Acute Cerebrovascular Accident after Cisplatin Treatment in a Patient Taking Letrozole

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Vascular thrombotic events · Cerebrovascular accident · Cancer · Chemotherapy

Abstract
Vascular thrombotic events are common in patients with cancer and chemotherapy is considered a contributing factor. Venous thrombotic events are more common than arterial ones which are less documented. In this report, we describe a patient with right homonymous hemianopsia following treatment with cisplatin for small cell lung carcinoma while also taking letrozole. A brief review of the literature on arterial thrombotic events after chemotherapy follows.

Introduction
Vascular thrombotic events are common in patients with cancer. The hyperthrombotic state that accompanies malignancies was reported as long ago as the 19th century by Trousseau [1]. Chemotherapy can also be a risk factor for vascular events. Twenty-five years ago, Goldhirsch et al. [2] reported an acute cerebrovascular accident (CVA) in a patient receiving a cisplatin-based treatment. Other case reports followed [3–5].

We describe a patient with left homonymous hemianopsia following the treatment of small cell lung carcinoma (SCLC) with cisplatin while also on letrozole.

Case Presentation
A 58-year-old woman diagnosed with SCLC extensive disease (metastases in the spine) was hospitalized for her first chemotherapy cycle.

Her medical history was noteworthy for a stage IIIA breast cancer diagnosed 3 years earlier and treated with mastectomy, adjuvant radiotherapy and chemotherapy of carboplatin/docetaxel/trastuzumab followed by hormone therapy with letrozole. She had no history of hypertension, hypercholesterolemia or diabetes, but had a current smoking history of 30 pack-years. The only other medication she was taking was 2.5 mg of letrozole daily. Her physical examination was normal.

The chemotherapy administered consisted of cisplatin 25 mg/m² and etoposide 80 mg/m² on days 1–3. On the 5th day after the start of chemotherapy, the patient noticed difficulty reading, especially the last letters of each line.

An ophthalmologic examination revealed normal pupils and normal ocular motility. The optic fundi were normal. Visual fields examination demonstrated a right homonymous hemianopsia. The rest of the neurologic examination was unremarkable. Laboratory studies including a coagulation profile, electrolytes and cholesterol were within normal limits. ECG showed a normal sinus rhythm.

Brain MRI showed a hyperdense lesion in the left occipital lobe in the T2 sequence, without gadolinium enhancement (fig. 1b).
This lesion was consistent with a thrombotic CVA. The lesion was not present in the brain MRI performed for staging 1 month before (fig. 1a). Doppler ultrasonography of carotids was normal.

Letrozole was stopped. Treatment with aspirin was started and the planned chemotherapy was continued every 3 weeks.

The neurological deficit remained stable and the patient had a partial response at the evaluation after 3 cycles of cisplatin/etoposide. MRI 2 months after the event showed a slight improvement of the left occipital lesion (fig. 1c). She received 2 more cycles of chemotherapy. No new thromboembolic events (TEs) happened until the patient died from progressive disease 10 months after the event.

Discussion

TEs occur frequently in cancer patients and constitute the second cause of mortality after cancer per se in these patients [6]. Conversely, about one fifth of patients with a venous thromboembolism have active cancer [7]. The mechanisms involved in the pathogenesis of TEs include aberrant activation of the coagulation cascade, defects in blood flow due to local tumor growth and the frequent presence of foreign bodies such as indwelling catheters in these patients and immobility due to cancer or surgery [6]. Furthermore, cancer treatment such as chemotherapy is an established risk factor for TEs in cancer patients in a variety of malignancies and many different treatment regimens. TEs are divided into venous (deep vein thrombosis and pulmonary embolism) and arterial (peripheral artery and cerebrovascular thromboembolism and myocardial infarction).

Several cases of ischemic cerebrovascular complications have been reported associated with the use of cisplatin-based chemotherapy.

A study that prospectively evaluated the incidence of major vascular events in 108 patients with non-SCLC receiving cisplatin and gemcitabine concluded that chemotherapy is a powerful risk factor. In this study, 10 of 22 recorded events were arterial including 1 patient who had an ischemic stroke [8]. Vascular events were detected between 4 and 234 days after the start of chemotherapy. The time to the first arterial event seemed to be shorter than the time to the first venous event (median 35 vs. 61.5 days) but it remains unclear if this observed numerical difference represents a true difference in the delay of these events, because it was not statistically significant. The role of gemcitabine as a contributing agent cannot be excluded [9]. A large retrospective analysis of 932 patients treated with cisplatin-based chemotherapy for various malignancies at a single institution confirms the high incidence of TEs in these patients. This analysis showed an incidence of 18.1% (169 patients) during or up to 4 weeks after chemotherapy. There were 18 arterial events, 10 of which were CVAs. Factors identified by multivariate analysis to increase the risk of TEs were advanced age, lower Karnofsky Performance Status score, the presence of a central venous catheter and higher Khorana score [10].

In another study of 179 patients with germ cell cancers receiving first-line platinum-based chemotherapy, 15 (8.4%) developed a TE; 3 of these TEs were arterial including 2 cerebral ischemic strokes [11].

Other case reports of CVAs in patients receiving cisplatin-based chemotherapy exist in the literature with various presentations. A patient with testicular cancer receiving cisplatin/vinblastine/bleomycin treatment was found to have left homonymous hemianopsia with encephalopa-
Patient Taking Letrozole

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References