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Oncology

CORTICAL BLINDNESS FOLLOWING CISPLATIN CHEMOTHERAPY : A Case Report

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ABSTRACT Acute blindness or seizures are usually the first signs of central neurotoxicity from cisplatin. We report a case of acute blindness caused by cisplatin. The loss of vision was the main observed sign.

The symptoms are usually reversible within weeks after cessation of the platinum treatment. The therapeutic strategy is stopping the platinum treatment.

KEYWORDS : .

INTRODUCTION

Cisplatin is a phase III chemotherapeutic agent, effective against a variety of tumors, which has many side effects, notably gastrointestinal, renal, audiological, haematological and neurological. We report a case where a patient experienced acute cortical blindness following Cisplatin chemotherapy.

MATERIALAND METHODS

A 45-year-old men with local relapse of UCNT after 3 cures of neoadjuvant chemotherapy (Cisplatin-doxorubicin) and 7cures of concurrent radio-chemotherapy with Cisplatin . He presents the local relapse after 1 year and 3months of the end of intial tratment confirmed in MRI . Baseline renal function was normal with a calculated creatinine clearance of 83ml/min (Cockroft formula). Chemotherapy consisted of a 3 cures every 3 weeks intravenous administration of Cisplatin 80mg/m with 5 Fluoro-uracil 1000mg/m for 4 days .The treatment was well tolerated . 20 days after the third cure of cisplatin and 5FU, he first complained about bilateral blindness .Other neurological signs were absent.

INVESTIGATIONS

An ophthalmologic examination revealed a bilateral corneal ulcer _ . Visual acuity was slightly reduced in both eyes. Differential diagnosis of increased intracranial pressure due to meningeosis carcinomatosa or cerebral metastasis and anterior ischemic optic neuropathy (AION) due to anemia were discussed. An MRI of the brain showed no signs of intracranial pressure, or leptomeningeal carcinomatosis (fig .1)

The cerebral and thoraco-abdominal CT scan showed a partial response in assessable disease site. Chemotherapy was therefore stopped because of the bilateral blindness . One week after the visual acuity was improved

DISCUSSION

Cortical blindness has been reported by Berman and Mann [1] in one patient receiving chemotherapy for testicular cancer; in one woman with carcinoma of the fallopian tube by Diamond et al [2] and another with squamous cell carcinoma of the cervix by Pippitt et al(3) .Analysis of these three cases and our own showed many similarities. Cisplatin was a common drug in all cases prior to the onset of blindness. Onset of blindness varies from several hours' to 13 days after Cisplatin treatment, suggesting a chronic rather than acute cause[3]

In adults, cisplatin toxicity of the central nervous system usually occurs suddenly after a total dose of 1200 mg/m2. The main symptoms are visual disturbances (often a sudden episode of blindness that has been attributed to cortical blindness , to retrobulbar neuritis , or to retinal toxicity), seizures, headaches, changes in mental status, and anxiety([4] .The neurological examination, including a fundoscopic examination, are normal. The neurological workup is non-contributive: the CT-scan of the brain is normal, the analysis of CSF is non-specific except for a possible protein elevation, and the EEG may show focal signs of slow or fast wave bursts, though usually only non-specific generalized slowing is noted. When visual-evoked potentials are done, an increase in the latency of the response is seen. These signs are usually reversible.

Neurologic, otologic, and ophthalmologic effects of CPDD have been reported in the literature Previous explanation of CPDD toxicity has been compared to the toxic effects of heavy metals, and recently cisplatin, have shown to cause a clinical picture consistent with retrobulbar neuritis with patients experiencing a “gray-out” of vision [4] .Lead may injure the optic nerve by causing either a generalized increase in intracranial pressure or a direct toxic action on the nerve itself. Kedar et al. reported a decrease in peripheral nerve conduction in a patient with osteogenic sarcoma treated with cisplatin . [5-6]

In our case report, we postulate a direct toxic effect of cisplatin, as it was described in the 1970s for cisplatin . In the case of cisplatin cortical blindness, macula degeneration, retrobulbar neuritis and papilledema were described [7] but not found in our case because of impossibility to realize a fundoscopic exam. Clinically, a loss of visual accuracy up to full blindness, often loss of color vision and scotomas were seen. Usually these symptoms are unilateral and initially mild, so that more chemotherapy is given before the diagnosis is made[8]. A correlation with renal insufficiency and arterial hypertension was reported . The symptoms are usually reversible within weeks to months after cessation of the platinum treatment , and the restoration of color vision can take up to 1 year[9-10]. It seems to be a cumulative toxicity, as all cases occurred after several cycles of chemotherapy [10] . Furthermore, pharmacokinetic studies of cisplatin show a continual rise of the drug concentration in the cerebrospinal fluid with each cycle [11]. It is possible that the cerebrospinal fluid concentration is important for the occurrence of this toxicity: in one patient with blindness and a seizure equally high concentrations of cisplatin in the cerebrospinal fluid and the serum were measured [12-13] .There are no proven therapeutic interventions; corticosteroids are used empirically. The early recognition of this potentially severe side effect is paramount, since stopping chemotherapy before irreversible damage occurs is crucial

CONCLUSION

Clinically relevant papilledema is a rare, but important side effect of cisplatin. It can occur at standard doses and it can be partly irreversible. Since cisplatin is extensively used in a variety of common tumors in the palliative as well as the curative setting, this potentially severe side effect has to be kept in mind. Early recognition followed by cessation of further cisplatin administration is crucial

Although cisplatin toxicity of the central nervous system usually occurs as an acute toxic encephalopathic syndrome with blindness and seizures as hallmark signs, subacute central neurotoxicity has to be recognized as part of the same symptomatology. It is crucial to differentiate subacute neurotoxicity from signs of tumor progression.

Discontinuation of cisplatin is usually curative , and the administration of steroids might speed recovery . An alternative chemotherapy should be used for further cancer treatment.

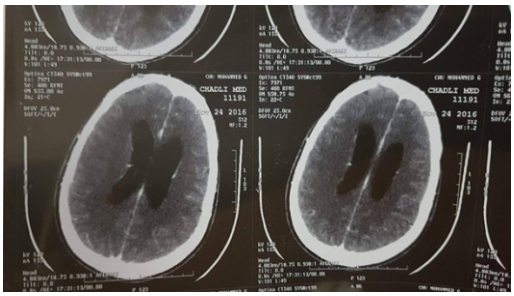

Fig.1

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