report a case of a 16-year-old girl with hyaline-vascular type of abdominal Castleman's disease. The patient presented with a history of palpable mass below left ribcage for 6 months. On admission the girl was in good general condition. Physical examination showed a palpable mass in the left hemiabdomen but was otherwise unremarkable. Laboratory findings were within normal limits except hypergammaglobulinemia with elevated immunoglobulin A level. Computed tomography (CT) revealed well-demarcated homogeneous mass, extending from left diaphragm to the lower pole of left kidney, as well as from peritoneum to the pancreas. CT-guided biopsy was performed. A biopsy material was considered insufficient for definitive diagnosis. A complete surgical resection was done, and a diagnosis of hyaline-vascular type of Castleman's disease was established. Eight years after surgery the patient is in complete remission. **Conclusion** - Castleman's disease is a rare benign lymphoproliferative disorder, whose early recognition can be difficult due to nonspecific symptoms and radiologic findings. The right pathohistological diagnosis and appropriate staging of the disease are crucial in the treatment planning.

**Key words:** Castleman's disease ▪ Lymphoproliferative disorder  
▪ Child

### Introduction

Castleman's disease (CD) is a benign lymphoproliferative disorder, with unknown aetiology. There are localized or unicentric and systemic or multicentric forms. CD most often presents as a solitary soft tissue mass in the mediastinum, and may be located extra-thoracically: in the neck,

mesenterium, the pancreas, the glands, retroperitoneum, the pelvis, the femoral region, the bone marrow and intracranially (1, 2, 3). It is divided histologically into three types: the hyaline vascular type, the plasma cell and mixed type (4, 5).

Surgery is the therapeutic method of choice when the disease is localized. In treating disseminated CB partial surgical resection is used, along with steroids, chemotherapy, and radiotherapy (6). This study presents a patient with a rare abdominal location of CB.

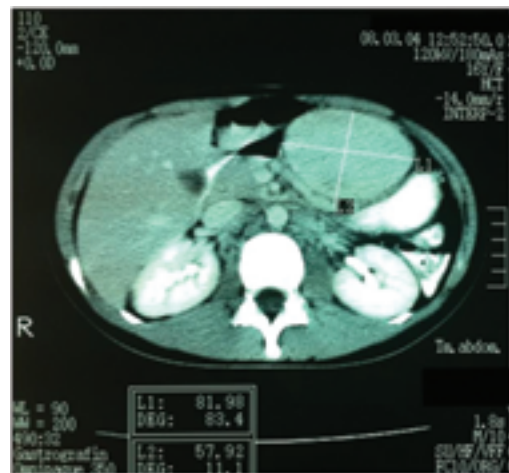
### Case report

A 16-year old girl was admitted to the Paediatrics Clinic of Clinical Hospital Centre Rijeka for to a palpable, painless swelling under the left rib cage, which she had noticed 6 months before admission. She did not have any other complaint. On admission the patient was in good general condition, non-febrile, with pale skin and pink visible mucous membranes. The peripheral lymph nodes were not palpable. There was a palpable mass under the left rib cage, 5 cm in diameter, painless, of a hard consistency and fixed to a base. Otherwise her somatic and neurological finding was normal.

Laboratory results, including sedimentation rate, complete blood count, kidney and liver function tests, C-reactive protein, lactate dehydrogenase, ferritin, copper, and coagulation tests were within reference values. Hypergammaglobulinemia was present ( $\gamma$ -globulins 16.3 g/l) with raised immunoglobulin A (3.39 g/l; reference values: 0.40–2.40 g/l). Serological tests for Epstein-Barr virus, cytomegalovirus, herpes simplex virus, human immunodeficiency virus and *Toxoplasma gondii* were negative.

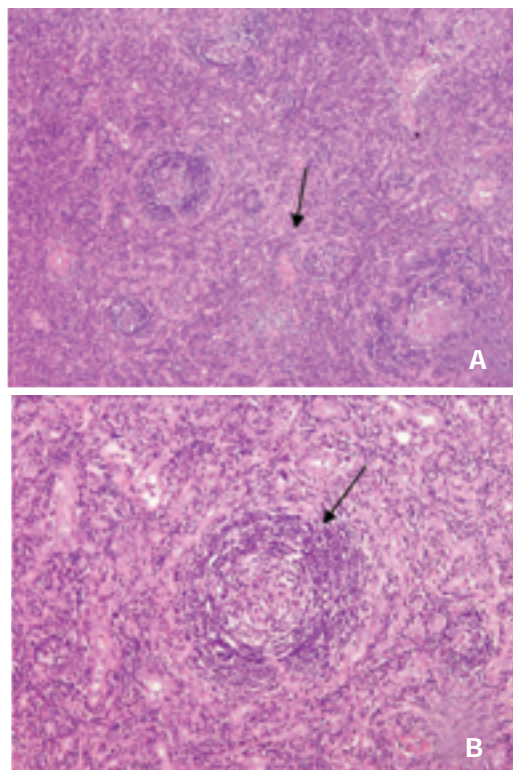
Chest X-ray and ultrasound (US) of the neck, the axillary and supraclavicular regions were normal. Abdominal US showed a homo-

geneous mass under the left rib cage, 100x60 mm in size, sharply delineated, and displacing the surrounding intestinal coil and stretching dorsally to the tail of the pancreas. CT confirmed a 110x85x60 mm mass, stretching from the left diaphragm to the lower half of the left kidney, and in the front from the peritoneum dorsally to the body and tail of the pancreas, which it was slightly depressing. The formation was well delineated, homogeneous, with native absorption values 50 Hounsfield units (HU), that is slightly lower than the surrounding muscle, and post-contrast it opacified evenly with values around 100 HU. There were no signs of retroperitoneal or mesenteric lymphadenopathy (Fig. 1).



**Fig. 1** CT image of the abdomen with contrast showing the well delineated homogeneous mass 110x85x60 mm in size.

A CT guided fine needle biopsy was done. The obtained material contained some tissue, imbued with multiplied capillaries or arborized shape, between which there was some mononuclear infiltrate composed of lymphocytes and many plasma cells. In the opinion of the pathologist the sample was scarce and the most probable diagnosis was an inflammatory pseudo-tumour.



**Fig. 2** The hyaline-vascular type of Castleman's disease with prominent interfollicular vascular proliferation (A) and palisade of small lymphocytes around the residual germinal centre (B) (arrow).

After presentation to the paediatricsurgical-radiological consultation board, the patient was referred for surgery. Complete surgical resection was performed. The post-operative course was normal. Patho-histological examination established the definite diagnosis of hyaline-vascular type of CD (Fig. 2). During the follow-up, the girl was monitored clinically and by US. Eight years after the surgery she is in good general condition and has no signs of illness.

## Discussion

Castleman's disease was first described by Benjamin Castleman in 1954 in a patient with a large mediastinal mass similar to a tumour

(7). The many titles used in literature for this disease are: angiofollicular lymph node hyperplasia (8), angiomatose lymphoid hamartoma (9), giant lymph-node hyperplasia (1), benign giant lymphoma, follicular lymphoreticular and lymph node hamartoma (10). Two entities are distinguished clinically: localized or unicentric CD (affecting one group of lymph nodes) and disseminated or multicentric (affecting two or more groups of lymph nodes). The peak of incidence is in the third and fourth decades for the localized form, and in the fourth and fifth decades for the disseminated form of the disease. CD is rare in children (11).

The precise pathogenesis of CD is unknown (12). The key role of interleukin-6 (IL-6) has been shown in lympho-vascular proliferation and systemic manifestations of the disease (13). Yorshizaki et al., first reported a patient with elevated concentrations of IL-6 which normalized after excision of the affected lymph nodes with the disappearance of all clinical symptoms (14). The universal presence of human herpes virus 8 (HHV-8) has been shown in multicentric CD in patients who are positive for human immunodeficiency virus (HIV), and its sporadic presence has been found in HIV negative patients. Although HHV-8 produces a viral analogue of IL-6, which is very similar to human IL-6 (15), it cannot be considered a risk factor for the occurrence of the disease (12).

Histologically, the disease is classified in three types: hyaline-vascular, plasma cell and mixed. There is also a plasmablast variant associated with HHV-8 and HIV. Localized CD is mainly of the hyaline-vascular type (5, 16). Most disseminated forms of CD are the plasma cell type or, in HIV positive patients, the plasmablast type.

Hyaline-vascular type of localized CD is mostly asymptomatic. In some cases there may be afever, night sweats or loss of weight (5, 16). Plasma cell type of localized CD and

multicentric CD present with many systemic symptoms: fever, night sweats, loss of body weight, anaemia, peripheral lymphadenopathy, hepatosplenomegaly, skin rash, respiratory and renal insufficiency (5). Disseminated CD is most often characterised by an aggressive clinical course, complicated with infections, autoimmune anaemia, sarcoidosis and amyloidosis. It has been described in association with POEMS syndrome (polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin changes) and malignant neoplasms, most often lymphoma, follicular dendritic cell sarcoma and Kaposi's sarcoma in HIV positive patients (5, 14, 17). Spontaneous remission is very rare. The prognosis of disseminated plasma cell CD is worse than disseminated hyaline-vascular or mixed hyaline-vascular and plasma cell types (4, 5, 18).

CD may develop in any part of the body where there are lymph nodes. In most adult patients it is localized in the mediastinum. The involvement of other thoracic structures has also been described: the pericardium, the lungs, the thoracic and intercostal spaces (19, 20). In children and adolescents it is most often located in the abdomen, the neck, the mediastinum and the pulmonary hilus (21).

Mediastinal tumours are usually asymptomatic. Sometimes problems are present resulting from localized compression (coughing, chest pain, dyspnea). Invasion and adhesion of blood vessels and the bronchi are frequent and make surgical excision more difficult (11, 20). Abdominal CD sometimes presents with abdominal pain (22). Also, it may be associated with rare clinical conditions such as amyloidosis, nephrotic syndrome, myasthenia gravis, peripheral neuropathy, pemphigus vulgaris, thrombocytopenia and thrombotic thrombocytopenic purpura (5, 23). In childhood the typical triad of symptoms is described: anaemia, hypergammaglobulinemia and developmental delay (12).

The most frequent cause of anaemia is a chronic/inflammatory disease, but there are also other unexplained causes (24). Extreme anaemia in mesenteric CD is the consequence of weak iron resorption from the mucous cells of the intestines in the interstitium and reduced mobilization of iron from the tissue stores (25). Complete surgical resection of the solid lesion is accompanied by normalization of all haematological abnormalities (3).

The radiological characteristics of CD are not specific. US most often shows a homogeneous hypoechogenic formation (26). On CT lesions with diameter less than 5 cm have homogeneous vascular appearance, whilst larger lesions are most often heterogeneous with central low attenuation, due to the presence of fibrosis and necrosis (27). The hyaline-vascular type presents in three ways on CT: as a solitary non-invasive mass, a dominant infiltrating mass accompanied by lymphadenopathy or matted lymphadenopathy with no dominant mass (20). It is difficult using radiological methods to differentiate CD from other malignant diseases, above all lymphomas and sarcomas (27).

Needle biopsy is not recommended in the diagnostic procedure, since it usually does not obtain a sufficient quantity of tissue for pathohistological analysis. Moreover, incision biopsy increases the risk of bleeding or dissemination of the tumour (26, 28). Therefore, open surgical biopsy with removal of the lesion, whenever this is possible, has the advantage in setting the diagnosis (29).

Treatment depends on the spread of the disease. The treatment of choice for the localized form is complete surgical resection (12, 16), which is followed by the disappearance of all the general symptoms present (1). The surgical procedure may be complicated by significant blood loss, because the formation is well vascularized. Shawn et al., described the positive effect of pre-operative

embolization of the tumour to prevent bleeding (29). In treating incompletely resectable or non-resectable lesions, adjuvant therapy is used and/or steroids and chemotherapy (12, 30, 31). In these cases promising results stem from neoadjuvant use of Rituximab, monoclonal anti CD20 antibody (32).

The optimal therapy approach for disseminated CD has not been agreed (18, 30, 31). Surgical resection has no purpose (5). In treatment corticosteroids cytotoxic drugs (most often chemotherapy protocols for non-Hodgkin lymphomas) (33) and immunotherapy (monoclonal antibodies, thalidomide, interferon) are given. Apart from Rituximab, monoclonal antibodies to receptors for IL-6 (Tocilizumab) are used (34), and results are also expected from Phase II clinical trial of Siltuximab, monoclonal antibody to IL-6 (35). The effectiveness has been described of immunomodulatory therapy with interferon alpha and Thalidomide (36) and Anakinra (antagonist of receptors for IL-1) (37).

This paper presents paediatric CD in a rare location. The disease presented clinically as a palpable abdominal mass. Hypergammaglobulinemia was the only laboratory abnormality. A definite diagnosis was made by pathohistological analysis of the extirpa-

ted lymph node. Our case indicates that CD, although very rare, should be considered in children with solid hypervascular abdominal masses. In localized forms, complete surgical resection is the method of choice. Recurrence, although extremely rare, is possible and therefore long-term monitoring is recommended for these paediatric patients.

## Conclusion

CD is a rare benign lymphoproliferative disorder, whose early recognition is made difficult by its non-specific symptoms and radiological characteristics. Precise pathohistological diagnosis and staging of the disease are key in planning therapy. The prognosis of the localized form is excellent after complete surgical resection.

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