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Research Paper

# A Case of 5 Fluorouracil Induced Leukoencephalopathy in a Patient on Treatment for Carcinoma Rectum

Medical Science

KEYWORDS :

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## ABSTRACT

*AIMS & OBJECTIVES: To review the clinical presentation and imaging findings in detection of 5-FU-induced Acute Leukoencephalopathy on MRI*

*MATERIALS & METHODS: A 33 year old male patient, known case of carcinoma rectum who underwent 3 cycles of chemotherapy on 5FU presented with complaints of giddiness, ataxia, headache and diplopia. Patient underwent MRI Brain.*

*RESULT: Patient underwent MRI Brain and showed diffuse bilateral symmetrical restricted diffusion and T2 Changes in cerebral white matter (sparing of subcortical U fibres).*

*CONCLUSION: Early detection of drug-induced leukoencephalopathy is important as the clinical symptoms can be reversed by early discontinuation of the causative drug. Diffusion-weighted magnetic resonance imaging is a useful modality for the early detection and definitive diagnosis of this characteristic encephalopathy. Drug-induced leukoencephalopathy is mainly caused by various chemotherapeutic agents, which include methotrexate, vincristine, ifosfamide, fludarabine, cytarabine, 5-fluorouracil, cisplatin and the interferons. 5-FU is a fluorine-substituted analogue of pyrimidine uracil. The main action of this agent is to block DNA synthesis by reducing the formation of thymidine monophosphate via the inhibition of the thymidylate synthetase and incorporation into RNA. 5-FU readily penetrates the blood-brain barrier; however, 5-FU-induced neurotoxicity is uncommon and has an incidence of less than 5% among patients treated with this agent. Drug-induced leukoencephalopathy is dose- and schedule-dependent and is reversible after drug withdrawal or dose reduction*

**Introduction**

5-Fluorouracil (5-FU) is a pyrimidine metabolite, widely used in the treatment of a spectrum of solid cancers, such as carcinoma of the head and neck, oesophagus, stomach, intestine and ovaries. Adverse reactions of the drug in the brain are rare and include encephalopathy and may present as disorientation, confusion, irritability, neurosensory hearing impairment, seizure and even deep coma. Diffusion-weighted magnetic resonance imaging (DW-MRI) is a useful modality for the early detection and definitive diagnosis of this characteristic encephalopathy. Herein, we reported a case of 5-FU-induced acute leukoencephalopathy.

We present a biopsy proven case of carcinoma colon, underwent 3 cycles of systemic chemotherapy with 5-fluorouracil.

**MATERIALS & METHODS:**

A 33 year old male patient, known case of carcinoma rectum who underwent 3 cycles of chemotherapy presented with complaints of giddiness, ataxia, headache and diplopia. Patient underwent MRI Brain.

MRI of the brain using Magnetom Symphony TIM System1.5 T machine.

Our brain MRI protocol included sagittal spin echo (SE) T1-weighted images (TR 550,

TE 8), axial and coronal fast spin echo (FSE) T2-weighted images (TR 4200, TE 97), axial fluid- attenuated inversion recovery (FLAIR) (TR 9000, TI 2500, TE 82), axial spin echo (SE) T1- weighted images (TR 535, TE 13) and axial diffusion weighted images (b0-1000). Post gadolinium sagittal and axial T1-weighted images were performed.

**RESULT:**

Patient underwent MRI Brain and showed diffuse bilateral symmetrical restricted diffusion, apparent diffusion coefficient (ADC) demonstrated hypointense signals correlating with DWI restriction and T2 hyperintense changes in cerebral white matter , including periventricular, peritrigonal regions, centrum semi ovale , corona radiata and corpus callosum with sparing of subcortical U fibres.

**Figure 1.a, b) FlAIR images shows symmetrical white matter hyperintensities ( arrows), In bilateral fronto-parietal white matter.c)T1 axial image shows no significant changes**

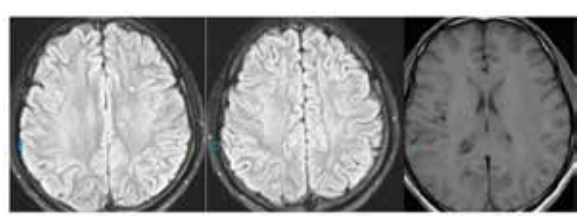
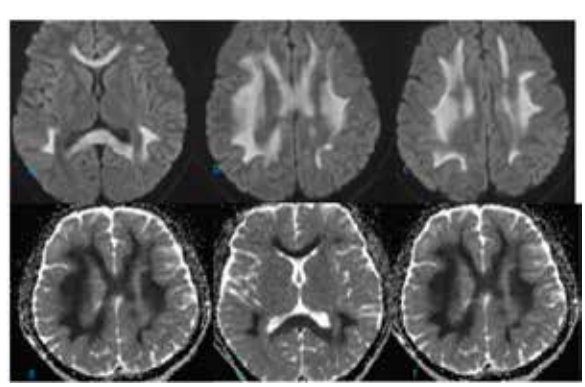


**Fig 2. a,b,c) DWI axial images shows restricted diffusion in the bilateral white matter in the fronto-parietal regions. d,e,f) ADC axial images shows hypointensiities in the corresponding white matter areas**



**Discussion**

5-FU-induced Leukoencephalopathy is a form of toxic encephalopathy (TE) Leukoencephalopathy initially manifests itself as dizziness, numbness, disorientation, memory deficit, confusion, agitation, cognitive impairment and unsteady gait. In severe cases, stupor, seizure,mutism, and even comas may occur . Drug-induced leukoencephalopathy is mainly caused by various chemotherapeutic agents, which include methotrexate, vincristine, ifosfamide, fludarabine, cytarabine,

5-fluorouracil, cisplatin and the interferons . 5-FU is a fluorine-substituted analogue of pyrimidine uracil. The main action of this agent is to block DNA synthesis by reducing the formation of thymidine monophosphate via the inhibition of the thymidylate synthetase and incorporation into RNA.

5-FU readily penetrates the blood-brain barrier; however, 5-FU-induced neurotoxicity is uncommon and has an incidence of less than 5% among patients treated with this agent. In general, 5-FU-induced leukoencephalopathy is more common in females and in patients with malnutrition or liver dysfunction. Dyhydropyrimidine dehydrogenase (DPD) is responsible for more than 85% of the catabolism of pyrimidine. Several studies suggest that DPD deficiency, in which the serum and urine levels of uracil and thymidine are increased, may be a risk

factor for 5-FU-induced leukoencephalopathy . Drug-induced leukoencephalopathy is dose-and schedule-dependent and is reversible after drug withdrawal or dose reduction; however, in some cases it may lead to life-threatening complications.The disease seems to be associated with two clinical courses, according to the time of onset.

The first is an acute phase, which develops within one week after administration of the medication. The second is a subacute phase, which develops within five months after administration of the medication. The treatment modalities proposed in the literature vary considerably and range from purely supportive measures to the use of corticosteroids, thiamine.

The common radiological imaging findings of leukoencephalopathy include symmetrical periventricular hypoattenuation on CT scan and diffuse high intensity signal in the white matter and corpus callosum on T2 weighted MRI DW-MRI. DW-MRI is more sensitive.

It has been known that DW-MRI detects molecular motion of water protons. The accumulation of many small vacuoles within the myelin may interfere with diffusion, thus leading to the appearance of high signal intensity on DW-MRI

**CONCLUSION:**

Early detection of drug-induced leukoencephalopathy is important as the clinical symptoms can be reversed by early discontinuation of the causative drug. Diffusion-weighted magnetic resonance imaging is a useful modality for the early detection and definitive diagnosis of this characteristic encephalopathy.

5-FU induced acute toxic leukoencephalopathy should be recognized early to avoid complications such as coma and death.

A proper understanding of the characteristic imaging features, in combination with detailed clinical history, can often aid in quickly establishing the correct diagnosis

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