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Meningeal Carcinomatosis in Urothelial Cancer

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MENINGEAL CARCINOMATOSIS is a rare manifestation of epithelial tumours. We report a 38-year-old patient with meningeal carcinomatosis who became symptomatic 27 months after treatment of a metastatic renal pelvic tumour.

Induction was with cisplatin 70 mg/m^2 and methotrexate 40 mg/m^2. Radical nephro-ureterectomy and retroperitoneal lymphadenectomy was done after the first cycle. Postoperative adjuvant chemotherapy was cisplatin and methotrexate (four cycles). 27 months later he was admitted with hypoacusis, balance troubles and headache without nausea and fever. Lumbar puncture revealed malignant cells. Magnetic resonance imaging, computed tomography (CT) and X-ray of the skull showed no sign of a space-occupying intracerebral process. No other metastases were found. Six intrathecal courses of methotrexate 7.5 mg/m^2 were given followed by five courses of 12 mg/m^2. The results of treatment were assessed by examination of the cerebrospinal fluid (CSF) (Table 1), CT of the brain, audiogram and observation of the eye-fundus. Headache, nausea and dizziness and choked papilla resolved after methotrexate treatment. The hypoacusis did not improve. The patient was admitted to the neurology department because of *grand mal* seizures, which occurred 3 weeks after stopping methotrexate. Neurological examination revealed a diffuse cerebral dysfunction, bicerebellar symptoms, distal polyneuropathia and lesion of the pyramidal tract on both sides without signs of paraplegia.

Gonzales-Vitale and Garcia-Bunuel found, in 2227 necropsies, 306 patients with cerebral metastasis. Only 18 had evidence of meningeal carcinomatosis [1]. There was only 1 patient with an ureteral tumour and meningeal carcinomatosis. Several routes of metastases have been discussed: Haematogenous to the choroid plexus, primary haematogenous by the leptomeningeal vessels, dissemination of tumour cells along the perineural lymphatics and sheats [1] and centripetal extension along the perivascular lymphatics [2]. Symptoms depend on the site: Cerebral symptoms due to diffuse spread to the leptomeninges, compression of the cerebral nerves caused by tumour cells with sheathing the nerves and radicular symptoms due to infiltration of the spinal roots.

Our patient had a lesion of the VIIth and VIIIth cerebral nerve with suspicion of metastasis to the hard bone and the internal auditory meatus. Little *et al.* also observed a reduction of CSF glucose [3] in 76% of patients with meningeal carcinomatosis. The cause may be the alternation of the blood–brain barrier or increased use of glucose by tumour cells [4, 5]. CSF protein is elevated in meningeal carcinomatosis, and CSF cytology leads to diagnosis. Sometimes several punctures are needed for a positive cytology result. The dose of methotrexate that is usually given is 0.2 mg/kg over 3–4 days [6]. Intrathecal methotrexate should be continued until the symptoms improve. Our patient received methotrexate intrathecally every 7 days to a total dosage of 109.5 mg/m^2. The clinical symptoms improved, but there was no improvement of hypoacusis. CSF glucose, protein and globulin did not normalise. We stopped methotrexate, because there is a risk of radiculopathia with symptoms of paraplegia with an increasing doseage of methotrexate. Little *et al.* and Grain and Karr reported survival times up to 6 months [7, 3]. Our patient had the first symptoms in March, 1987. The *grand mal* seizures indicated tumour progression, he died 7 months after beginning intrathecal chemotherapy.

Table 1. CSF examination

Date	Cytology (PAP)	Colour	Globulin	No. of cells (μl)	Glucose (mg/dl)	Protein (mg/dl)	Cells
8.3	II	Clear	+++−	80	42	49	—
17.3	II	Opal	—	120	51	39	—
24.3	IV	Clear	—	100	—	—	Atypical
30.3	V	Clear	—	144	36	58	Atypical
4.4	X	—	—	—	—	—	—
15.4*	X	—	—	—	—	—	—
23.4	X	—	—	—	—	—	—
30.4	X	—	—	—	—	—	—
13.5	V	Clear	—	32	35	71	Atypical
18.5	IV	Clear	—	—	—	—	Atypical
25.5	V	—	—	—	—	—	Atypical
1.6	IV	Clear	+	50	42	103	Atypical
9.6	IV	Clear	—	39	43	163	—
15.6	V	—	—	—	—	—	Atypical
22.6	IV	Clear	+++	6	—	151	Atypical
29.6	II	Clear	+	56	34	129	—

*Methotrexate stopped. Normal values: glucose, 45–70 mg/dl; protein, 15–45 mg/dl; and cells, up to 12 μl.

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