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Atypical PRES with diffusion restriction or neurotoxicity– ? part of same spectrum—after oxaliplatin (FOLFOX-4 regimen) for colonic cancer

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ABSTRACT

Atypical features of Posterior reversible encephalopathy syndrome (PRES) (diffusion restriction, involvement of corpus callosum & white matter tracts along posterior limbs of internal capsule) were seen in a patient after oxaliplatin administration (FOLFOX- 4 regimen). Findings were most obvious on diffusion weighted images, similar to acute methotrexate neurotoxicity, and resolved completely on follow up.

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To the Editor,

A 49-year-old female was diagnosed with stage IV colonic cancer (adenocarcinoma on colonoscopic biopsy, with liver, bone & lung metastasis, and ascites). She was started on palliative chemotherapy with oxaliplatin, 5-fluorouracil and leucovorin (FOLFOX-4 regimen; 1 cycle is given over 2 days). Two days after completing first cycle of chemo, she had difficulty in opening mouth (for speaking and swallowing). She was admitted in a local hospital; CT scan was normal;

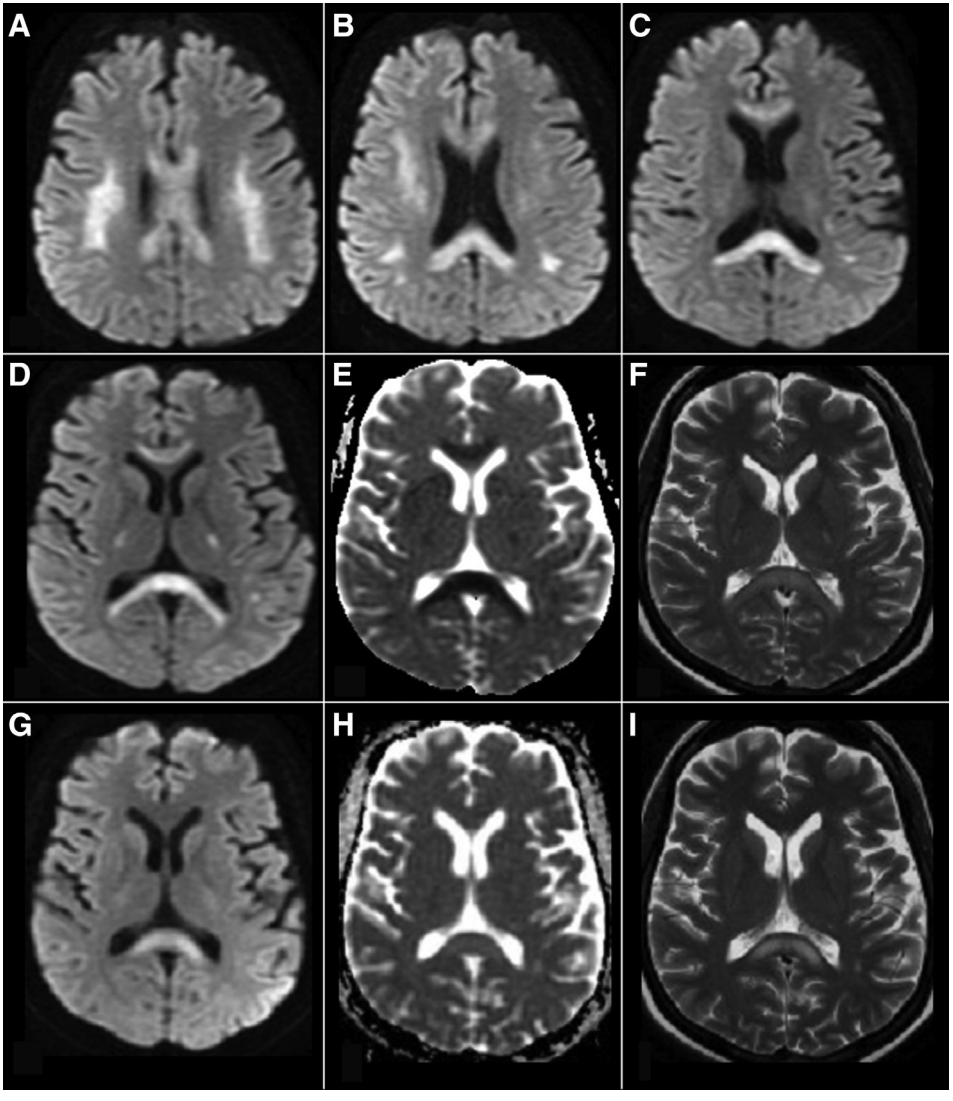

Fig. 1. Diffusion weighted images (A-D) show hyperintensities in corpus callosum (A-D), centrum semiovale, and corona radiata (A, B), along posterior limbs of internal capsule (D). Apparent diffusion coefficient (ADC) image (E) confirms diffusion restriction, while T2 weighted image (F) shows less obvious hyperintensities. Repeat MRI taken on 29th day after chemotherapy (G-I) shows that changes in diffusion weighted image (G) have reduced considerably; ADC image (H) shows resolution of diffusion restriction; hyperintensity in splenium of corpus callosum on T2 weighted image (I) has become more prominent.

she improved clinically and was discharged. On the next day, she had recurrence of the symptoms: she could understand everything and indicate 'yes or no' by nodding her head, but was unable to speak; there was no palatal palsy on examination; she became asymptomatic by the evening. Magnetic resonance imaging (MRI) on the fourth day after completing chemo showed diffusion restriction in white matter (centrum semiovale, corona radiata, corpus callosum, and white matter tracts along posterior limbs of internal capsule) (Fig 1A-E), while changes on T2 weighted images were less obvious (Fig 1F). Repeat MRI done on 29th day after chemotherapy showed that diffusion restriction had disappeared, with only diffusion hyperintensity remaining in splenium of corpus callosum (Fig 1G, H). T2 hyperintensity in splenium of corpus callosum was more prominent this time (Fig 1I). Oxaliplatin was withheld from second to fifth chemotherapy cycles and she remained asymptomatic. Follow up MRI after 4 months (not shown) was completely normal. After the fifth cycle, chemotherapy was stopped due to deterioration of performance status; she later expired. She had been hypertensive and dyslipidemic, but high blood pressure had not been recorded during this treatment.

Oxaliplatin, a third generation platinum compound used for treatment of metastatic colon cancer, is known to have two types of side effects—an acute neurosensory complex that appears shortly after the first few infusions and a cumulative sensory neuropathy, with distal sensory loss and dysesthesias. Acute manifestations were reported in 85.9% of patients; of these 95.2% patients showed perioral and 91.8% patients showed pharyngolaryngeal dysesthesias[1]; other symptoms included jaw spasm, swallowing difficulty, and slurred speech. Acute symptoms are known to improve after peaking on the third day.[2] Symptoms and time frame of onset in our case are consistent with these studies.

Posterior reversible encephalopathy syndrome (PRES) has been reported in oxaliplatin neurotoxicity,[3,4] but diffusion restriction and deep white matter involvement (atypical features) are not common. Involvement of basal ganglia, thalami, deep white matter (including internal capsules), splenium of corpus callosum, as well as diffusion restriction are known atypical features of PRES.[5,6] Diffusion restriction of white matter has been reported in a patient after oxaliplatin and 5-fluorouracil chemotherapy.[7]

Diffusion restriction is known to be a reliable early sign of acute methotrexate toxicity.[8] We found diffusion restriction in acute phase of oxaliplatin neurotoxicity which decreased considerably (and later resolved) on follow up. Diffusion changes were followed later by changes on T2 weighted images, similar to methotrexate toxicity.[8] We wonder whether PRES and MRI findings of neurotoxicity are part of the same spectrum.

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