Abstract We describe a rare case of multiple spinal meningiomas and evaluate the possible relationship with tamoxifen treatment. We observed a 74-year-old woman who showed a spastic paraparesis gradually developed in the last year. The patient underwent left mastectomy for a breast cancer ten years earlier and was treated with tamoxifen for four years after surgical intervention. Magnetic resonance imaging revealed three spinal meningiomas at C6-C7, D6-D7 and D9 levels. Taking in account the tumor-inducing properties of tamoxifen and the extreme rarity of multiple spinal meningiomas, we suggest that tamoxifen may be the cause play a role in the genesis of the spinal meningiomatosis in the observed patient. Therefore, we propose the long-term clinical and neurological surveillance of patients who assumed tamoxifen, even for a short time, in order to survey the possible appearance of secondary tumours.

Key words Tamoxifen • Spinal multiple meningiomas • MRI

Introduction

Multiple spinal meningiomas are relatively rare neoplasias, accounting for only about 3% of all spinal meningiomas [1]. Although in most cases the aetiology remains unknown, mutagenic effects of radio- and chemotherapy have been hypothesized to play a role in the genesis of spinal meningiomas in patients treated for lymphoma or leukaemia [2, 3].

The chemotherapy-induced meningiomas have been described only as isolated tumours and no cases of multiple localization of the tumours have been reported so far [2, 3]. Tamoxifen, which is a non-steroidal mixed estrogen agonist/antagonist drug widely used for patients with metastatic and primary breast cancer, and utilized in the treatment of malignant gliomas with some efficacy [4], is able to induce neoplasms such as endometrial carcinomas [5]. However, no cases of association between spinal cord tumours and therapy with tamoxifen have been previously described. On the other hand, based on the frequent observation of estrogenic receptors in meningiomas, Goodwin et al. [6] even evaluated high doses of tamoxifen in unresectable or refractory meningiomas, moreover without any significant efficacy, further increasing the ambiguousness concerning the antitumoral and tumor-inducing properties of this drug.

We report the case of a 74-year-old woman affected by multiple spinal meningiomas that appeared after four years of therapy with tamoxifen for breast cancer. To our knowledge, this is the first report of an association between multiple spinal meningiomas and tamoxifen.

Case report

A 74-year-old woman was referred for neurological observation for a 1-year history of progressive gait disorders, poor balance, weakness of the right hand and urinary symptoms. At the age of 64 years, she underwent left mastectomy for breast tumour. Histological examination showed an infiltrant...
ductal carcinoma without lymphnode involvement. The patient was successfully treated with tamoxifen 20 mg b.i.d. for four years and after ten years neither recurrences nor metastases of the breast cancer were evident. During the treatment the patient suffered from slight leucopenia, ankle swelling and gastric symptoms such as nausea and vomiting, considered common side effects of tamoxifen therapy.

Neurological examination revealed paretic-spastic gait and unsteadiness. Romberg’s sign was positive. There was slight distal weakness in the right upper limb. Reflexes were brisk in the lower limbs. Babinski’s sign was present on the left side and plantar response was absent on the right side. There was hypoesthesia with sensory level up to D9. There was urge incontinency.

The patient underwent magnetic resonance imaging (MRI) of the spinal cord, performed with a 0.5 T superconducting magnet (Philips Gyroscan II). We acquired sagittal T1-weighted spin-echo images with a repetition time (TR) of 550 ms, an echo time (TE) of 22 ms, a field of view (FOV) of 284 mm, and a slice thickness of 4.0 mm; T2-weighted images used a TR of 3360 ms, TE of 150 ms, FOV of 284 mm, and slice thickness of 4.0 mm. A second set of T1-weighted images (TR=579 ms; TE=30 ms; FOV=220 mm; slice thickness, 5.0 mm) was acquired in the axial plane before and 5 minutes after an injection of a double dose of gadolinium DTPA (0.2 mmol/kg) (Magnevist, Shering). Three isolated areas of isointensity were present on T2- and T1-weighted images at C6-C7, D6-D7 and D9 levels (Fig. 1).

These areas showed a mild enhancement after the injection of gadolinium and appeared to compress the spinal cord. Taking in account the location and the morphology of the lesions and the characteristics of their enhancement, a radiological diagnosis of multiple meningiomas was made.

Brain MRI was then performed in order to exclude the presence of cerebral lesions. The following sequences were acquired in the axial, sagittal and coronal planes: T1-weighted images (TR=500 ms; TE=25 ms; FOV=220 mm; slice thickness, 5.0 mm), T2- and proton-density weighted images (TR=3000 ms; TE=90/30 ms; FOV=220 mm; slice thickness, 5.0 mm), and fluid-attenuated inversion recovery (FLAIR) images (TR=6000 ms; TE=150 ms; FOV=220 mm; slice thickness, 6.0 mm; inversion time (TI), 2200 ms) after an injection of 0.2 ml/kg gadolinium. The examination did not reveal the presence of any brain lesions suggestive of meningioma.

Removal of the tumours was performed by standard neurosurgical techniques for cervical and dorsal meningiomas in a 2-step procedure. In the first operative session, the cervical tumour was excised and, two weeks later, the dorsal tumours were removed. Histological examination of the tumours showed a grade I meningotheliomatous meningioma according to the World Health Organization (WHO).

The patient recovered well from the surgery and suffered no neurological deterioration. At the one-year follow-up, the patient showed a slight improvement in symptoms.

Discussion
We reported a case of multiple spinal meningiomas after therapy with tamoxifen for a primary breast carcinoma. This drug is largely used for patients with metastatic and primary breast cancer, and in the last decade, on the basis of in vitro studies that showed its antiproliferative properties in cultured human gliomas, it was experimented even in neuroon-