Hemophagocytic lymphohistiocytosis: spectrum of neuroimaging findings in a family

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OBJECTIVE

To describe the spectrum of neuroimaging findings in three children of a consanguineous Pakistani couple suffering from hemophagocytic lymphohistiocytosis (HLH) on computed tomography (CT) and magnetic resonance imaging (MRI).

MATERIALS AND METHODS

Descriptive study with retrospective review of imaging studies (CT and MRI) of three patients diagnosed with hemophagocytic lymphohistiocytosis.

RESULTS

CT and MRI studies showed a spectrum of neuroimaging findings which ranged from brain parenchymal abnormalities (white matter lesions, rim-enhancing lesions, cerebral hemorrhage, atrophy), leptomeningeal involvement to metabolic disturbances on MR spectroscopy.

Previous reports have described a correlation between the neuroradiological findings and histopathological grading of HLH.

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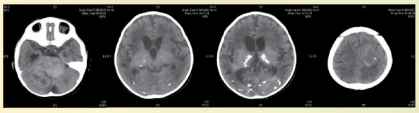

Fig. 1 CT. Bilateral cortical and thalamic calcifications.

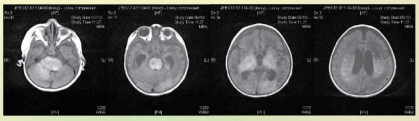

Fig. 2 T1W. Heterogeneous infiltrative T1 signal involving bilateral deep gray matter, cerebral white matter, cerebellum and brainstem.

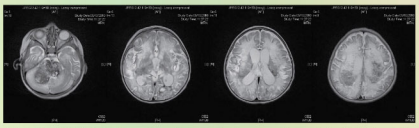

Fig. 3 T2W. Extensive hyperintense signal in bilateral cerebral white matter with blooming phenomenon suggestive of calcifications and hemosiderin deposition.

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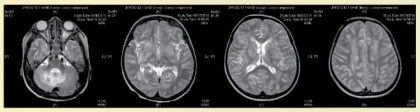

Fig. 4 T2W. High signal at bilateral cerebral and cerebellar white matter, bilateral deep gray nuclei and brainstem.

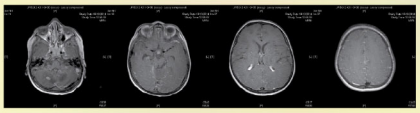

Fig. 5 T1W + contrast. Right cerebellar rim-enhancing lesion with diffuse leptomeningeal enhancement affecting both supra- and infratentorial regions.

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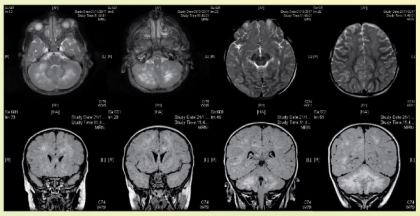

Fig. 6 T2W and FLAIR. Hyperintense signals along the gyri and subcortical white matter of bilateral cerebral and cerebellar hemispheres.

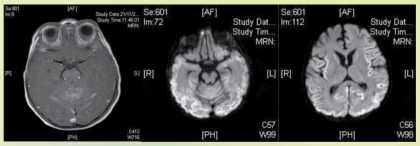

Fig. 7 T1W + contrast. Cluster of tiny enhancing foci at the superior aspect of cerebellar vermis suspicious of leptomeningeal enhancement.

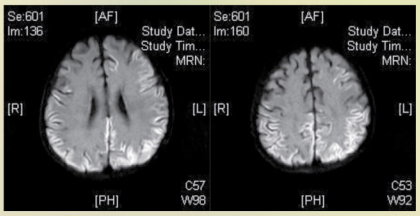

Fig. 8 DWI. More extensive restricted diffusion along bilateral cerebral gyri and subcortical white matter and new restricted diffusion at bilateral insular cortex and caudate nuclei.

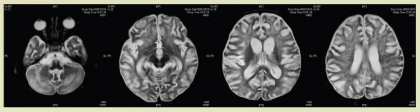

Fig. 9 T2W. Serial MRI shows progressive atrophy of brain parenchyma with extensive white matter high signal.

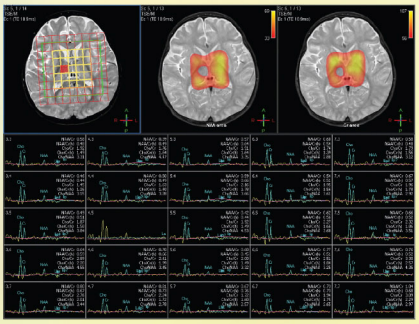

Fig. 10 MR spectroscopy at basal ganglia (above), cerebellum and gray-white junction (not pictured) show decreased choline, creatine and NAA and focal areas of lactate peak.

Correlation between histopathologic stage and imaging findings described in the literature

	Histopathologic stage	Imaging findings
Stage I	Leptomeningeal lymphocyte and histiocyte infiltration	Diffuse leptomeningeal enhancement
Stage II	Adjacent parenchymal involvement with perivascular infiltrations	Diffuse white matter changes with variable enhancement, hemorrhage, and restricted diffusion
Stage III	Widespread tissue infiltration, demyelination, blood vessel destruction, gliosis, and tissue necrosis	

CONCLUSION

Neuroradiological findings in HLH are not sufficiently specific to achieve the diagnosis. The diagnosis of HLH is based on established diagnostic criteria including clinical findings, biochemical abnormalities and the detection of genetic mutations.

Depending on the patient's clinical presentation and neuroimaging findings, other differential diagnoses may be considered, such as infection (brain abscess), malignancy (primary glioma or metastasis), demyelination (multiple sclerosis), inflammation (acute disseminating encephalomyelitis) or even child abuse.

In summary, hemophagocytic lymphohistiocytosis, although an uncommon disease, should be kept at the back of our mind when reviewing imaging especially when clinical colleagues have an underlying suspicion.