

## Langerhans' cell histiocytosis as a cause of periportal abnormal signal intensity on MRI

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Received: 29 July 1998/Accepted: 23 September 1998

### Abstract

Three cases of hepatic Langerhans' cell histiocytosis (LCH) manifesting as periportal abnormal signal intensity on magnetic resonance images are described. One case also demonstrated intrahepatic bile duct dilatation due to secondary sclerosing cholangitis. Hepatic involvement of LCH could be included in the differential diagnosis of periportal abnormal signal intensity in children.

**Key words:** Liver—Langerhans' cell histiocytosis—Children—Magnetic resonance imaging.

Children with Langerhans' cell histiocytosis (LCH) usually present hepatomegaly associated with multiorgan involvement. In these patients, hepatic dysfunction may occur at the time of diagnosis or later. The basic pathologic features of the liver in children with LCH has been well described [1–3]. Different imaging findings of the liver, however, have been described in children and adults with LCH [4–8]. A review of the literature shows that the findings may depend on the difference of duration of the disease and the main pathological features in each case. Ultrasonographic (US) or cholangiographic findings of the liver have been discussed in a few cases of young children with disseminated LCH [2, 4, 5]. In adult cases, magnetic resonance imaging (MRI) has demonstrated periportal fat infiltration or fibrosis mimicking multiple hepatic tumors [6, 8]. We encountered three young children with LCH with hepatic involvement characterized by different degrees of periportal abnormal signal intensity (PASI) on MRI. These cases are presented, and their clinical outcome and pathologic findings are discussed.

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### Case reports

A brief summary of clinical data is given in Table 1. In all three cases, we obtained MR images of the liver immediately before or after the diagnosis of LCH. Those MRI and pathologic findings are summarized in Table 2.

#### Case 1

An 11-month-old boy was transferred to our hospital due to hepatosplenomegaly. He had been well until 2 months before admission when he had developed poor oral intake. On physical examination, lymph nodes were palpated in both cervical and left inguinal areas in addition to hepatosplenomegaly. Serum levels of alkaline phosphatase (708 IU/L), aspartate aminotransferase (52 IU/L), and alanine aminotransferase (46 IU/L) were elevated.

Ultrasound (US) of the liver showed periportal hypoechogenicity and multiple hypoechoic nodules, some of which had a target-like appearance. MRI of the liver was obtained 2 weeks after the US. Axial T1-weighted images (WIs) showed hepatomegaly and lesions with intermediate to low signal intensity around the portal branches (Fig. 1A). On T2-WIs, periportal lesions appeared to have moderate to high signal intensity (Fig. 1B). The periportal lesions enhanced after injection of Gd-DTPA (0.1 mmol/kg; Magnevist, Schering, Germany; Fig. 1C). On the 20th hospital day, purpuric papules or macules involving the anterior abdominal wall developed. The skin and lymph node biopsies were diagnosed as LCH. Liver biopsy was not performed.

Chemotherapy was initiated with prednisolone and vinblastine. After three cycles of treatment, the oncologist changed the regimen to etoposide and cyclophosphamide. Although chemotherapy had been continued over a period of 1.5 years, the patient eventually developed upper gastrointestinal bleeding, jaundice, hypoalbuminemia, and diabetes insipidus. He later received a cadaveric liver transplantation.

On pathological examination of the explanted liver, there were bile ductular proliferation, periductal fibrosis and histiocytic infiltration, and micronodular cirrhosis. Histiocytes infiltrating around the dilated bile ducts were positive for S-100 protein and CD1a.

#### Case 2

A 24-month-old boy presented with progressive abdominal distention for 1 year and vomiting and diarrhea for 1 week. Physical examination

**Table 1.** Clinical data and outcome in three children

| Case | Age (mo) | Sex | Presenting symptoms                          | Organs involved          | Outcome, treatment                                      |
|------|----------|-----|--|--------------------------|---|
| 1    | 11       | M   | Poor oral intake                             | Skin, lymph nodes, liver | Hepatic dysfunction, <sup>a</sup> liver transplantation |
| 2    | 24       | M   | Abdominal distension, vomiting, and diarrhea | Scalp, liver             | Hepatic dysfunction, <sup>a</sup> liver transplantation |
| 3    | 18       | M   | Limping gait                                 | Ilium, spine, liver      | Stable, chemotherapy                                    |

<sup>a</sup> Hepatic dysfunction developed 1½ years after an initial presentation

**Table 2.** Summary of MR imaging and pathologic findings of the liver in three children

| Case | MR imaging  | Pathology  |
|------|---|--|
| 1    | Smooth hepatic surface, diffuse PASI  | Biliary cirrhosis, extensive periportal fibrosis                                   |
| 2    | Nodular hepatic surface, diffuse PASI, unevenly dilated intrahepatic bile ducts | Biliary cirrhosis, extensive periportal fibrosis, secondary sclerosing cholangitis |
| 3    | Smooth hepatic surface, mild PASI in central portal tract                       | Bile ductular proliferation, periductal histiocytes, and inflammatory cells        |

PASI; periportal abnormal signal intensity on T1, T2, and contrast-enhanced T1 weighted images

showed hepatosplenomegaly and thickly crusted patches on the scalp. Laboratory examination showed an elevated serum level of alkaline phosphatase (1075 IU/L), aspartate aminotransferase (134 IU/L), and alanine aminotransferase (121 IU/L).

US showed heterogeneous hepatic parenchymal echoes and periportal hypoechogenicity. MR images of the liver showed thick, abnormal PASI, intrahepatic bile duct dilatation, and nodular appearance of the enlarged liver (Fig. 2A,B). On contrast-enhanced T1-WIs, relatively hypointense nodular lesions were found adjacent to an abnormal periportal enhancement (Fig. 2C).

In addition to the findings typical of LCH from biopsy of the scalp and liver, secondary changes of extrahepatic bile duct obstruction and cholangitis were seen. Although chemotherapy had been continued for 1.5 years, he developed hematemesis and melena. He received a liver transplantation from a cadaveric donor. Gross and microscopic examination of the explanted liver showed nodular hepatic surface, severe secondary sclerosing cholangitis, and bile duct proliferations.

### Case 3

A 18-month-old boy presented with a limping gait. Physical examination showed hepatomegaly. Laboratory examination showed an elevated serum level of alkaline phosphatase (626 IU/L), aspartate aminotransferase (53 IU/L), and alanine aminotransferase (186 IU/L). An osteolytic lesion of the right iliac bone and flattening of the 8th and 9th thoracic vertebrae were found on plain radiographic examination.

US of the liver showed slightly increased parenchymal echoes and small round hypoechoic nodules in the left lobe. MR images of the liver showed PASI confined to the central portal tract (Fig. 3A,B).

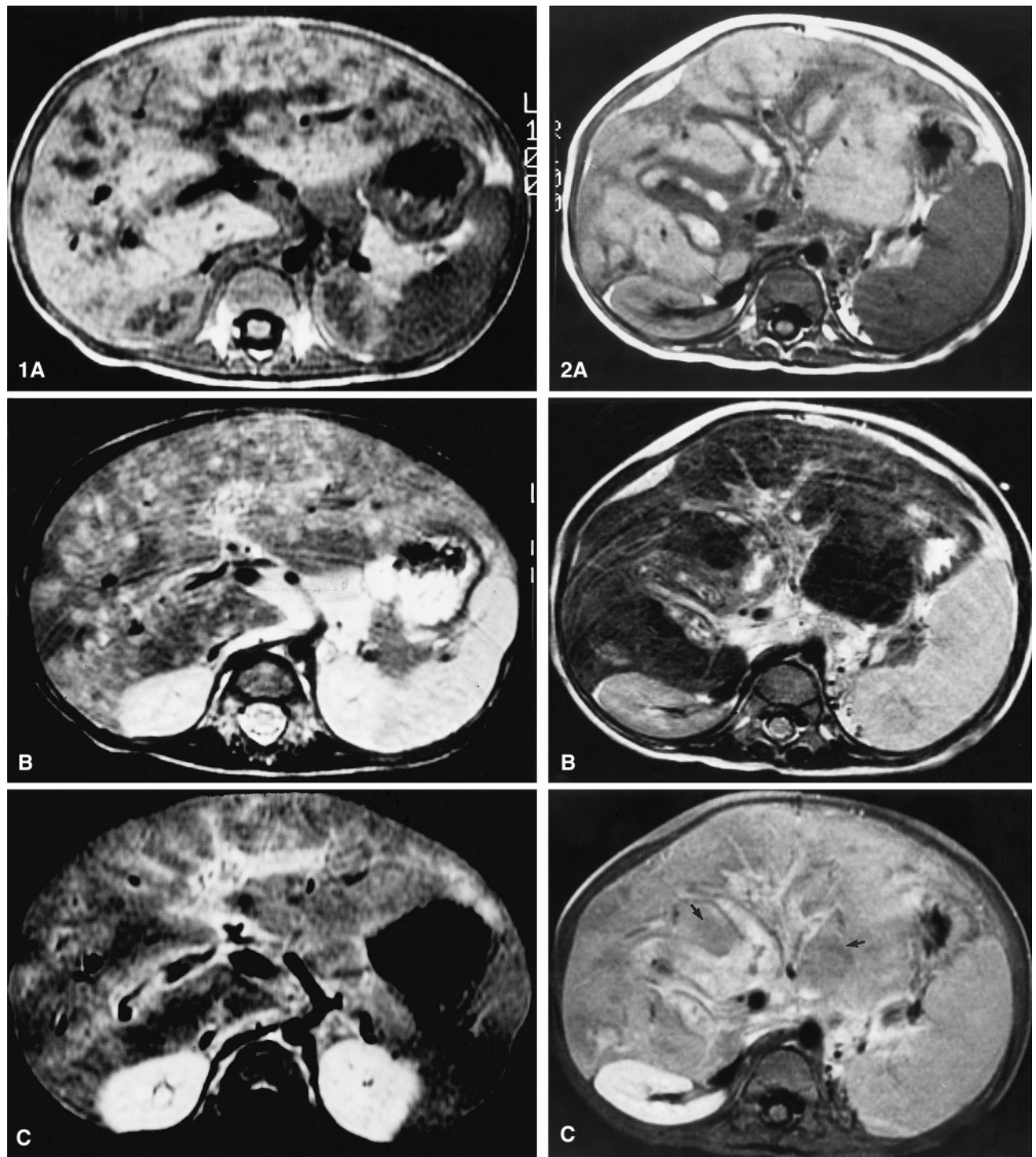
The diagnosis of LCH was made from biopsy of the right ilium and the liver. Liver biopsy showed bile ductular proliferation, periductal histiocytic, and lymphocytic infiltration. Chemotherapy was initiated with prednisolone and vinblastine and was then continued with cyclophosphamide and VP-16. On follow-up MR images obtained 2 years later, PASI showed near complete resolution (Fig. 3C). The patient has not developed any clinical manifestations of hepatic dysfunction for 3 years after diagnosis.

### Discussion

In children with LCH, hepatic involvement is common. At presentation, hepatomegaly is observed in up to 60% of patients with disseminated LCH [3], but hepatomegaly does not always portend a poor prognosis. Hepatic dysfunctions such as jaundice, hypoproteinemia, and portal hypertension may be present at the time of diagnosis or may develop over months or years [1–3]. In all three patients, clinical manifestation of hepatic dysfunction was not evident at the time of diagnosis.

Morphologic changes of the liver in LCH have been described in a number of previous studies. A report from the Children's Cancer Study Group has described four patterns: (a) portal triaditis with infiltrating neutrophils, eosinophils, or mononuclear cells; (b) bile duct proliferation with triaditis; (c) fibrohistiocytic change; and (d) nodular parenchymal lesion with triaditis [1]. Other reports have described triaditis, periportal fibrosis, or liver cirrhosis and bile stasis and bile duct proliferation in some cases [2, 3, 9–11]. We could not confirm the sequential change of hepatic pathology in each patient, but bile ductular proliferation and periductal inflammatory cell infiltration were noted in the pretreatment liver biopsy of patient 3. Biliary cirrhosis and extensive periductal fibrosis was seen in the explanted liver of patients 1 and 2, who had developed hepatic dysfunction. In patient 2, secondary sclerosing cholangitis was also noted.

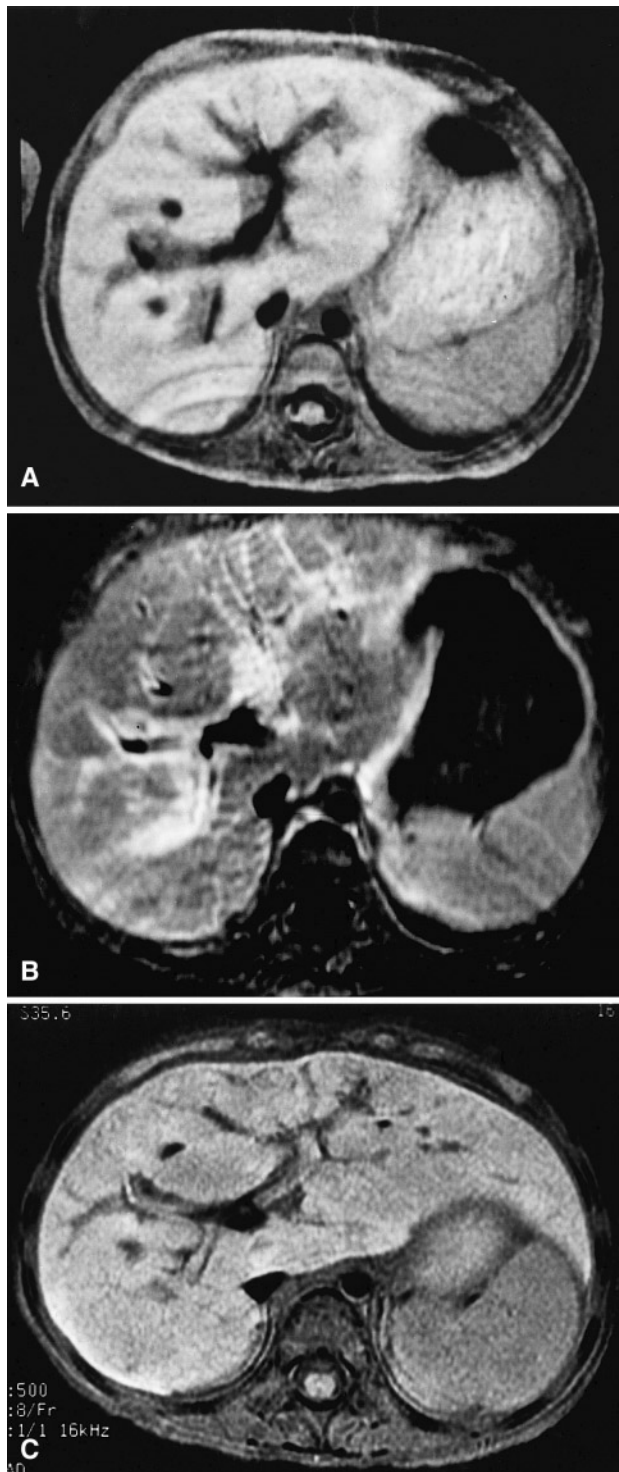
US finding of the liver in LCH has been described as hypoechoic nodule or periportal hyperechogenicity that may be attributed to inflammatory cell infiltration or fat content [4, 5, 7, 8]. US in the present cases showed periportal hypoechogenicity that was band-like



**Fig. 1.** Case 1. **A** T1-weighted image (500/11 TR/TE) shows periportal low signal intensity surrounding the portal veins that extends peripherally from the porta hepatis. **B** Fast spin-echo T2-weighted image (4000/85) shows diffuse periportal high signal intensity as a periportal ring or tramline, some of which have a hyperintense nodular appearance. **C** Contrast-enhanced T1-weighted image (500/11) with fat suppression shows periportal enhancement.

portal low signal intensity and nodular hepatic surface. Unevenly dilated intrahepatic bile ducts or bile lakes appear to have high intensity due to stagnant bile. **B** Fast spin-echo T2-weighted image (4000/98) shows moderate to high signal intensity along the portal tracts. **C** Strong periportal enhancement is seen on contrast-enhanced T1-weighted image (650/13). Hypointense periportal fibrosis mimicking a mass (*arrows*) is more clearly defined than in the T1-weighted image.

**Fig. 2.** Case 2. **A** T1-weighted image (650/13) shows thick, peri-



**Fig. 3.** Case 3. **A** T1-weighted image (550/17) with fat suppression shows periportal low signal intensity that is confined to the central portal tracts. **B** Periportal enhancement is clearly seen on contrast-enhanced T1-weighted image (600/11) with fat suppression. **C** T1-weighted image (500/8) obtained 2 years later shows no periportal low signal intensity.

or nodular. Some hypoechoic nodules looked like targets. We suspect that periportal hypoechogenicity may be attributed to the infiltration of histiocytes and inflammatory cells based on our biopsy result, which accorded with the reports of Hara et al. [4] and Mukakkit et al. [5].

MRI findings of the liver in LCH have been noted in two case reports [6, 8]. These cases presented as mass lesions of the liver, which had imaging characteristics of periportal fibrosis and focal fatty infiltration. In the present cases, MRI showed PASI rather than a focal mass. Matsui et al. [12] described periportal abnormal intensity on MRI from patients with cholangitis, obstructive jaundice that was due to edema, inflammatory cell infiltration, and proliferation of bile ductules. On each T1-WI and T2-WI, signal intensity of periportal lesions in our patients was lower and higher than that of surrounding hepatic parenchyma, respectively. Signal intensity of these lesions was increased on contrast-enhanced T1-WI with fat suppression. PASI extended diffusely from the central large portal tracts to peripheral small ones in patients 1 and 2, who eventually developed hepatic dysfunction. In addition to the extensive PASI, intrahepatic bile duct dilatation and nodularity due to secondary biliary cirrhosis were noted in patient 2. This finding is in contrast to PASI confined to the central large portal tract in patient 3 who has not yet developed hepatic dysfunction. Pathologic examination of this patient showed bile ductular proliferation and periductal histiocytic and lymphocytic infiltration. On follow-up MRI obtained 2 years later, PASI was not seen in all sequences as compared with that of the initial study. We consider that MRI of the liver in children with disseminated LCH may be different according to the pathological change, ranging from triaditis to periportal fibrosis and biliary cirrhosis.

In summary, we could find PASI as a common feature on initial MRI of three children with disseminated LCH. As already known, PASI itself is nonspecific. However, in conjunction with clinical and laboratory data, MRI can be valuable in the estimation of morphologic change of the liver in children.

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