Liver Involvement in Langerhans’ Cell Histiocytosis. Case Report

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Abstract

Langerhans’cell histiocytosis (Histiocytosis X) is a rare disease of unknown cause characterized by oligoclonal proliferation of Langerhans cells. It occurs mostly in children and young adults and involves one or more body systems such as bone, hypothalamus, posterior pituitary gland, lymph nodes, liver or various soft tissues. The diagnosis is always made by a histological approach. We report a case of Langerhans’cell histiocytosis in a young patient with clinical signs of diabetes insipidus and hepatic involvement in whom the immunohistochemical analysis of the liver tissue led to the definitive diagnosis.

Key words

Langerhans’cell histiocytosis - diabetes insipidus - S100 protein

Introduction

Langerhans’cell histiocytosis (Histiocytosis X) is a clonal proliferative disorder of the Langerhans cells (1,2). The clinical presentation may be variable, either solitary disease of the bone, or severe multisystemic involvement (lung, bone, liver, spleen, lymph nodes, hypothalamus, pituitary gland, gastrointestinal tract). Langerhans’cell histiocytosis typically occurs in children and adolescents, but can develop in all age groups, with a male predominance (3). The diagnosis is based on cytology or histology in combination with immunohistochemical tests for S100 protein expression (4,5). We present a case of Langerhans’ cell histiocytosis in a young male patient with neurological symptoms (diabetes insipidus) and subclinical hepatic involvement that helped us establish the diagnosis using histological and immunohistochemical techniques.

Case report

A 31 year old man came to our attention for non specific symptoms such as progressive lethargy, fatigue, anorexia and a 30 kg weight loss in association with polydipsia (5-6 l fluids per day) and polyuria. These symptoms had developed over an 8 month period. His family history was unremarkable and no toxic habits apart from cigarette smoking were present. Physical examination showed a skinny, ill appearing patient with a mild pallor. He was afebrile and anicteric and systemic examination revealed no abnormality. The laboratory data evidenced a marked inflammatory syndrome - erythrocyte sedimentation rate (ESR) 84mm/h, leucocytosis 18x10³/mm³, fibrinogen 800mg/dl (NV<550), a mild anemia – hemoglobin 11.8g/dl, cholestasis - alkaline phosphatase 499U/L (NV<126) and GGT 514 U/L (NV<85) with normal bilirubin and aminotransferase levels. Hepatitis B virus surface antigen as well as hepatitis C antibodies and human immuno-deficiency virus antibody were negative. Alpha-fetoprotein, carcinoembryonic antigen (CEA) and CA19-9 concentrations were also normal. Urinalysis evidenced isostenuria. Abdominal ultra-
sonography revealed a diffusely inhomogeneous echotexture of the liver suggestive of parenchymatous infiltration or liver metastases as well as multiple celiac lymph nodes (<1 cm in greater diameter). There were no lytic bone lesions of the skull or spine on radiological examination. Sella was normal in size and contour. The chest X-ray film detected no pulmonary infiltration. Computerized tomography (CT) of the abdomen confirmed the findings on sonography, and brain CT scanning showed no abnormality. In order to complete the investigations, gastroscopy and colonoscopy were performed but revealed no involvement of the gastrointestinal tract.

Finally, the patient underwent diagnostic laparoscopy which evidenced multiple liver nodules of variable size ranging from 0.5 to 1 cm (Fig.1); celiac lymph nodes were also detected. Liver biopsies were taken and the histological examination with immunohistochemical analysis led to the diagnosis of Langerhans’cell histiocytosis. The hepatic granulomas consisted predominantly of macrophages, intermixed with eosinophils (Fig.2). The macrophages showed strong positivity to antibodies to S100 antigen, indicating the diagnosis of histiocytosis X (Fig.3). Mib1 (proliferation marker Ki-67) was positive in 5 – 10% of cells (Fig.4). The patient was referred to the hematological department for specific treatment.

**Discussion**

Langerhans’cell histiocytosis is a rare proliferative disorder (1) of the Langerhans cells (2). The term encompasses the formerly known entities of histiocytosis X that included Letterer Siwe disease, Hand Schuller Christian disease and eosinophilic granuloma. It occurs mostly in children and young adults, with males being affected more frequently than females (3). The clinical spectrum is broad, ranging from localized bone disease to severe multisystemic involvement (bone, pulmonary, pituitary, gastrointestinal tract, hepatic, cutaneous, lymph nodes). Clinical diagnosis largely depends on a high degree of suspicion. Diabetes insipidus together with the
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Liver parenchyma infiltration and the cholestatic pattern of liver tests found in our patient raised the suspicion of a granulomatous disease such as histiocytosis X, but we also considered other diagnosis such as hepatic metastasis or a lymphoproliferative disorder.

The definitive diagnosis is always based on histological examinations and confirmed by immunohistochemical tests. Data from literature showed that cells in Langerhans’cell histiocytosis are usually positive for S100 protein (4,5) and local proliferation is shown by immunostaining for Ki-67 (6), markers that helped establishing diagnosis in our case, too. Although CD1a is the most specific marker of Langerhans’cell histiocytosis, it was not detected in this patient. According to the Histiocyte Society classification (7) of Langerhans’cell histiocytosis that takes into account the number of organs involved (one or two organs: localized forms; at least 3 organs: multisystemic forms) we considered that our patient presented a multisystemic form of Langerhans’cell histiocytosis with hepatic, lymph node and pituitary involvement.

The extent of the disease has a significant effect on the course of the disease and on its prognosis. Multivisceral forms are associated with a 4-year survival rate of 60-80% (8,9). However, it seems that pituitary involvement is a protective factor for survival.

In conclusion, hepatic disease, although subclinical, was the clue of the diagnosis in this case of Langerhans’cell histiocytosis.

References