Folfox encephalopathy: A rare case series

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Dear Editor,

Encephalopathy is a rare and usually reversible toxicity following FOLFOX 4, a well-established and well-tolerated chemotherapeutic regimen for gastrointestinal cancers. We report two cases of encephalopathy occurring after FOLFOX4 chemotherapy presented with confused mental status and recovered completely.

**Case Report 1**

A 37-year-old woman diagnosed with carcinoma colon with Krukenbergs tumor was started on FOLFOX 4 regimen. During infusion of 5-flourouracil (FU), the patient developed severe headache, intractable vomiting. Subsequently, she became drowsy, developed altered sensorium, and aphasia. She also developed bilateral ptosis, hypertension. Magnetic resonance imaging (MRI) was done which was suggestive of acute toxic encephalopathy [Figure 1]. Toxic and metabolic screen was negative. An electroencephalogram showed a diffuse slowing of waves. Two-dimensional (2D) echo showed ejection fraction of 40%, compared to baseline of 58% before starting chemotherapy. The patient was started on intravenous methyl prednisolone, lactulose enema, hydration, and oxygen support. After 7 days, her ptosis and sensorium gradually improved but improvement in speech from incomprehensible sounds through monosyllable speech to normal speech took about 14 days. MRI and 2D echo at the time of discharge were normal.

**Case Report 2**

A 55-year-old patient of carcinoma esophagus, on disease progression was started on FOLFOX-based chemotherapy. She tolerated the first three cycles of chemotherapy fairly well. However, on 5th day of cycle four, she presented to emergency room with the complaints of altered sensorium and hypertension. Investigations revealed increased creatinine, decreased left ventricular ejection fraction (27%). An MRI brain was suggestive of acute toxic encephalopathy [Figure 2]. She was treated with antihypertensives and other supportive

Figure 1: Case 1: Diffusion-weighted magnetic resonance imaging showing diffusion restriction in bilateral subcortical white matter
Dear Editor,

A 35-year-old lady underwent total abdominal hysterectomy with bilateral salpingoovariotomy and omentectomy for stage IIIb GCT. She refused adjuvant chemotherapy and was lost to follow-up.

She was evaluated for abdominal discomfort and detected to have ascites with pelvic and hepatic recurrence in 04/02/2003. She was managed with four cycles of bleomycin, etoposide and cisplatin, followed by debulking of pelvic disease with removal of remnant omentum and pelvic node sampling. She developed right-sided pneumothorax which was managed conservatively. No adjuvant treatment was offered, this being a solitary nature of the lesion a decision for surgical resection of the lesion was taken. Intraoperatively, there was a mass of 5 cm × 5 cm arising from the diaphragm and partially infiltrating segment VII of the liver. During her postoperative stay, CT abdomen showing a large hypodense lesion in segment VII of the liver. Tumor markers alfa fetoprotein, carcinoembryonic antigen and CA 125 were normal. She developed a second hepatic recurrence in 21/01/2010 with a solitary lesion which was completely excised.

Hepatic metastasis occurs in 4% of cases and the treatment in this scenario is usually palliative. In most cases, patients recovered completely after supportive care. Gradually, her kidney function tests normalized, and her sensorium normalized within 72 hours.

**Discussion**

Encephalopathy can occur as an adverse effect of FOLFOX regimen in 5.7%.\(^1\) This can be of three different types. They are posterior reversible encephalopathy, Wernicke’s encephalopathy, and hyperammonemic encephalopathy.\(^2,3\) It is the diagnosis of exclusion.

When 5-FU-induced encephalopathy is suspected, the immediate step is to stop 5-FU infusion. Laboratory tests include but not limited to serum electrolytes, serum ammonia levels, kidney, and liver function tests. MRI is the imaging modality of choice.\(^4\)

In most cases, patients recovered completely after supportive treatment. Our patient was treated with intravenous methyl prednisolone, hydration, branched chain amino acid infusions, and lactulose enema.

**Conclusion**

Removal of the cytotoxic drug is usually recommended once encephalopathy occurs. Early diagnosis and treatment play a pivotal role in the management of FOLFOX-induced encephalopathy as it is a reversible condition with good supportive care.

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**Conflicts of interest**

There are no conflicts of interest.

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**Figure 2: Case 2: Bilateral symmetrical cerebral white matter diffusion restriction**