İnönü Üniversitesi Tıp Fakültesi Dergisi
8(2) 92-94 (2001)

Castleman's Disease Associated with Annular Pancreas and Down Syndrome in An Infant

Sema Uguralp*, Murat Mutus*, Oğuz Turhan**, Mehmet Demircan*

* İnönü University School of Medicine, Departments of Pediatric, Malatya, TURKEY
** State Hospital, Rize, TURKEY

A patient with Down syndrome who had an operation for proximal intestinal atresia in the newborn period and had the diagnoses of annular pancreas, duodenal atresia, and malrotation was admitted a second time when he was 13 months old with intestinal obstruction due to adh esions. Histopathology of the resected necrotic ileal segment in the operation was reported as Castleman's disease of hyaline vascular type.

Key words: Infant, Annular Pancreas, Castleman's Disease, Down Syndrome

Bir İnfantta Down Sendromu Ve Annüler Pankreasla Birlikte Castleman Hastalığı

Yenidoğan döneminde proksimal intestinal atrezi nedeniyle opere edilmiş ve laparotomisinde annüler pankreas, duedonal atrezi ve malrotasyon tanıları alan Down sendromlu bir olgu 13 aylıkken brid ileus nedeniyle tekrar başvurdu. Yapılan operasyonda nekroz nedeniyle rezeke edilen ileum segmentinin histopatolojik muayenesi hyalen vasküler tip Castleman hastalığı olarak rapor edildi.

Anahtar kelimeler: Süt Çocuğu, Annüler Pankreas, Castleman Hastalığı, Down Sendromu

Angiofollicular lymph node hyperplasia or Castleman's disease (CD) was first descri bed by Castleman and colleagues in 1956.[1] Keller et al. classified the lesions into two types based on clinical and pat hological criteria. Castleman's disease can be divided into three types on the b asis of clinical features and histolog ical findings: hyaline vascular (HV) type, plasma cell type, and intermediate variant type. [2] The plasma cell type seems to be more common in children than in adults. Recently, multicentric CD defined as a lymphoprolife rative disorder with similar histologic features but more generalized or extensive lymph node involvement has been reported. [3] It was noted that the HV type is rarely associated with symptoms except when these lesions compress adjacent structures. Castleman 's disease usually appears as a localized form, especially in children. In contrast to the relativel y benign clinical course of the localized forms, the multicentric form of the disease carries significant morbidity and mortality. [4,5] The latter type is associated with a poor prognosis and can be associated with the development of lymphoma and infections. [6] The most common sites for CD in childhood and adolescence are the abdomen, the m ediastinum, and the hila of the lungs. Although it has been reported at a ll ages, most patients are between 30 and 40 years of age at presentation. [5]

This report described coexistence of Down Syndrome and HV type CD origina ting from the mesentery in a 13 month-old-boy.

CASE

A 13-month-old-boy presented with high fever, vomi ting, and signs of intestinal obstruction in the past 48 hours.

In his history, the neonate had a laparotomy with the preoperative diagnosis of prox imal intestinal atresia when he was 72 hours old. At exploratory laparotomy, extrinsic du odenal atresia due to annular pancreas, and intestinal

malrotation was found, and retrocolic isoperistaltic duodenojejunostomy and Ladd procedure had been performed. Chromosome analysis showed trisomy 21.

At admission, mongoloid face, apathic appearance, mental retardation, pale skin, failure to thrive, decreased skin turgor-tonus, 39^0C fever were present. There were no abdominal distention or rigidity, but bowel sounds were hyperactive. He had no other abnormal physical findings.

The whole blood count revealed $14x10^3$/uL of white blood cell, 9 g/dl of hemoglobin, and 29,1 % of hematocrit, $496X10^3$/uL of platelet. Upright abdominal radiography showed multiple air-fluid levels.

Although nasogastric decompression, antibiotic treatment and parenteral nutrition were administered, intestinal obstruction signs did not improve.

During the exploratory laparotomy, a necrotic ileal segment due to adhesions was found and an end to end ileoileal anastomosis was done. Histologically, mesenteric lymph node of the resected segment showed non-active lymphoid follicles showing hyalinized vascularization without germinal centers. There were extensive proliferation of capillaries and plasma cells in the interfollicular area (Figure 1).

A five-year follow-up period was asymptomatic.

DISCUSSION

Castleman's disease is a lymphoproliferative disorder of unknown and controversial etiology and has been mainly reported in adults.[5] In the recent review by Parez et al. on 76 pediatric cases of CD, 20 were older than the age of 15 and mesenterial involvement were present in 14 cases. There were 7 patients under the age of 2, and 3 of these were symptomatic.[7] A noteworthy finding in this report was the difficulty of diagnosing the asymptomatic patients of younger age. Diagnosis in our case could only be achieved when operated for bowel obstruction, otherwise the lesion would have remain undiagnosed until adulthood. Early diagnosis of mesenteric CD, especially in children is difficult.[8] This may be explained by the long-standing nature of the disease. Retrospective evaluation of our patient suggests that the anemia and failure to thrive might have been related to the disease.

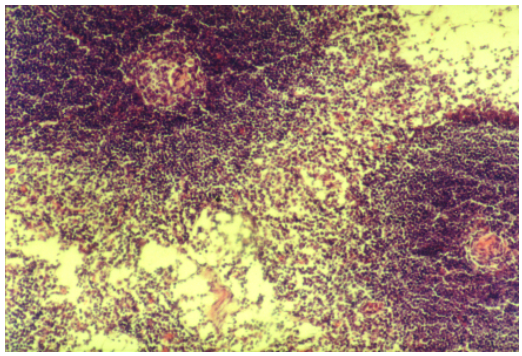

Figure 1. Lymphoid tissue showing hyalinized central vessel (H.E. x 100)

Although the etiology of CD is unclear, the hyaline vascular type seems to be a chronic reactive lymphoid hyperplasia. Possible etiologic factors include an abnormal immune reaction or immune dysregulation, or an endothelial proliferation or proliferation of autoantibody producing B cells. Even though the etiologic agent remains unclear, the stimulus for the B-cell proliferation intervening the production of interleukin 6 (IL-6), a B cell growth factor, being secreted by germinal centers is a recently proposed cause of the disease. The symptoms, signs and abnormal laboratory findings of CD may resolve with monoclonal anti IL-6 antibody treatment.[9,10]

Most pediatric cases are asymptomatic and detected incidentally, or present with the signs of local growth.[5] The symptoms are generally nonspecific (fever, anemia, failure to thrive, weight loss, fatigue, pain, recurrent infections). Laboratory abnormalities were more often associated with the plasma cell type and were mainly represented by anemia and hypergammaglobulinemia. Treatment of the localized tumor consisted of surgical excision, whereas treatment of the multicentric form was medical, comprising retinoic acid, prednisone and other immunosuppressor drugs.[7,11]

In the review of Turkish literature, Arslan et al. have reported a multicentric CD in a 8 year old patient that have been treated medically. The lesion relapsed in 6 months of follow up due to resistance of multicentric form to medical treatment. Hepatic and splenic enlargement is observed in majority of multicentric form. Lymphadenopathy is universal. Skin rashes, neurologic and rheumatologic manifestations are common.[4]

In CD the reported tumor sizes were ranging from 0,5 to 15 cm.[7] In our case, the 13-month-old baby had a single lymph node of 0,5 cm in diameter. The smallest mass reported in the literature was an asymptomatic neck CD in a 1,5 ye ar old patient of 0,5 cm in size, with mixed type of pathology.[12] Due to early diagnosis, our patient has shown a small sized CD case with typical lymph node morphology.

Immune system disorders are frequently seen in Down syndrome patients. Castleman's d isease is also a lymphoproliferative system disorder, and commonly coexist with diseases suppressing the immune system.[13] Development of malignant lymphoma and Kaposi's sarcoma has been reported especially in patients with multicentric CD, and rarely in lo calized disease.[14,15] This finding stresses the importance of long-term follow-up in these patients. Localized disease can be treated successfully by surgical removal of the mass.[14] Therefore, early diagnosis and interventions are essential in the localized form of the disease. Although the coexistence of CD, annular pancreas and Down syndrome in our patient may be incidental, we suggest that when nonspecific sign and symptoms of unknown origin are present in trisomy 21 patients, CD may be considered in the differential diagnosis.

REFERENCES

1- Castleman B, Iverson L, Menendez VP. Localized mediastinal lymph -node hyperplasia resembling thymoma. Cancer 1956;9:822 -30.
2- Keller AR, Hochholzer L,Castleman B. Hyaline vascular and plasma cell types of giant lymph node hyperplasia of mediastinum and other locations. Cancer 1972;29:670-83.
3- 0'Reilly Jr PE, Joshi VV, Holbrook CT, Weisenburger DD. Distinctive case. Multicentric Castleman's disease in a child with prominent thymic involvement. A case report and brief rev iew of the literature. Modern Pathol 1993;6:776 -80.
4- Arslan D, Öztürk F, Patıroğlu T, Küçükaydın M, Gündüz Z. Castleman's Disease. A case report. Turkish J Pediatr 1996;38:361 -66.
5- Salisbury JR. Castleman's disease in childhood and adolescence: report of a case and review of the literature. Pediatr Pathol 1990;10:609 -15.
6- Advani R, Warnke R, Rosenberg S. Treatment of multicentric Castleman's disease complicated by the development of non -Hodking's lymphoma with high -dose chemotherapy and autologous peripheral stem -cell support. Ann Oncol 1999;10:1207-9.
7- N.Parez, B. Bader-Meunier, C.C.Roy, J.P.Dommergues. Paediatric Castleman disease: report of seven cases and review of the literature. Eur J Pediatr 1999;158:631-37.
8- Rieu P, Droz D, Gessain A, Grunfeld JP, Hermine O. Retinoic acid for treatment of multicentric Castleman's disease. Lancet 1999;354:1262-3.
9- Hung I-J, Kuo T, Lin J-N. New observations in a child with angiofollicular lymph node hyperplasia (Castleman's Disease) originated from the mesenteric root. Am J Pediatr Hematol/Oncol 1992;14:255 -60.
10- Yoshizaki K, Matsuda T, Nishimoto N, et al. Pathogenic significance of interleukin-6 (IL-6/BSF-2) in Castleman's disease. Blood 1989;74:1360 -67.
11- Beck JT, Hsu SM, Wijdenes J, et al. Alleviation of systemic manifestations of Castleman's disease by monoclonal anti -interleukin-6 antibody. N Engl J Med 1994;330:602-605.
12- Baruch Y, Ben-Arie Y, Kerner H, Lorber M, Best LA, Gershoni -Baruch R. Giant lymph node hyperplasia (Castleman's disease). A clinical study of eight patients. Postgrad Med J 1991;67:366 -70.
13- Frizzera G. Castleman's disease an d related disorders. Semin Diagn Pathol 1988;5: 346-64.
14- Weisenburger DD, Nathwani BN, Winberg CD, Rappaport H. Multicentric angiofollicular lymph node hyperplasia. Hum Pathol 1985;16:162 -72.
15- Vasef M, Katzin WE, Mendelsohn G, Reydman M. Report of a case of localized Castleman's disease with progression to malignant lymphoma. Am J Clin Pathol 1992;98:633-36.

Correspondence Address:
Sema Uguralp MD,
Department of Pediatric Surgery
Turgut Özal Medical Center, Malatya, Turkey.