Capecitabine and sixth cranial nerve palsy

ABSTRACT

Capecitabine is an oral chemotherapeutic agent converted to 5-fluorouracil (5-FU). Neurotoxicity associated with the medication encompasses both central and peripheral nervous systems. We describe a 60-year-old man with colonic carcinoma who developed diplopia due to a sixth nerve palsy following the use of capecitabine which is an orally administered prodrug of 5-FU. An MRI of brain did not reveal a space occupying lesion or vascular insult to account for his cranial nerve palsy. The sixth nerve palsy resolved spontaneously once capecitabine was withdrawn. Physicians in all walks of life are increasingly likely to come across such patients and should familiarize themselves with toxicities consequent to chemotherapy. Further research is needed to elucidate the cause of capecitabine associated neurotoxicity.

KEY WORDS: Capecitabine, cancer, neurotoxicity

INTRODUCTION

Capecitabine is an orally administered prodrug that is converted in the body by thymidine phosphorylase to its active metabolite, 5-fluorouracil (5-FU). 5-FU subsequently leads to inhibition of DNA synthesis resulting in cell death. 5-FU is best known for its use in metastatic breast and colorectal cancers but has also been used in the treatment of gastro-oesophageal, prostate, and renal cell cancers. Neurotoxicity manifesting as cerebellar ataxia[1] and multifocal leukoencephalopathy[2] have been described with this drug.

CASE REPORT

A 69 year old man with an adenocarcinoma of the transverse colon underwent a right hemicolectomy with curative intent. This was followed by adjuvant chemotherapy with capecitabine in a dose of 3200 mg daily. Three days after the first cycle of chemotherapy, he developed sudden onset of diplopia on horizontal gaze but with no associated symptoms including headaches and painful eye movements. He had a previous history of hypertension which was well controlled with ramipril 10 mg daily and bendrofluamethazide 2.5 mg daily and had no other history of note. He was seen within 24 h of the onset of symptoms. and on clinical examination he was found to have a left sixth nerve palsy but with no other neurologic deficit. An MRI diffusion-weighted imaging was performed the next day which showed no evidence of restriction to suggest hyperacute infarction. The MRI did show old ischemic changes and lacunar infarcts but with no evidence of a spaceoccupying lesion or significant brain stem abnormality to account for the sixth nerve palsy. In the absence of any other etiology, and because the symptoms came on within days of starting therapy with capecitabine, the sixth nerve palsy might have been caused by capecitabine. His double vision resolved gradually over the ensuing month.

DISCUSSION

Capecitabine-induced multifocal leukoencephalopathy has been described in the scientific literature.[2] Another case report highlighted two patients who developed peripheral neuropathy during treatment of pancreatic cancer with capecitabine; one developed perioral and upper extremity paresthesias during treatment and the other, a right foot drop. An electromyogram and nerve conduction studies showed sensorimotor peripheral neuropathy in both patients but central nervous system imaging showed no abnormalities. Neurologic symptoms resolved in both patients[3] with no long term sequelae. One case report described a severe disabling sensory-motor polyneuropathy with oxaliplatin and capecitabine chemotherapy, which rendered the patient wheelchair bound.[4] Neuromuscular symptoms, including trismus, slurred speech, confusion, gait abnormalities, and ocular changes have all been reported with capecitabine.[5]

To the best of our knowledge, this is the first description of a sixth nerve palsy in association with capecitabine therapy. The onset of symptoms (diplopia) within days of starting chemotherapy with capecitabine suggests that the drug may
be the culprit in this case. The underlying etiology of neurotoxicity (peripheral and central) remains unclear in patients receiving capecitabine.

5-FU has been implicated in cerebrovascular accidents in patients receiving this drug. It has been suggested that since capecitabine is rapidly metabolized to 5-FU, it is likely that it is the 5-FU and its metabolites that are the main culprits in its toxicity.

**CONCLUSION**

Capecitabine has an established role in the treatment of cancer but is an important albeit infrequent cause of central nervous system toxicity. Therefore, clinicians should carefully weigh the benefits and burden of this drug in individual patients. There is a need for further research to better elucidate the pathophysiology of capecitabine-induced cytotoxicity.

**REFERENCES**


**Source of Support:** Nil, **Conflict of Interest:** None declared.