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Case report

Cortical blindness—a catastrophic side effect of vincristine

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The term 'cortical blindness' indicates loss of sight due to bilateral lesions of the occipital lobes. It is a rare, but severe, side effect of chemotherapeutic agents. Cortical blindness was diagnosed in a 67 year old woman with leiomyosarcoma of the large bowel, treated by vincristine-containing chemotherapy. Cortical blindness without focal neurological signs and with two repeated normal brain computed tomography scans, in which there was no structural damage to the occipital lobes, suggests a metabolic or toxic reaction as a cause in our patients. The temporal relationship between vincristine treatment and cortical blindness implicates vincristine as the possible causative agent for this catastrophic phenomenon.

Key words: Acute vision loss, cortical blindness, neurotoxicity, vincristine.

Introduction

Acute blindness, particularly in a cancer patient, is a catastrophic event that aggravates disability and severely impairs performance status and quality-of-life. It might result from a disease-related complication such as optic nerve involvement of malignant cells,[1] metastasis to the eye or to the orbit,[2] primary or metastasis in the pituitary gland[3] or primary tumors of the optic pathway.[4] It might also be a toxic manifestation of anti-cancer treatment. Cranial irradiation[5] as well as several drugs have been reported to cause acute blindness: cisplatin,[6–9] BCNU, VM-26,[9] oral CCNU,[5] methotrexate,[10] vincristine[11] and α-interferon.[12] Various mechanisms for this side effect have been suggested, including retrobular neuritis,[12] optic nerve swelling,[8] cone dysfunction,[14] ischemic damage to the anterior visual system[5] and cortical blindness.[12,15,16]

Herein, we report a case of acute cortical blindness related to treatment with vincristine and review the literature regarding this toxic manifestation.

Case report

A 67 year old female with leiomyosarcoma of the large bowel underwent right hemicolectomy and panhysterectomy in August 1990. After a disease-free period of 3 months abdominal cavity recurrence, presented by a mass and ascites, was diagnosed. Chemotherapy was administered: etoposide (VP-16; 100 mg/m^2/day) and a continuous drip of ifosfamide (1.8 g/m^2/day), for five consecutive days. Uroprotection with mesna was given together with the ifosfamide. Severe toxicity was observed within 2 days following the course including ifosfamide-related acute encephalopathy, myelosuppression and fever, electrolyte disturbances, mild renal failure, and general deterioration. The patient recovered completely, but refused to continue this protocol. Therefore, she received one course of cyclophosphamide (500 mg/m^2) on day 1, vincristine (1 mg/m^2) on days 1 and 5, adriamycin (50 mg/m^2) on day 1, and DTIC (200 mg/m^2) on days 1–5. The patient was discharged from the ward on the sixth day, but was re-admitted the following day because of paralytic ileus, which was treated conservatively. On the 10th day fever (38.5°C) and leukopenia (200 cells mm^3) were observed. Blood culture yielded staphylococcus coagulase positive, which

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was successfully treated by a vancomycin and Garamycin combination. On the 21st day, the paralytic ileus resolved. On the next day, she developed a neurological syndrome of confusion and acute bilateral complete vision loss. Her general condition deteriorated again: she became febrile, had leukopenia (1800 cells/mm^3) and severe thrombocytopenia (8000 mm^3) without purpura or bleeding. Examination of the fundi was normal and no hemorrhage was seen in the retinae of both eyes. Neurological examination suggested cortical blindness. Electro-encephalogram (EEG) demonstrated left occipital slowness and no photic drive was evoked. Repeated computed tomography (CT) studies of the brain did not disclose structural damage to the occipital cortices, the optic radiations or the adjacent cerebrospinal fluid (CSF) spaces. Lumbar puncture was performed after which the thrombocyte count improved, and the liquor was clear, with normal protein, glucose and without blood cells or malignant cells. The patient deteriorated, became comatose and succumbed on the 33rd day. Autopsy was not permitted.

Discussion

The term 'cortical blindness' indicates loss of sight due to bilateral lesions of the occipital lobes. The pupillary light reflexes are preserved, the retinas are usually normal but the optokinetic nystagmus is lost. These findings may be transient, lasting from 24 h to 14 days.[17]

Cortical blindness might result from various pathological states involving the occipital lobes.[17] The etiologies of cortical blindness include trauma, hypoxia, cerebrovascular accident, paraneoplastic disseminated intravascular coagulation, non-Hodgkin's lymphoma, leukemia and others.[6,15,17,18]

Cortical blindness is a rare, unexpected and severe side effect of chemotherapeutic agents such as cisplatin,[16] vincristine[15] and α-interferon.[12] In no case was cortical blindness the sole neurological manifestation related to vincristine or cisplatin, but rather part of a generalized acute encephalopathy or neurotoxicity. Concomitant manifestations were grand mal seizures and respiratory arrest. CSF analysis and brain CT scan were usually not contributory,[6,12,15,16] as in our case, while EEG presented a pattern of diffuse encephalopathy.[6,12,15,16] In our patient the EEG demonstrated left occipital slowness and bilateral lack of photic drive.

Our patient was treated by a combination containing vincristine and developed a wide spectrum of vincristine toxic manifestations. The most common neurological manifestations of vincristine toxicity include polyneuropathy, cranial nerve paralysis, a syndrome of inappropriate ADH secretion, autonomic dysfunction and diffuse cerebral dysfunction with seizures.[7,11,15,19] Less frequent manifestations are optic neuropathy and short-term cortical blindness.[7,11,15] The mechanism of this vincristine toxicity is not clear, but may be related to the effect of the drug on the microtubules.[15] Studies on nerve conduction indicated axonal degeneration.[20]

Cerebrovascular disease and brain metastases are common causes of cortical blindness in elderly patients.[17,19] Cortical blindness without focal neurological signs and from two consecutive brain CT scans, which did not show any pathology in the occipital lobes, suggests a metabolic or toxic reaction as a cause in our patient. The temporal relationship between vincristine treatment and cortical blindness implicates that vincristine is the possible causative agent for this phenomenon.

Interestingly, our patient had experienced ifosfamide-related encephalopathy followed by complete clinical recovery before the development of vincristine-related neurotoxicity. There are no data regarding the influence of previous encephalopathy due to one drug on the probability of having another event of encephalopathy induced by a second, non-cross-active drug. It might be assumed that the risk is increased and that vincristine-related neurotoxicity is promoted by previous ifosfamide-related damage. The mechanism is, however, unclear, because vincristine crosses the blood–brain barrier and ifosfamide causes this toxicity by its metabolites.

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