Temozolomide: Anti-tumor effect on giant, invasive and resistant pediatric prolactinoma

Sir,

Prolactinomas are more common in women than in men. They are usually well-controlled by dopamine agonists that normalize prolactin (PRL) and reduced the pituitary tumor. Resistant forms are relatively rare and their treatment is challenging. Pediatric forms are rarer and usually respond

to medical treatment, except in some exceptional cases. Our aim was to report a miraculous and spectacular shrinkage of a giant (≥4 cm in height), invasive pediatric prolactinoma, resistant to dopamine agonists and somatostatin's analogs, which responded favorably to Temozolomide: A cytostatic alkylating agent.

A woman aged 27, consulted for the first time at 17 years old for primary amenorrhea caused by an invasive and aggressive prolactinoma: PRL = 1350 ng/ml (n < 30), measuring 23 mm × 30 mm × 17 mm (height, transversal diameter and anteroposterior diameter) invading the right cavernous sinus [Figure 1a] and inducing two pituitary deficits: Gonadotroph and somatotroph.

She was treated successively by bromocriptine, cabergoline, then both for 8 years. Pituitary tumor remained stable, but PRL was never normalized. After a while, PRL increased and the tumor became giant and multidirectional [Figure 1b], but without any metastasis.

After an unsuccessful treatment by somatostatin's analogues, she was operated on twice, but unfortunately, there was not any modification of the tumor size and PRL. Immunohistochemical study was positive for PRL and the ki67 was equal to 5%, P53 was negative. Post-operative PRL was 19,984 ng/ml and tumor size was equal to 55 mm × 63 mm × 48 mm.

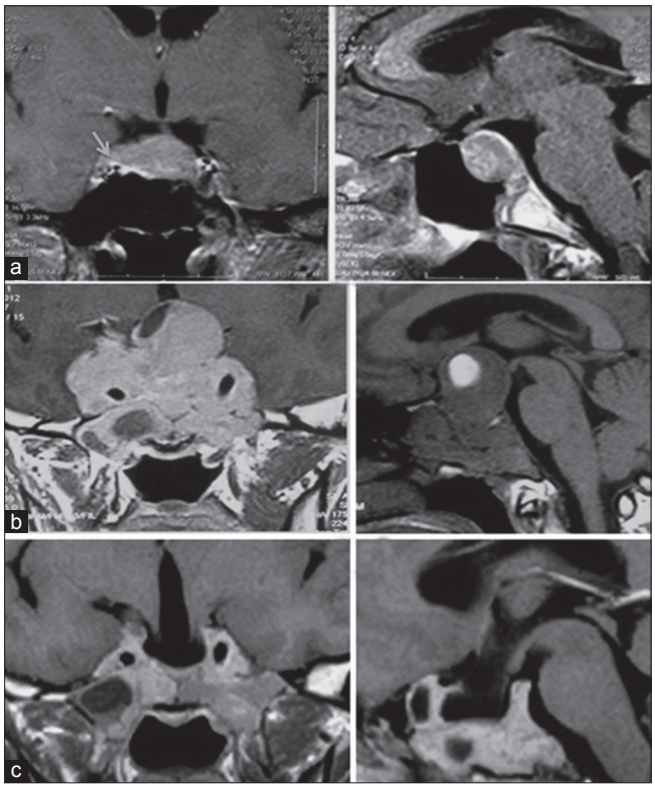

Figure 1: (a) Pituitary tumor with suprasellar extension and invasion of the right cavernous sinus. (b) Increase in tumor volume. (c) Important reduction in tumor size after temozolomide

For treatment, as radiotherapy was refused by patient and her parents, she continued medical treatment for some months with a strict follow-up. Then, she had several apoplectic episodes with a decrease in visual acuity. The intra tumoral hemorrhagic complication was treated with corticoids, but the steroid treatment did not improve visual acuity and tumor volume, which pushed us to prescribe Temozolomide: 5 mg/day, 5 days/28 days. After four cycles, visual acuity improved, PRL dropped from 19,984 to 11,085 ng/ml and tumor volume decreased from 55 to 12 mm [Figure 1c].

Tomozolomide usually used to treat glioblastomas, oligodendrogliomas and melanomas[1] seems to provide promising results for pituitary tumors, which are resistant to classical treatments. It is also efficient in aggressive or malignant tumors. The first pituitary tumor that responded to Temozolomide was published in 2004; since then other cases have been reported. In 2012, a literature review including 51 aggressive tumors showed that 15 out of 20 prolactinomas (75%) treated with Temozolomide exhibited a good response.[2] It was concluded that Temozolomide can be used as a salvage treatment for resistant or malignant tumors. Three cycles are usually necessary to identify responders,[3] but acquired resistance is possible.[4]

As other authors, we can conclude that giant and/or resistant prolactinomas are really difficult to manage especially in young people and children. Temozolomide, which is a cytostatic agent, is a very good alternative for refractory tumors as in our case. However, a long clinical, biological, ophthalmological and radiological follow-up is mandatory to detect an acquired resistance.

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