Introduction

Castleman disease (giant lymph node hyperplasia, angiomatous lymphoid hamartoma) refers to an accumulation of non-neoplastic lymphoid tissues interspersed with plasma cells and blood vessels (1,2). The most frequent site is the thorax (33%), but lesions may also be found in the abdomen (30%), peripheral lymph nodes (30%), pelvis and various organs (10%) (3,4,5). Three histologic variants (hyaline vascular, plasma cell, and mixed) and two clinical types (localized and multicentric) have been described for Castleman disease (CD). Localized disease generally presents with a single enlarged lymph node or a widening of the mediastinum, whereas multicentric disease is a systemic lymphoproliferative disorder characterized by lymphadenopathy, hepatosplenomegaly, constitutional symptoms, anemia, hypoalbuminemia, and hypergammaglobulinemia (6). The hyaline vascular variant is typically characterized by a benign clinical course with no constitutional symptoms other than pressure of the mass itself (7).

With this report, a case of localized, hyaline vascular type CD admitted with a productive cough and recurrent pulmonary infections and diagnosed as bronchiectasis, is presented. In the follow-up period, imaging techniques demonstrated the existence of a subcarinal mass leading to the diagnosis of CD. Bronchiec-
tasis may be present from birth or may develop as a result of airway obstruction or inflammation in response to chronic or repeated infection. It may also occasionally occur secondary to the pressure of a mass (8). CD is a rare disease which may present as a mass leading to bronchiectasis in childhood. In presenting this patient, we suggest that CD needs to be considered in the differential diagnosis of mediastinal mass leading to bronchiectasis.

Case Report
A 12-year-old boy was admitted with the complaints of productive cough and frequently recurring pulmonary infection. At 6 months of age, he had first experienced bronchopneumonia, accompanied by oral moniliasis and impetigo and was hospitalized. At that time he was found to have thalassemia trait.

From that time on, he had suffered from recurrent respiratory tract infections, all of which were mild to moderate in intensity, not requiring hospitalization. During the last two years, his symptoms recurred more frequently and he was admitted to different health centers, but unfortunately a definite diagnosis could not be reached. Ultimately he was referred to our hospital for further evaluation and diagnosis. He had a history of allergy for sulfonamides. The family history revealed that both his mother and brother had thalassemia trait.

Physical examination: Body weight was 30 kg (3-10th perc.), height was 135 cm (3-10th perc.), arterial blood pressure was 110/60 mmHg, and heart rate was 100 per minute. Bilateral crepitations were heard in lung auscultation, predominantly in the right middle lobe. This finding initially supported pneumonia being more prominent in the right middle lobe. The liver and the spleen were nonpalpable. The examination of other systems was normal.

Laboratory analyses: Hematologic parameters were: hemoglobin 9.8 g/dl, hematocrit 27.4%, red blood cell count 5 080 000/mm³, MCV 54, MCH 19.3, MCHC 35.8, platelet count 580 000/mm³, white blood cell count 8100/mm³ with a differential count of 58% neutrophils and 42% lymphocytes. Microcytic anemia was considered and the hemoglobin electrophoresis revealed a HbA2 of 3.6% and a HbF of 8%, supporting the diagnosis of thalassemia trait. Urine examination, serum electrolytes, renal and hepatic function tests, total protein, and albumin were in normal ranges.

Immunologic studies on the patient revealed a normal neutrophil burst test by flow cytometry. Serum immunoglobulin (Ig)G, IgM, IgA, IgE levels were 1475 mg/dl, 76 mg/dl, 272 mg/dl, 21.1 IU/m, respectively and in the normal ranges. Lymphocyte phenotyping by flow cytometry were as follows: CD3+ T lymphocytes 60%, CD19+ B lymphocytes 19%, CD4+ T lymphocytes 30%, CD8+ T lymphocytes 32%, CD16+56+ cells 2%, HLA DR+ active T cells 9%; all being in the normal range. Total hemolytic complement activity was normal. Size of the induration of the Candida dermal test was normal (10 mm), size of the induration of the tuberculin test was 3 mm. Serology was negative for HIV.

A chest x-ray demonstrated infiltrations in the middle lobe of the right lung. This finding, along with the history of frequent pulmonary infections and associated productive cough, led us to consider bronchiectasis. Computerized thorax tomography (CT) revealed collapse and bronchiectasis of the middle lobe and bronchiectasis in the posterior and lateral segments of the right lower lobe (Figure 1). Additionally a subcarinal mass 3.5 cm in diameter was detected. Magnetic resonance imaging showed that the subcarinal mass was a cystic lesion extending towards the azygosophageal recessus on the right side (Figure 2). With a tentative diagnosis of a bronchogenic cyst or cystic lymphadenopathy the patient underwent surgical operation, also for diagnostic purposes. The right middle lobe was found to be collapsed and bronchiectatic. Only the subcarinal mass underwent complete resection. Histopathological examination of the mass was consistent with hyaline vascular type CD (Figure 3).

Discussion
Since Castleman and Towne first described hyperplasia of the mediastinal lymph nodes in 1954, many cases of CD have been reported (9). Castleman disease is a heterogenous group of lymphoproliferative disorders of uncertain cause. The disease takes its place in the group of disorders leading to lymphadenopathy and its incidence among the nodal pathologies with indication of excisional biopsy is 1/68 (10). Castleman disease is also accepted as one of the nonlymphomatous pulmonary lymphoproliferative disorders. Nonlymphomatous pulmonary lymphoproliferative disorders other than CD include plasma cell granuloma, pseudolymphoma,
lymphocytic interstitial pneumonitis, angioimmunoblastic lymphadenopathy, and lymphomatoid granulomatosis. All these disorders are thought to represent a hyperplasia of the pulmonary immune system in response to chronic antigenic stimulation (11).

Two distinct histologic variants have been described in CD. At present, it is not clear whether the variants represent two stages of one syndrome, two different host reactions to the same etiologic agent, or two unrelated clinicopathologic entities (1). The cause of localized CD is still unknown. Human herpes virus 8 (HHV-8) or Capost’s sarcoma-associated herpes virus are suggested to be responsible for the etiology of multicentric CD (12). Interleukin 6 is another factor that may contribute to the etiology. Continuous overproduction of IL6 is observed in patients with some immune-inflammatory diseases such as CD and rheumatoid arthritis. The lack of cytogenetic abnormalities in CD supports the hypothesis that CD is an interleukin-6-driven lymphoproliferative disorder (13).

Castleman disease is divided histologically into 3 types: hyaline vascular, plasma cell type and mixed. The hyaline-vascular type is more common. In a study presenting 17 cases of CD with abdominal localization; 11 localized (8 hyaline, 3 plasma cell types) and 6 multicentric (3 hyaline, 3 plasma cell types) CD cases have been reported (14). Although the hyaline-vascular type appears to have a benign course, it has been demonstrated to lead to follicular dendritic cell sarcoma in the nasopharynx (15). Our patient also showed the histological characteristics of the hyaline-vascular type.

Two-thirds of the cases with the localized type occur in the mediastinum. Atypical thoracic CD involving the pleura, the intercostal fossa, the intercostal spaces, the pericardium, and the chest wall have all been reported (16,17,18). In our patient, a solid, well-circumscribed, expansive mass in the subcarinal region was detected preoperatively by imaging procedures. Parenchymal lung involvement is also rare in the localized type CD. Two examples for this type of involvement have been presented by Spedini and Leung (19,20). The first one was a 51-year-old male who had a thick, not homogenous lesion of lobular shape, localized between the right middle and lower lobes; and the other was a 30-year-old female having a localized, hyaline-vascular type CD localized in the interlobar fissure between the right middle and lower lobes.

Parenchymal lung involvement is more common in the systemic type. An evaluation of CT findings in 12 cases with intrathoracic multicentric CD revealed the presence of bilateral hilar and mediastinal lymphadenopathy and centrilobular nodular opacities. The pulmonary parenchymal findings were thought to be secondary to the associated interstitial pneumonitis. Subpleural nodules, ground-glass attenuation, airspace consolidation, and bronchiectasis have been reported by the same authors as less common findings (21). Bronchiectasis has been reported as a rare finding even in the systemic form of CD. Our patient is one of these rare cases.

Our patient was evaluated for possible immune deficiency because of a history of recurrent lower respiratory tract infections. However, immune deficiency was ruled out because the basic immunologic evaluations were normal and also because the bronchiectasis was localized. Subsequently, we focused on etiologies causing a subcarinal mass and a diagnosis of CD was finally reached by surgical intervention. We could not determine a relationship between CD and the presence of a thalassemia trait. However, the triad of anaemia, hypergammaglobulinaemia, and failure to thrive has been described in patients with CD (3).

Our case was accepted as a localized form of CD because of its subcarinal localization and lack of systemic findings such as hepatosplenomegaly, constitutional symptoms, anaemia, hypoalbuminemia, and hypergammaglobulinaemia. Although localized type is classically asymptomatic, our case presented with recurrent respiratory tract infections. It is likely that recurrent pulmonary infections in our patient are a major contributor to the development of the bronchiectasis. We sug-
gest that bronchiectasis in this patient was the result of drainage failure due to the pressure of the subcarinal mass and that the recurrent infections may have contributed to its spread to a wider area.

Surgery is indicated in localized CD. Cure is obtained by the total resection of the mass (17,22). Although surgery is considered as the therapy of choice for localized CD, favourable responses to radiotherapy also have been documented. Surgery results in excellent rates of cure in patients with localized CD; radiotherapy can also achieve a clinical response and cure in selected patients. Multicentric CD is a more aggressive clinical entity and is most effectively treated with combination chemotherapy (23). Recently interferon-alpha has been introduced for the treatment of multicentric CD, since it is an atypical lymphoproliferative disorder (24). The new therapeutic strategy for CD is the administration of humanized antibody to human IL 6 receptor (25).

In our patient, the subcarinal mass was totally resected and a follow-up protocol was started. Radical tumour resection was performed with successful results in a patient with paracardiac pleural CD, a similar location to that of our patient (26). In conclusion, we advance that CD, although a rare disorder, needs to be considered in the work up of bronchiectasis in children.

References