Neuroimaging Highlight

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MRI Findings in an Immunocompromised Boy with CNS Fungal Infection

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An immunosuppressed 11-year-old with relapsed T-cell leukemia presented with subacute onset fever, headache and a "heavy" right hand. Neurologic examination revealed right-sided hemiparesis and hypesthesia.

Magnetic resonance imaging (MRI) 24 hours after symptom onset disclosed lesions involving the right cerebellar hemisphere, left putamen, and cortex in the right frontal lobe and left frontoparietal region (Figure 1). The lesions were gyriform, T1 hypointense, non-enhancing, and T2 hyperintense, with blooming of the larger lesions on the gradient echo sequence consistent with hemorrhage. Interestingly, on fluid attenuation inversion recovery (FLAIR) imaging, the lesions were predominantly isointense with only a small peripheral rim of increased signal. The lesions demonstrated increased signal on the diffusion weighted sequences (DWI) and decreased signal on the apparent diffusion coefficient (ADC) map in keeping with restricted diffusion. There was minimal edema and mass effect.

Cerebrospinal fluid (CSF) showed normal glucose, protein, red and white blood cell counts. Flow cytometry did not reveal leukemic cells. There was no serum or CSF evidence of acid-fast bacilli, toxoplasma, enterovirus or herpes simplex virus. Echocardiogram was normal. Biopsy of a lung infiltrate was non-diagnostic.

The clinical course fluctuated, with worsening hemiparesis, expressive language difficulties and depressed level of consciousness, which responded only temporarily to corticosteroids. The lesions progressed in size despite maximal empiric broad-spectrum antimicrobial treatment against bacteria, viruses, fungi and toxoplasma.

Repeat MRI one week after onset showed enlargement of the lesions. They were hyperintense on T1 sequences and without clear contrast-enhancement. They continued to show restricted diffusion. MRI 17 days after symptom onset again showed lesion growth. There was ring enhancement and significant vasogenic edema with mass effect (Figure 2). The lesions no longer showed restricted diffusion.

Due to disease progression despite maximal therapy, the brain lesions were not biopsied and the child was transferred to the palliative care service. He died at home six weeks after symptom onset.

Postmortem brain examination showed multifocal chronic fungal abscesses in the frontal lobes, left putamen and right cerebellum. Central coagulative necrosis harboured thrombosed blood vessels bearing fungal angioinvasion. Though morphologically suggestive of *Aspergillus*, the hyphae were degenerate, precluding definitive identification (Figure 3). Abscess capsules were well-formed and contained multinucleated giant cells and focal granulomata (Figure 4). Adjacent parenchyma was gliotic and focally degenerate, suggesting chronic edema. Leukemic infiltrates were not present.

We report a case of multifocal fungal cerebritis with MRI showing restricted diffusion. At the time of presentation, the

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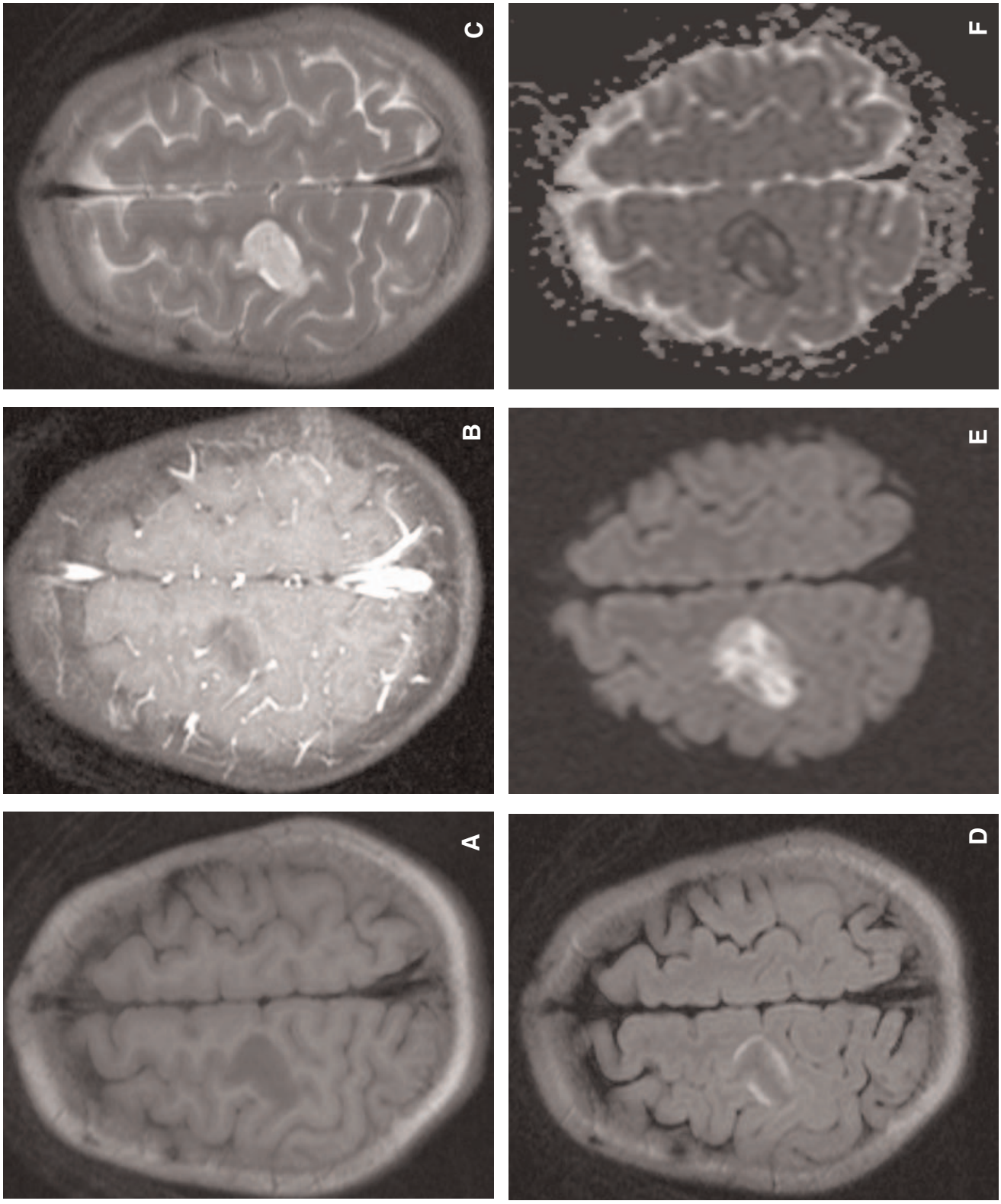

Figure 1: *Magnetic resonance imaging of the right frontal lesion 24 hours after symptom onset. Axial T1 weighted images without (A) and with (B) gadolinium show a discrete, hypointense, non-enhancing lesion with a gyriform appearance in the right frontal lobe. The lesion is hyperintense on axial T2W (C) but shows minimal increased signal on the FLAIR images (D). The lesion is hyperintense on DWI (B1000 series) (E) and hypointense on the ADC map (F), in keeping with restricted diffusion.*

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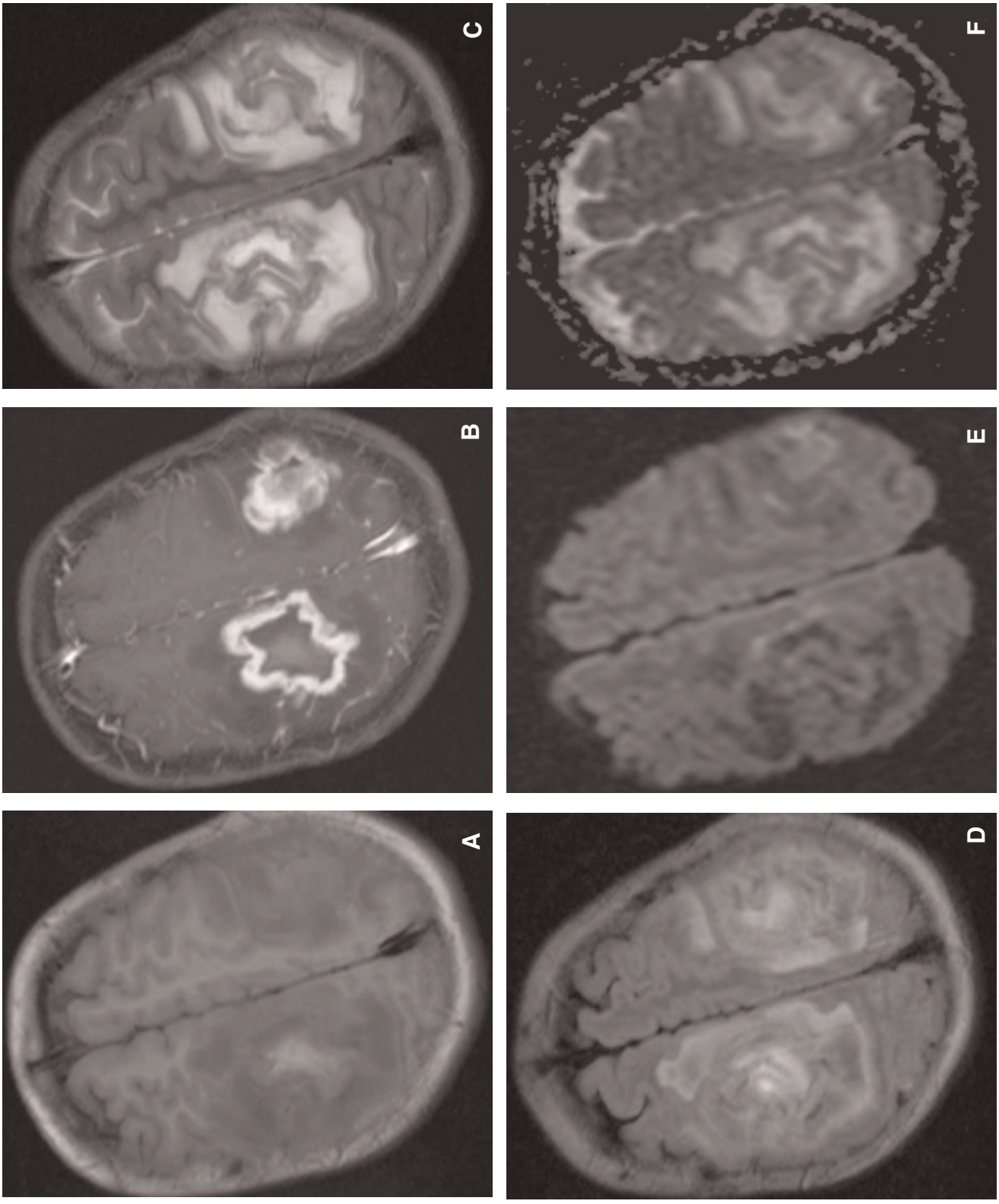

Figure 2: *Magnetic resonance imaging at the same level 17 days after symptom onset shows marked interval enlargement of the right and left frontal lesions. Axial T1 weighted images without (A) and with (B) gadolinium now show significant ring-enhancement of the lesions. T2W (C) and FLAIR (D) images show pronounced edema of the surrounding parenchyma. Restricted diffusion is no longer apparent (E) and (F).*

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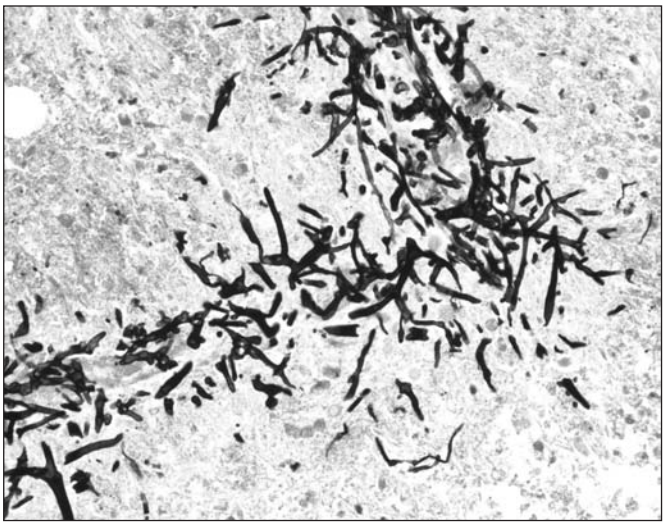

Figure 3: *Grocott Methenamine silver stain – 400x. Fungal hyphae are seen invading a small blood vessel. Morphology, including septations, is suggestive of Aspergillosis spp.*

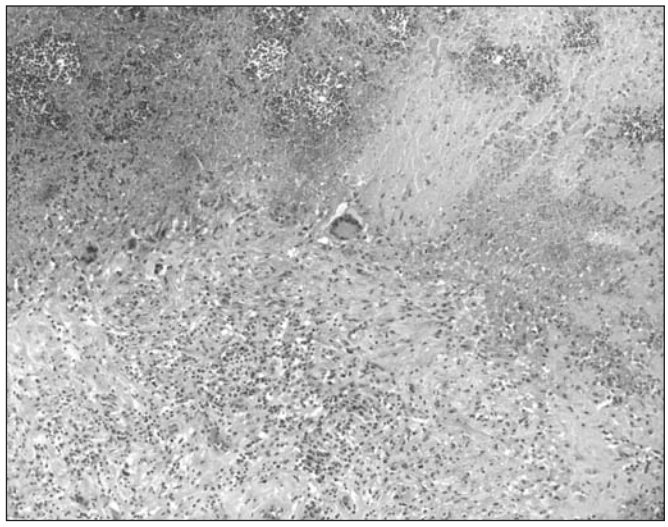

Figure 4: *Haematoxylin-eosin, X100. Left frontal lobe abscess with coagulation necrosis and inflammatory infiltrates. There is a large multinucleated giant cell at the center of the field, and two smaller giant cells toward the left of the image.*

differential diagnosis included embolic infarcts, infection and leukemic infiltrate. Ischemic stroke was initially favoured given the lesions' gyriform appearance and restricted diffusion. However, the FLAIR appearance was atypical for an acute-subacute stroke in that the lesions were predominantly isointense. Because of the subsequent clinical course, evolution of the lesions on MRI and lack of proximal embolic source, a presumed diagnosis of fungal infection was made prior to autopsy confirmation.

Diffusion-weighted imaging (DWI) is an MRI technique that measures the restriction of water diffusion. It is widely-used to diagnose early cerebral ischemia, though restricted diffusion is not specific for stroke.[1] Restricted diffusion in fungal cerebral infection is common, and was seen in all eight patients reviewed recently by Gaviani et al. These authors suggest cellular infiltrate, multi-infarct ischemia, hemorrhage and accumulation of proteinaceous fluid as possible causes for restricted diffusion.[2]

In the appropriate clinical situation, fungal disease should be considered in the differential diagnosis of restricted diffusion. We are uncertain as to why the lesions in this case are predominantly isointense on FLAIR. The gradient echo images demonstrate susceptibility artifact within the lesions, consistent with hemorrhage. This susceptibility effect may shorten the T2 relaxation time of the lesions so that they appear isointense on FLAIR. Further similar examples will be necessary to determine if this distinct FLAIR appearance may be helpful in distinguishing stroke from fungal infection.

References

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2. Gaviani P, Schwartz RB, Hedley-Whyte ET, Ligon KL, Robicsek A, Schaefer P, et al. Diffusion-weighted imaging of fungal cerebral infection. AJNR Am J Neuroradiol. 2005;26(5):1115-21.