A RARE MULTISYSTEM LANGERHANS CELL HISTIOCYTOSIS PRESENTED WITH SCLEROSING CHOLANGITIS: CASE REPORT AND LITERATURE REVIEW

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ABSTRACT

Introduction*: Langerhans cell histiocytosis is a rare disease with unknown etiology. It occurs more in children and also in adults and involves one or more organs such as skin, bone, lung, hypothalamus, posterior pituitary gland, lymph nodes and other tissues. But liver involvement is rarely reported and pathological manifestation of sclerosing chlongitis is rare.*

Metholds*: We reported a case of langerhans cell histocytosis with multisystem involvement including skin, lungs, thyroid gland, rare liver, nails and possible spleen in a young adult man.*

Results*: Though he developed cholestasis and came to liver disease center firstly, he was diagnosed by infiltration of Langerhans cell in the skin and thyroid gland biopsy, with pathological manifestation of sclerosing cholongitis in liver biopsy.*

Conclusion*: It is a rare case with multi-organ involved.*

Keywords*: Langerhans cell histiocytosis, Sclerosing cholongitis, Skin, Lung, Nail.*

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Introduction

Biological studies have shown that systemic Langerhans cell histiocytosis (LCH) is a clonal proliferative disorder of the langerhans cells(1). Langerhans'cell histiocytosis typically occurs in children and rarely in adults, but can develop in all age groups, with a male predominance. The clinical presentation may be variable, either solitary disease of the bone, or severe multisystem involvement (lung, bone, liver, spleen, lymph nodes, hypothalamus, pituitary gland, gastrointestinal tract)(2).

We present a case of LCH in a young male patient with rare more than 5 organs involvement which the skin biopsy lead to the diagnosis of LCH and detection of other organs involvement including liver, thyroid gland, lungs and nails. But liver biopsy didn't show infiltration of Langerhans cells but sclerosing cholangitis(SC).

Case report

The 20 years-old young male was admitted into our liver disease department with chief complains low appetite, fatigue and jaundice for more than one year. At physical examination, he had normal vital signs such as blood pressure and tempreture, BMI is 23.6. An extensive coalescing, scaling, or crusted papules was found on his skin (Fig. 1A) and onycholysis, loss of nail plate, subungual hyperkeratosis could be seen in most of his fingernails (Fig. 1B). The yellow-stained sclera was also found. The bilateral thyroid was tumescent, the liver and spleen were not palpable under the cost arch. Family history was negative for rheumatic or inherited liver disease. No history of ethanol consumption and blood transmission. His family history was unremarkable and no toxic habits were present.

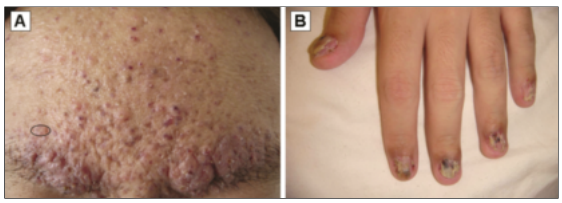

Fig. 1A. The facial skin is present with extensive coalescing, scaling, or crusted papules; **Fig. 1B**. Onycholysis, loss of nail plate, subungual hyperkeratosis of his fingernails in one hand.

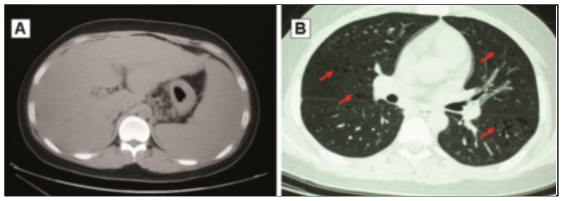

Fig. 2A. Computed tomography (CT) shows slpenomegaly, megaly of lymph node and low-density node of liver. **Fig. 2B**. Computed tomography (CT) showing multiple cystic pulmonary lesions indicating pulmonary LCH(Arrow target).

The laboratory data evidenced a mild anemia(hemoglobin 9.90g/dl) and higher cholestasis-alkaline phosphatase 456U/L (NV<126) and GGT 189 U/L (NV<85), total bilirubin 184.99 umol/l (NV<17.1), direct bilirubin 150.76 umol/l, aline aminotransferase 18 U/L (NV<40), T3, T4 were within normal range, but TSH was 14.88 UIU/ml (NV<6). The immunoglobin IgG was 3060mg/dl higher than normal. Viral hepatitis markers and antibody such as ANA and AMA were negative. All tumor antigens were normal. Urinalysis analysis showed urine specific gravity is 1.000 with no other abnormality.

Abdominal computed tomography (CT) revealed enlarged bile duct (Fig. 2A). Then the patient underwent diagnostic skin and liver biopsy. Liver biopsy showed that the formation of bile pigment granules and irregular intrahepatic duct wall, small bile duct proliferation and periductal fibrosis which is associated with SC (Fig. 3A,B). Skin biopsies were taken and the histological examination with immunohistochemical analysis led to the diagnosis of LCH. The skin pathology consisted predominantly of macrophages, intermixed with eosinophils. The macrophages showed strong positivity to antibodies to CD1a antigen, indicating the diagnosis of LCH (Fig. 3C).

The chest Computerized tomography (CT) scan detected the diffuse small cyst of lungs indicating involvement of these organs (Fig. 2B). At last the patient also received fine needle aspiration biopsy of thyroid gland again which also confirmed the diagnosis of LCH with positive CD1a immunohistochemical staining (Fig. 3D).

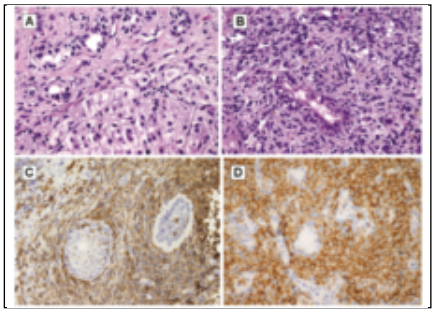

Fig. 3A. The liver biopsy show irregular bile duct wall, loss of bile duct and periductal fibrodis. **Fig. 3B**. Proliferation of ductile, enlarged bile duct(pyknic Arrow figure), infiltration of intestinal cells and mild periductal fibrosis(tenuis Arrow figure) in liver biopsy. **Fig. 3C**. Skin Biopsy: Immunohistochemical stain showing the macrophages being strong positivity to antibodies against CD1a antigen. **Fig. 3D**. Positive CD1a immunohistochemical staining around the thyroid gland lumina.

Disccusion

A review about current recommendation of LCH from Histocyte Society recommended that a definitive diagnosis requires that lesional cells exhibit positive staining with S-100 or CD1a[1,3]. In our case, the skin biopsy prompted us to defective diagnosis of LCH. The skin biopsy showed infiltration of large mount of langerhans cell and the cells were positive for CD1a immunohistochemical staining which confirm and coincidence with diagnosis of LCH. Biopsy of thyroid gland also found infiltration of langerhans cell and positive immunohistochemical presentation of CD1a protein which reinforced the diagnosis of LCH.

Although the liver biopsy showed no positive CD1a protein, the liver involvement can't be excluded. According to report, presentation of liver involving in Langerhans cell histiocytosis can be variable. Infiltration of the intra- and extra-hepatic biliary tree, sclerosing cholangitis, hepatomegaly, hepatic heterogenous node and hepatic fibrosis has been reported[4-22]. Among, the incidence of sclerosing cholangitis in LCH ranges from 10 to 18%.We summaried the reported cases with live involvement which presented with sclerosing cholangitis(Table 1). As the table showed, the SC presented more in children and elder, rarely in young man. The symptoms also varied as jaundice, prurotus, hepatomegaly and portal hypertation.

Reference	Pub year	Case number	Age(year)	sex	Extrahepatic involvement	treatment	outcome
4	1981	6	children	5M,1F	S, LN, L, CNS, B, DI	C	4 died
6	1984	3	17,44,65	1M ,2F	B, LN,L	S+C	3 died
7	1987	1	26	F	S,L,T, DI	C	Not well
8	1988	1	43	M	S,LN	S	unknown
9	1988	1	18	M	none	unknown	died
10	1990	1	3	M	unknown	C	died
11	1993	1	7	M			
12	1995	5	12.6±3.6	3M,2F	B,S, DI	LT	2died
13	1999	9	Jan-62	6F,3M	S,L,B,LN	LT+C	4 died
14	2000	2	1.5, 0.5	F	S,E	LT+C	Live well
15	2002	1	29	F	DI,T	C	Live well
16	2002	12	Mar-36	unknown	S,B,E	LT+C	3 died
17	2003	1	56	M	L,B	P	Live well
18	2004	1	40	F	B,CNS,L	S	Died
19	2004	1	41	F	B,CNS,L,S	LT+C	Live well
20	2004	1	1.5	F	H,S	S	Died
21	2005	1	66	M	CNS	C	Died
22	2006	1	65	F	LN	LT	Live well

Table 1: Summary of sclerosing cholangitis due to LCH.

Note: B:bone, C:chemotherapy, CNS:central nervous system, DI: diabetes insipidus, E:ear, F:female, H: hematopoietic system, LT:Liver transplantation, L:lung, LN:lymph node, M:male, S:skin, ST:supportive treatment, T:thyroid.

And when LCH presented with SC, LCH generally have involved other systems, that is to say SC may be a complication of disseminated LCH. Only one reported case of multisystem LCH involved more than 5 organs, so our cases is rare[4]. But why the liver biopsy is negative with CD1a? One is that LCH infiltration area may be missed by liver biopsy. Second is a lesion of LCH may progress through four histopathological stages : proliferative phase, granulomatous, xanthomatous and fibrous phase. Once a lesion has entered the last phase, it loses the histological features and demonstrable langerhans cells[11,12,19]. In this case, the liver biopsy showed that presentation of proliferation, loss of bile duct and fibrosis of periportal district. This is a cause that CD1a immunohistochemistry was negativein this case. Another is biopsy error. Kaplan KJ et al summarized even when Langerhans' cells are not demonstrable, sclerosing cholangitis can be seen in LCH[12].

With defective diagnosis of LCH involving skin and thyroid gland, liver, lung and other organs, the patients was treated with VP-16, prednisolone, cyclophosphamide and vinblastine, ursodeoxycholic acid (UDCA) for his cholestasis and Euthyrox for hypothyrosis according to recommendation[3]. After two full-duration treatment, the liver function of the patient has improved and thyroid deflated, but the exact prognosis still is puzzling as no specific predictive factors[23-24].

So in our case, liver involvement in multisystem LCH presented with cholestasis and pathological sclerosing chonlongitis. Although there is no characteristic manifestation in liver pathology, it is important to have LCH induced sclerosing cholongitis in mind, and should give further investigation to find out positive langerhans cells.

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