Malignant Transformation of an Aggressive Pituitary Prolactinoma After Radiotherapy and During Dopaminergic Agonist Treatment: Case Report

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Introduction:

Pituitary carcinomas are rare tumors that are most commonly prolactinomas and present heterogeneous behaviors. Their carcinogenesis is unknown, they present mostly in men and their treatment is multimodal & non-standardized. They are mainly diagnosed through the appearance of distant metastases and radiotherapy can be used for local control of invasive adenomas.

Case Report:

A 47-year-old man consulted for headaches, decreased libido, impaired vision and gynecomastia. A CT scan revealed a pituitary macroadenoma with suprasellar extension and invasion of the left sinus cavernosus and sphenoidal sinus. Prolactin levels were of 2750 ng/mL (reference value:<25 ng/mL). The patient began treatment with bromocriptine 2.5 mg/day, and underwent a transsphenoidal adenomectomy (TSA). Post-operatively the patient began prednisone, testosterone and levothyroxine therapy. Due to tumoral persistence with invasion to adjacent structures a transfrontal craniotomy was realized in the following year with sellar radiotherapy of 50 Gy. Subsequently, the patient presented a normal campimetry, prolactin levels of 88 ng/mL and symptomatic improvement.

The patient remained asymptomatic for 5-years with concurrent bromocriptine treatment. Due to bromocriptine intolerance, he began cabergoline 1 mg/week. Posteriorly, prolactin rose gradually reaching levels of 1800 ng/mL. After confirming cabergoline resistane, the patient he started therapy again with bromocriptine until reaching a dose of 40 mg/day. However, 6-years later he reported lumbar pain and a MRI scan showed a hypointense lesion in L1; confirming with biopsy a prolactinoma metastasis. Spine radiotherapy was administered with symptomatic improvement. Three TSA were later needed due to recurrence of the sellar lesion, with prolactin averaging levels of 1000 ng/mL. The patient, then with oligo-metastatic disease, declined any further treatment. He had a death associated with extensive cranial involvement, and survival of 6-years after initial metastatic diagnosis.

Conclusions:

The clinical course in this patient was very unusual. He had a very aggresive tumor, with extensive and recurrent local invasion, metastases, and dopaminergic analogue (DA) resistance. Nonetheless, he presented a 14-year overall survival without any systemic antitumor therapy. Furthermore, while radiotherapy is used in recurrent and aggressive pituitary tumors in which surgery fails, we hypothesize that it contributed to the tumoral malignant transformation and the late resistance to DA in our patient.

Learning Objectives:

By the conclusion of this session, participants should be able to:

1. Know that pituitary carcinomas present heterogeneous behaviors with patient's overall survival being 14 years even after initial tumoral aggressiveness and metastatic diagnosis.
2. Understand that previous radiotherapy treatments may play an influential role in malignant tumor transformation and dopaminergic analogue resistance of these types of tumors.
3. Understand why new randomized trials regarding survival and therapeutic strategies of pituitary carcinomas to further understand their pathophysiology are needed.

Appendix 1:

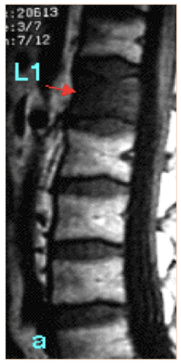

Figure 1a

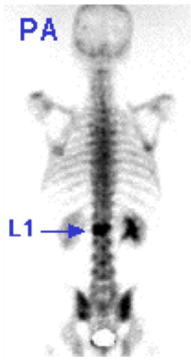

Figure 1b

1a - Magnetic resonance image (MRI) of the lumbar spine that reveals a hypointense lesion in the vertebral body of L1.

1b - Bone scan of the patient that shows hypercaption of radiotracer at L1 vertebrae level

Appendix 2

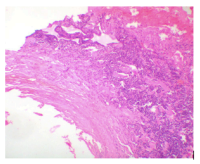

Figure 2a

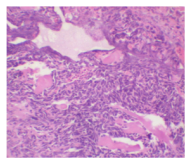

Figure 2b

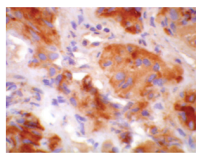

Figure 2c

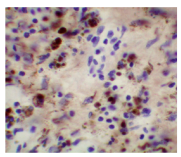

Figure 2d

2a – Histopathology of the initial pituitary adenoma. H-E at x10 magnification

2b – Histopathology of the lumbar spine metastatic lesion. H-E at x10 magnification

2c – Immunohistochemistry positive for prolactin presence, negative for other pituitary hormone

2d – Immunohistochemistry for Ki-67, with a proliferation index > 10%

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