CASE REPORT

DOI: 10.37047/jos.galenos.2025.2025-3-5

J Oncol Sci 2025;11(2):179-181

Cytotoxic Lesion of the Corpus Callosum Associated with 5-Fluorouracil: A Case Report and Review of Literature

Maral Martin MİLDANOĞLU[1], Banu KARAALİOĞLU[2], Ebru ENGİN DELİPOYRAZ[1], Mehmet Haluk YÜCEL[1], Ömer Fatih ÖLMEZ[1]

[1]İstanbul Medipol University Faculty of Medicine, Department of Medical Oncology, İstanbul, Türkiye
[2]İstanbul Medipol University Faculty of Medicine, Department of Radiology, İstanbul, Türkiye

ABSTRACT

Cytotoxic lesions of the corpus callosum (CLOCC) represent a rare neurological complication. 5-fluorouracil (5-FU) has been associated with CLOCC; however, its precise pathophysiology remains poorly understood. We present the case of a 64-year-old woman with recurrent head and neck squamous cell carcinoma who developed CLOCC following treatment with a regimen including 5-FU, carboplatin, cetuximab, and pembrolizumab. The patient had previously undergone surgery and adjuvant chemoradiotherapy, but later progressed to metastatic disease. After initiating 5-FU-based chemotherapy, she developed neurological symptoms. Diffusion-weighted magnetic resonance imaging revealed cytotoxic lesions in the splenium of the corpus callosum, consistent with CLOCC. Despite discontinuation of chemotherapy and administration of corticosteroids, the patient's condition deteriorated, and she ultimately died due to severe pneumonia and septic shock. This case underscores the rare yet serious risk of CLOCC in patients receiving 5-FU. Further research is needed to elucidate the underlying mechanisms and to identify risk factors associated with 5-FU-related neurotoxicity.

Keywords: Cytotoxic lesion; corpus callosum; 5-fluorouracil

INTRODUCTION

The corpus callosum is a bridge of nerve fibers that connects the right and left cerebral hemispheres. It is traditionally divided into four parts: the rostrum, genu, body, and splenium. The splenium plays a pivotal role in the transfer of visuospatial information, language processing, reading comprehension and consciousness.[1]

Cytotoxic lesions of the corpus callosum (CLOCC) are rare clinical phenomena. While the precise incidence remains uncertain, prior studies have reported a prevalence ranging from 1.1-3%.[2] Various systemic, metabolic, toxic, and infectious processes have been proposed as potential etiologies. CLOCCs present as small, round, or oval lesions, most commonly located on or near the splenium of the corpus callosum.[3] Furthermore, these lesions often demonstrate restriction of diffusion, which may be attributed to complex cell-cytokine interactions leading to neuronal water influx and the subsequent development of cytotoxic edema.[4,5]

Despite the rarity of its occurrence, 5-fluorouracil (5-FU) and its oral prodrug capecitabine have previously been associated with acute central nervous system toxicity. Such toxicities include transient leukoencephalopathies involving the splenium of the corpus callosum.[6] The aim of this report is to present a case of a patient who developed a cytotoxic corpus callosum lesion associated with 5-FU, a rare adverse effect observed in our clinic.

CASE REPORT

A 64-year-old woman with a history of hypothyroidism and no other significant comorbidities presented with bilateral foot

Correspondence: Maral Martin MİLDANOĞLU MD,
İstanbul Medipol University Faculty of Medicine, Department of Medical Oncology, İstanbul, Türkiye
E-mail: mmildanoglu@gmail.com
ORCID ID: orcid.org/0000-0002-4587-0726

Received: 12.03.2025 **Accepted:** 21.07.2025 **Epub:** 13.08.2025 **Publication Date:** 28.08.2025

Cite this article as: Mildanoğlu MM, Karaalioğlu B, Engin Delipoyraz E, Yücel MH, Ölmez ÖF. Cytotoxic lesion of the corpus callosum associated with 5-fluorouracil: a case report and review of literature. J Oncol Sci. 2025;11(2):179-181

*This case report was previously presented as a poster at Master Oncology Congress, in September 2024.

Available at journalofoncology.org

swelling. Her oncological history included surgery for a right mandibular mass in July 2022, followed by neck dissection. Pathological examination confirmed squamous cell carcinoma with negative surgical margins and no malignancy detected in 35 dissected lymph nodes. The patient then received adjuvant chemoradiotherapy and was maintained under active surveillance. After one year, the disease recurred with the development of new pulmonary lesions. Treatment with capecitabine and cisplatin was initiated, but after three cycles, progression to bone metastases was noted, prompting the initiation of palliative radiation therapy for symptom control.

Subsequent restaging with 18- fluorodeoxyglucose positron emission tomography-computed tomography revealed new metastatic lesions in the liver, lungs, and bones. A tru-cut biopsy of the newly developed bone metastasis demonstrated a programmed death ligand 1 combined positive score of 10%, and treatment was modified to include 5-FU (4000 mg/m^2/4-day infusion), cisplatin 75 mg/m^2, cetuximab (400 mg/m^2), and pembrolizumab (200 mg).

One day following completion of the 5-FU infusion, the patient presented to the emergency department with anorexia, fatigue, dizziness, and confusion. Neurological examination revealed disorientation to time and place, with muscle strength of 4/5 in the upper extremities and 3/5 in the lower extremities. No focal deficits were observed. Laboratory tests showed mild anemia, elevated creatinine (1.98 mg/dL), urea (88 mg/dL), and C-reactive protein (103 mg/dL), while electrolytes and liver function tests remained within normal limits.

Diffusion-weighted magnetic resonance imaging demonstrated a characteristic cytotoxic lesion with restricted diffusion in the splenium of the corpus callosum, along with additional diffusion restriction in the cortical regions of the bilateral posterior sulci (Figure 1). No neoplastic or ischemic lesions were identified. The patient was admitted for supportive care, including hydration, broad-spectrum antibiotics, and corticosteroids (methylprednisolone at 1 mg/kg). Based on the patient's neurological presentation and anticipated response to corticosteroid therapy, further evaluation for paraneoplastic syndromes or leptomeningeal disease was considered. However, on day 5, the patient developed respiratory distress, necessitating transfer to the intensive care unit. Despite aggressive management, she succumbed to severe pneumonia and septic shock two days later. Patient consent was obtained.

DISCUSSION

CLOCCs are rare manifestations of neurotoxicity, often occurring within days of initiating chemotherapy with agents like 5-FU. This case clearly demonstrates the temporal relationship between the start of 5-FU therapy and the development of CLOCC. Previous reports have suggested that individual patient factors, rather than the cumulative dose of 5-FU, play a more pivotal role in the development of this complication.[6] Although CLOCC has been observed in patients treated with 5-FU for breast and colorectal cancers, there are fewer documanted cases in patients with head and neck malignancies. Upon reviewing the literature for case

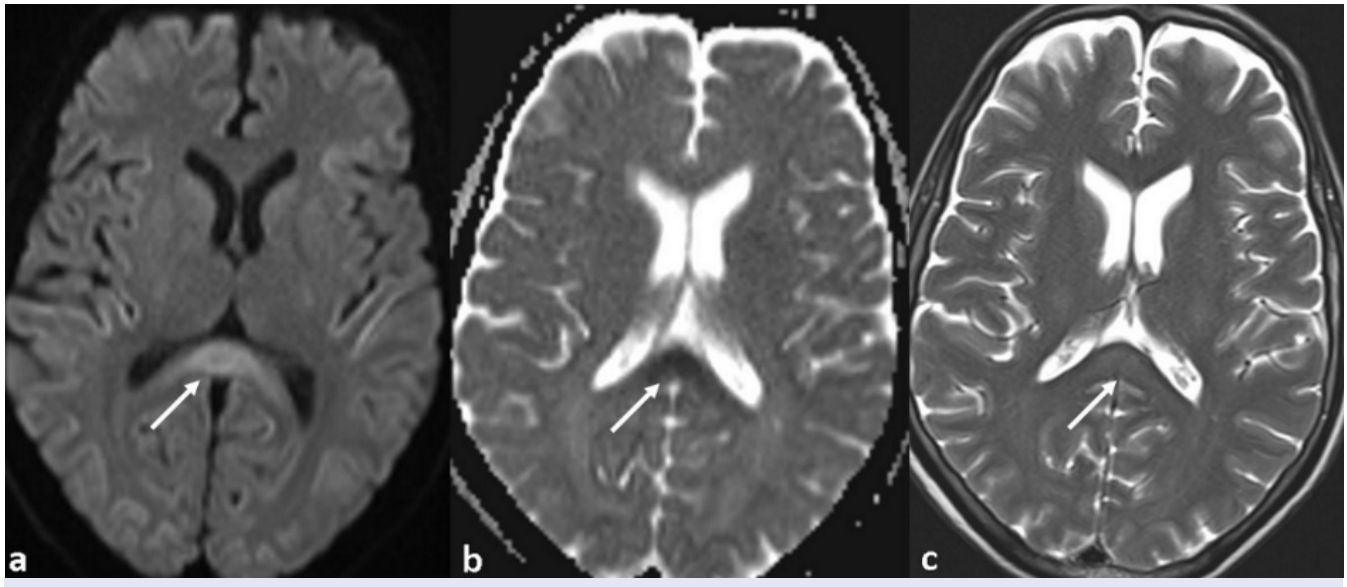

FIGURE 1. (a, b) Drug induced isolated corpus callosum splenium lesion is shown; localized diffusion restriction seen as hyperintense signal on DWI and confirmed with hypointense signal on corresponding ADC maps, representing isolated splenial excytotoxic edema. **(c)** On axial T2WI, splenial subtle hyperintensity can be depicted (arrow).

ADC: Apparent diffusion coefficient

reports and reviews of 5-FU–associated CLOCC, our case was identified as the only reported instance in which this adverse effect developed following combination therapy with 5-FU, cisplatin, cetuximab, and pembrolizumab. While cerebellar dysfunction, particularly dysarthria, is commonly observed in CLOCC cases, our patient primarily presented with confusion, which is the second most frequent symptom.[6] For patients receiving 5-FU, monitoring for neurotoxicity is critical, and some studies have suggested assessing dihydropyrimidine dehydrogenase (DPD) enzyme activity in patients with a history of neurotoxicity. However, routine screening for DPD deficiency is not currently endorsed.[7] In our case, DPD deficiency was not prioritized, as the patient had previously undergone capecitabine therapy without experiencing any significant adverse events, and, during the current course of 5-FU, did not develop mucositis, stomatitis, or other prominent toxicities typically associated with DPD deficiency. Most patients with CLOCC respond well to the discontinuation of the offending agent and corticosteroid therapy; however, the poor outcome in our patient underscores the potential severity of this toxicity. The patient was admitted to the intensive care unit due to severe pneumonia and sepsis, which developed as a result of immunosuppression and a possible opportunistic infection secondary to initiated corticosteroid therapy. Despite intensive care management, the patient ultimately died.

CONCLUSION

CLOCC are a rare but serious complication of 5-FU-based chemotherapy, and their recognition is essential for prompt management. Clinicians should remain vigilant for neurological symptoms in patients undergoing treatment with 5-FU, particularly when combined with other chemotherapeutic or immunotherapeutic agents. Early intervention, including discontinuation of the offending agent and administration of corticosteroids, may improve outcomes; however, further research is needed to better elucidate the pathophysiology and identify risk factors associated with CLOCC.

Ethics

Informed Consent: Patient consent was obtained.

Footnotes

Authorship Contributions

Surgical and Medical Practices: M.M.M., Concept: M.M.M., E.E.D., Ö.F.Ö., Design: M.M.M., M.H.Y., Data Collection or Processing: M.M.M., B.K., Analysis or Interpretation: M.M.M., M.H.Y., Ö.F.Ö., Literature Search: M.M.M., E.E.D., Writing: M.M.M., B.K., Ö.F.Ö.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

REFERENCES

1. Mathews MS, Linskey ME, Binder DK. William P. van Wagenen and the first corpus callosotomies for epilepsy. J Neurosurg. 2008;108(3):608-613. [Crossref] [PubMed]
2. Yum KS, Shin DI. Transient splenial lesions of the corpus callosum and infectious diseases. Acute Crit Care. 2022;37(3):269-275. [Crossref] [PubMed] [PMC]
3. Rolshoven J, Fellows K, Ania R, Tabaac BJ. Vertigo and cytotoxic lesions of the corpus callosum: report with review of the literature. Case Rep Neurol Med. 2021;2021:5573822. [Crossref] [PubMed] [PMC]
4. Tetsuka S. Reversible lesion in the splenium of the corpus callosum. Brain Behav. 2019;9(11):e01440. [Crossref] [PubMed] [PMC]
5. Starkey J, Kobayashi N, Numaguchi Y, Moritani T. Cytotoxic lesions of the corpus callosum that show restricted diffusion: mechanisms, causes, and manifestations. Radiographics. 2017;37(2):562-576. [Crossref] [PubMed]
6. Perrain V, Bihan K, Bompaire F, et al. Leukoencephalopathy with transient splenial lesions related to 5-fluorouracil or capecitabine. Eur J Neurol. 2021;28(7):2396-2402. [Crossref] [PubMed]
7. Li J, Lee JJ, Chu E, Baehring JM. Reversible leukoencephalopathy with stroke-like presentation in a patient with 5-dihydropyrimidine dehydrogenase deficiency treated with continuous 5-fluorouracil infusion. Clin Colorectal Cancer. 2012;11(3):215-217. [Crossref] [PubMed]