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Neuroradiology report

Spectrum of imaging appearances in Australian children with central nervous system hemophagocytic lymphohistiocytosis

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ABSTRACT

Hemophagocytic lymphohistiocytosis (HLH) is a rare multisystem disorder characterised by the proliferation and infiltration of lymphocytes and histiocytes. Central nervous system (CNS) infiltration is particularly devastating. Neuroradiological findings have been reported predominantly as individual case reports due to the rarity of the condition. To our knowledge there have been no published studies of imaging in Australian patients. This study aimed to retrospectively describe and illustrate the MRI appearances of CNS involvement by HLH in a cohort of seven Australian children from two paediatric centres between 2000 and 2011. MRI appearances demonstrate intersubject and intrasubject variability over time, likely reflecting the severity of CNS infiltration and associated demyelination. Familiarity with MRI patterns is important for assessing and monitoring disease activity.

1. Introduction

Hemophagocytic lymphohistiocytosis (HLH) is a rare multisystem disorder characterised by the proliferation and infiltration of lymphocytes and histiocytes in the liver, spleen, lymph nodes, bones and central nervous system (CNS).[1] Two subtypes of HLH occur: familial (X-linked recessive) and acquired (associated with infections and malignancies).[1] CNS infiltration is particularly devastating and frequently difficult to diagnose due to the extreme variability of the neuroradiological findings. The low incidence of this condition is reflected in the small number of published case reports.[2–9] This study aimed to describe and illustrate the MRI appearances of CNS HLH in a cohort of Australian children.

2. Materials and methods

A retrospective audit of MRI brain studies of patients with CNS HLH was performed at The Royal Children's Hospital, Melbourne and The Royal Children's Hospital, Brisbane from 2000–2011. Three patients with cerebrospinal fluid (CSF) proven CNS HLH had normal MRI scans and were excluded from this study.

The studies were acquired on a variety of scanners (Siemens 1.5T, Siemens 3T [both Siemens AG, Munich, Germany], GE 1.5 T [GE Healthcare, Fairfield, CT, USA]) using different protocols. All studies were good quality multiplanar acquisitions which included T1-weighted pre- and post-gadolinium, fluid attenuated inversion recovery (FLAIR), T2-weighted, diffusion weighted imaging and apparent diffusion coefficient (ADC).

MRI studies were systematically reviewed by a paediatric neuroradiologist and paediatric medical imaging fellow. The spectrum of imaging findings were collated, summarised and presented in pictorial format.

3. Results

Seven patients (aged 6 weeks to 14 years) were identified. There were six boys (86%) and one girl. All six boys were 4 years of age or younger with a mean age of 20.8 months at the time of first MRI. The single female patient was 14 years old (Table 1).

MRI appearances demonstrated intersubject and intrasubject variability over time.

3.1. T2-weighted/FLAIR hyperintensity

All seven patients demonstrated supratentorial and infratentorial T2-weighted/FLAIR hyperintensities with variation in each patient over time. The T2-weighted/FLAIR hyperintensities affected grey or white matter or a combination thereof. There was marked intersubject variability in appearance with these lesions manifesting as nodular or diffuse abnormalities (Fig. 1).

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Table 1
MRI findings in hemophagocytic lymphohistiocytosis patients

Patient	Age at diagnosis	Sex	T2/FLAIR hyperintensity	Enhancement	Atrophy	Restricted diffusion	T1 hyperintensity	Subdural collection	Optic nerve/ orbit
1	12 mo	M	X	X	X	X	X	X	–
2	11 mo	M	X	X	X	X	–	–	–
3	14 yrs	F	X	–	–	–	–	–	X
4	4 yrs	M	X	X	X		–	–	X
5	2 yrs	M	X	X	X	X	–	–	–
6	2 yrs	M	X	–	–	–	–	–	–
7	6 mo	M	X	X	–	–	–	–	–

F = female, FLAIR = fluid attenuated inversion recovery, M = male, mo = months, yrs = years, X = present, – = absent.

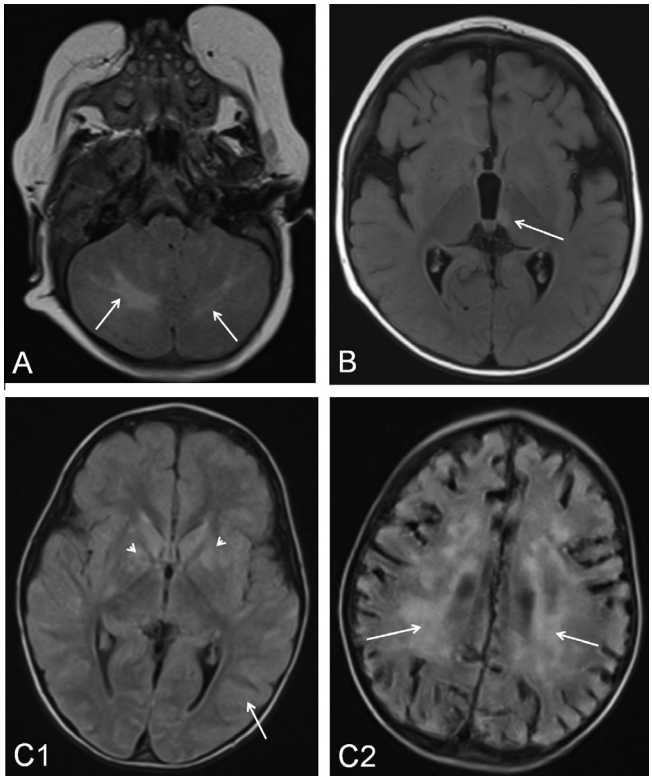

Fig. 1. Axial fluid attenuated inversion recovery images showing hyperintensity involving the cerebellar deep white matter (arrows) of Patient 2 (A), left medial thalamus (arrow) of Patient 1 (B) and basal ganglia (arrow heads) and cortex (arrow) of Patient 5 (C1) with MRI 2 weeks later (C2) showing marked cerebral deep white matter involvement (arrows) and cerebral atrophy in the same patient.

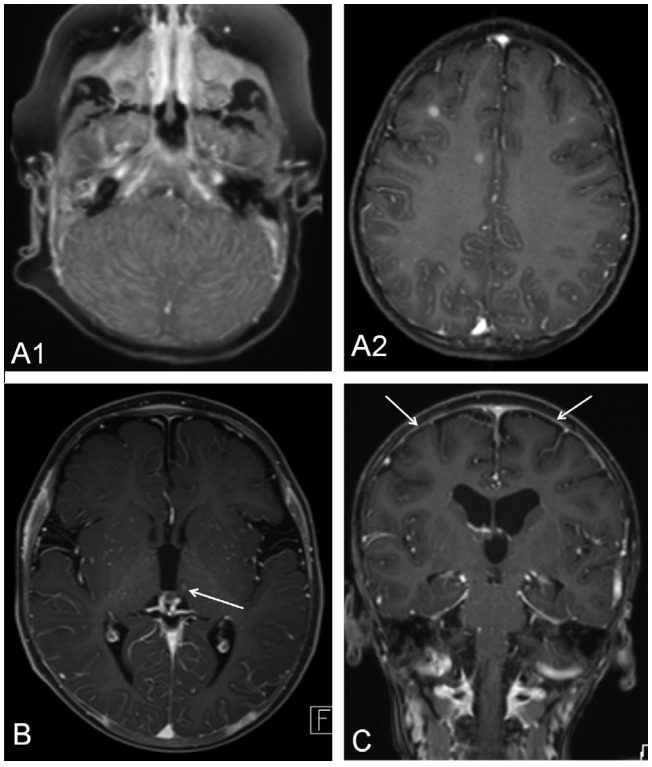

Fig. 2. Axial T1-weighted post-contrast images from Patient 5 (A1, A2) showing diffuse cerebellar and cerebral leptomeningeal enhancement and enhancing parenchymal nodules. Patient 1 (B) has similar posterior leptomeningeal enhancement and an enhancing nodule left medial thalamus (arrow) corresponding to the fluid attenuated inversion recovery hyperintensity in Fig. 1B. Patient 4 (C) manifested diffuse dural enhancement (arrows) as seen on the coronal view.

3.2. Contrast enhancement

Six (86%) patients had contrast enhancement following intravenous gadolinium injection on at least one MRI scan. Contrast enhancement was variable between patients and in the same patient over time. Structures that enhanced included parenchymal nodules and cerebral or cerebellar leptomeninges. Leptomeningeal enhancement was usually diffuse while parenchymal enhancing lesions were small and discrete. Several of the T2-weighted/FLAIR hyperintense lesions also enhanced. One patient had an enhancing T2-weighted/FLAIR hyperintense nodule in the left thalamus (Fig. 1, 2).

3.3. Cerebral atrophy

Four (57%) patients had cerebral atrophy with variable white matter signal changes, ventriculomegaly and enlarged extra-axial CSF spaces. The cerebral volume loss was shown to be progressive and severe from the time of diagnosis over a period of weeks to months. There appeared to be some reversibility of the volume loss in a 4-year-old patient on an MRI 5 months after bone marrow transplant (Fig. 3).

3.4. Restricted diffusion

Lesions in three (43%) patients demonstrated restricted diffusion. All three had restricted diffusion involving part or all of the thalamus with variable restriction of diffusion in the additional basal ganglia structures. In one patient there was restricted diffusion involving the entire cerebral cortical mantle. Another patient had restriction of diffusion involving the periventricular and deep white matter (Fig. 4). Some of these areas demonstrated contrast enhancement.