Cancer Chemother Pharmacol (1992) 29: 329–330

Cancer Chemotherapy and Pharmacology

Short communication

Interferon-related cortical blindness

Ofer Merimsky[1], Puiu Nisipeanu[2], Anat Loewenstein[3], Irith Reider-Groswasser[4], and Samario Chaitchik[1]

[1] Departments of Oncology[1], Neurology[2], Ophthalmology[3] and the Section of Neuroradiology[4], Tel-Aviv Medical Center and Sackler Faculty of Medicine, Tel-Aviv University, Tel-Aviv, Israel

Received 1 July 1991/Accepted 16 October 1991

Summary. The term cortical blindness indicates loss of sight due to bilateral lesions in the occipital lobes. It is a rare but severe side effect produced by chemotherapeutic agents. Cortical blindness was diagnosed in a 75-year-old man who had been treated with alpha-interferon for metastatic renal-cell carcinoma. The absence of focal neurological signs and of abnormal findings as determined by two repeated computed tomography (CT) scans of the brain, which excluded structural damge to the occipital lobes, suggest that metabolic or toxic reactions may have caused the cortical blindness diagnosed in our patient. The temporal relationship between the treatment with alpha-interferon and the development of cortical blindness indicates that this substance may have been the causative agent for this phenomenon.

Introduction

The term cortical blindness indicates loss of sight due to bilateral lesions in the occipital lobes. The pupillary light reflexes are preserved and the retinas are usually normal, but optokinetic nystagmus is lost. These findings may be transient, lasting from 24 h to 14 days [1]. Cortical blindness might result from various pathological states involving the occipital lobes [1]. The etiology of this phenomenon includes trauma, hypoxia, cerebrovascular accident, paraneoplastic disseminated intravascular coagulation, non-Hodgkin's lymphoma, and leukemia, among other causes [1–4, 7]. Cortical blindness is a rare but severe side effect produced by chemotherapeutic agents such as cisplatin and vincristine [4, 5].

Offprint requests to: Ofer Merimsky, Department of Oncology, Ichilov Hospital, 6, Weizman Street, Tel-Aviv 64239, Israel

This report describes a patient who developed acute cortical blindness associated with severe and fatal encephalopathy subsequent to treatment with alpha-interferon.

Case report

Patient 1. A 75-year-old man presented with histologically proven renal-cell carcinoma (RCC) arising in a congenital solitary kidney and metastasizing to the para-aortic lymph nodes. He was treated with intramuscular injections of recombinant interferon alpha-C (Interpharm Ltd., Israel) at doses of 3×10^6 IU daily for 2 weeks followed by 3×10^6 IU/m^2 every other day. Side effects were moderate and included fever of up to 38.5°C, loss of appetite, weakness, and lethargy. Within 3 weeks of interferon treatment, he developed a neurological syndrome comprising of a confusional state and cortical blindness. Examination of the fundi revealed normal findings. Blood counts and chemistry were all normal. Lumbar puncture (LP) yielded clear liquor at normal opening pressure, with normal protein and glucose levels and no blood cells being observed. No malignant cells were evident after centrifugation. A computed tomography (CT) scan of the brain revealed normal ventricles and sulci. In the centrum semiovale of both hemispheres, a diminution in the density of the white matter was noted. No enhancement occurred after contrast injection. The occipital lobes were normal. The second brain CT scan, which was obtained 10 days later, failed to disclose any pathology in the occipital lobes. Interferon treatment was discontinued. No antibodies to interferon were found in the patient's serum. There was no reversal of the neurological manifestations, and the patient died 6 weeks later. Unfortunately, autopsy was not permitted.

Discussion

Cortical blindness is a rare complication induced by several drugs that are used in the treatment of various malignancies. Data from the literature concerning this severe side effect are summarized in Table 1.

Our patient was treated with recombinant alpha-interferon and developed neurobehavioural toxic manifestation. Adverse neurologial reactions to interferon include somnolence, fatigue, lethargy, psychiatric symptoms, conceptual disorganization, neurological deficits, mental deterioration and coma. Interferon-related cortical blindness has not yet been reported. The mechanism underlying inter-

Table 1. Literature data on patients exhibiting cortical blindness following chemotherapy

Sex	Age (years)	Primary cancer	Drug regimen	Associated findings	Outcome	Reference
M	7	Abdominal NHL Burkitt's type	Cyclophosphamide, vincristine prednisone, methotrexate	Grand mal seizure, respiratory arrest, neurotoxicity normal brain CT, normal fundi	Complete recovery	[4]
M	4	Paratesticular Rhabdomyosarcoma	Actinomycin D vincristine	Neurotoxicity, encephalopathy, normal fundi and LP normal brain CT	Complete recovery	[4]
F	11	NHL in ileum, histiocytic	Methotrexate, L-asparaginase, prednisone, vincristine, ara-C, Adriamycin	Seizures, normal EEG and brain CT normal fundi and LP, cardiorespiratory arrest, positive vincristine challenge	Complete recovery	[4]
M	30	Embryonal cell in testis	Vinblastine bleomycin, cisplatin	Vomiting, grand mal seizures, normal brain scan and CT scan diffuse encephalopathy on EEG normal fundi and LP high cisplatin level in CSF	Complete recovery	[3]
F	62	fallopian tube	Cisplatin, Adriamycin	Normal brain scan and CT scan, delay in VEP latency, normal fundi	Visual acuity recovered, right homonymous hemianopsia	[5]

VEP, Visual evoked potential

feron-induced cortical blindness is obscure but may involve the direct toxic effect of this agent on the brain tissues [6].

Cerebrovascular disease and brain metastases are common causes of cortical blindness in elderly patients [1, 7]. The absence of focal neurological signs and of abnormal findings as determined by two consecutive brain CT scans, which revealed no pathology in the occipital lobes, suggested that metabolic or toxic reactions caused the cortical blindness diagnosed in our patient. The temporal relationship between the treatment with interferon and the development of cortical blindness indicates that this substance may have been the causative agent for this phenomenon. However, the possible influence of an RCC-related paraneoplastic syndrome manifesting as cortical blindness and neurobehavioral changes cannot be excluded with certainty.

References

1. Adams RD, Victor M (1989) Principles of neurology. McGraw Hill, New York, pp 347, 617
2. Bergman PS (1957) Cerebral blindness. Arch Neurol Psychiatr 78: 568
3. Berman IJ, Mann MP (1980) Seizures and transient cortical blindness associated with *cis*-platinum(II) diamminedichloride (PDD) therapy in a thirty-year-old man. Cancer 45: 764
4. Byrd RL, Rohrbaugh TM, Raney RB, Norris DG (1981) Transient cortical blindness secondary to vincristine therapy in childhood malignancies. Cancer 47: 37
5. Diamond SB, Rudolph SH, Lubicz SS, Deppe G, Cohen CJ (1982) Cerebral blindness in association with cisplatinum chemotherapy for advanced carcinoma of the fallopian tube. Obstet Gynecol 59: 84
6. Merimsky O, Reider-Groswasser I, Inbar M, Chaitchik S (1990) Interferon related mental deterioration and behavioural changes in patients with renal cell carcinoma. Eur J Cancer 26: 596
7. Posner JB, Schori M (1980) Cerebrovascular complication of cancer. Clin Bull 10: 158