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Sellar collision tumor involving a primary fibrosarcoma: Clinical, morphological and immunohistochemical study of a case and review of the literature

Tumor de colisión hipofisario con fibrosarcoma primario: estudio clínico, morfológico e inmunohistoquímico y revisión de la literatura

Collision tumors represent two morphologically different tumors attached to one another at a single anatomical site. While collision tumors have been reported in various organs, the concomitant presence of a pituitary adenoma with a second sellar lesion is an uncommon occurrence. When this does occur, radiation-induced sarcomas may coexist with a pituitary adenoma as result of previous radiation therapy aimed at treating the pituitary adenoma. Of these, fibrosarcomas are the most common, but rhabdomyosarcomas and chondrosarcomas have also been reported. If patients who have undergone previous radiation therapy are excluded from scrutiny, the presence of these two types of tumor in the same patient becomes even rarer.[1]

This report describes the case of a 41-year-old male, without personal or hereditary antecedents of relevance, who was referred to our Neuroendocrinology Unit presenting insidious discomfort and paresthesia in both hands that had developed over the previous 6 months. The patient also reported reduced visual acuity and partial loss of lateral vision over the previous year, accompanied by recurring headaches, which were relieved by analgesic administration.

Confrontation visual field tests found bitemporal hemianopsia. Magnetic resonance imaging (MRI) of the sellar region detected a pituitary mass of heterogeneous signal intensity but with well-defined borders, measuring 28 mm × 39 mm × 22 mm, pressing on the optic chiasm. Hormonal study found slight secondary panhypopituitarism due to tumoral compression (FT4: 0.79 ng/dl [0.90–1.70 ng/dl]; TSH: 2.09 μIU/ml [0.4–4 μIU/ml]; testosterone total 3.1 nmol/L [10–28 nmol/L]; FSH 5.2 mIU/ml [2–8 mIU/ml]; LH 3.2 mUI/ml [2–12 mIU/ml]; cortisol 49.8 ng/ml [50–250 ng/ml]; ACTH 12.8 pg/ml [8.0–66.0 pg/ml]; IGF-1 89.5 ng/ml, with adequate suppression of GH levels after an oral glucose tolerance test). Diagnosis established a suspected pituitary macroadenoma.

Endoscopic endonasal transsphenoidal resection of the pituitary tumor was performed. Post-operative histopathologic analysis revealed a proliferation of fusiform cells in a lax stroma, with moderate atypia and a proliferation index (Ki-67) of around 10%; vimentin and SMA (smooth muscle actin) were immunophenotype-positive, while other markers showed negative (CD31, CD34, EMA, S100, PGFA, CKAE1/AE3). Islands with an epithelial aspect of pituitary origin were mixed in with the neoplasia, which expressed chromogranin and showed negative for all pituitary hormones (ACTH, GH, PRL, TSH, FSH and LH) (Fig. 1). Histopathological diagnosis identified a collision tumor composed of low-grade mesenchymal spindle cell neoplasm and a non-secreting pituitary adenoma. Histopathologic features and the presence of a small residual tumor observed in post-operative MRI justified fractionated stereotactic radiotherapy, which was clinically well tolerated by the patient. After surgery and radiotherapy, the patient showed a notable clinical improvement, particularly in visual acuity and remained neurologically asymptomatic. In subsequent follow-up examinations, images showed no sign of remains or recurrence of the pituitary tumor. The patient continues to attend the clinic for regular check-ups.

This case presents several notable characteristics. Firstly, the coexistence of two pituitary tumors of different histogenesis. The presence of a collision sellar lesion is a very uncommon event. To date, the concomitance of two different pathologies within the sella have mainly been described in individual case reports; very few surgical series have been published that describe specific combinations of sellar lesions such as a double pituitary adenoma,[2,3] a combination of an adenoma and Rathke's cleft cyst,[4] or a gangliocytoma associated with a pituitary adenoma.[5] In one of the very few case series published, Koutourousiou et al. reported an incidence of 1.46% of collision lesions among a group of 548 patients who underwent transsphenoidal surgery for pituitary adenoma resection. Among these pituitary adenomas with different features, the authors found one case of sarcoidosis, three cases of gangliocytoma, one schwannoma, one case of double pituitary adenoma, and two Rathke's cleft cysts.[6]

Secondly, the present case of a sellar collision tumor is of particular interest due to the discovery of a primary fibrosarcoma in a patient with no history of radiation exposure. This

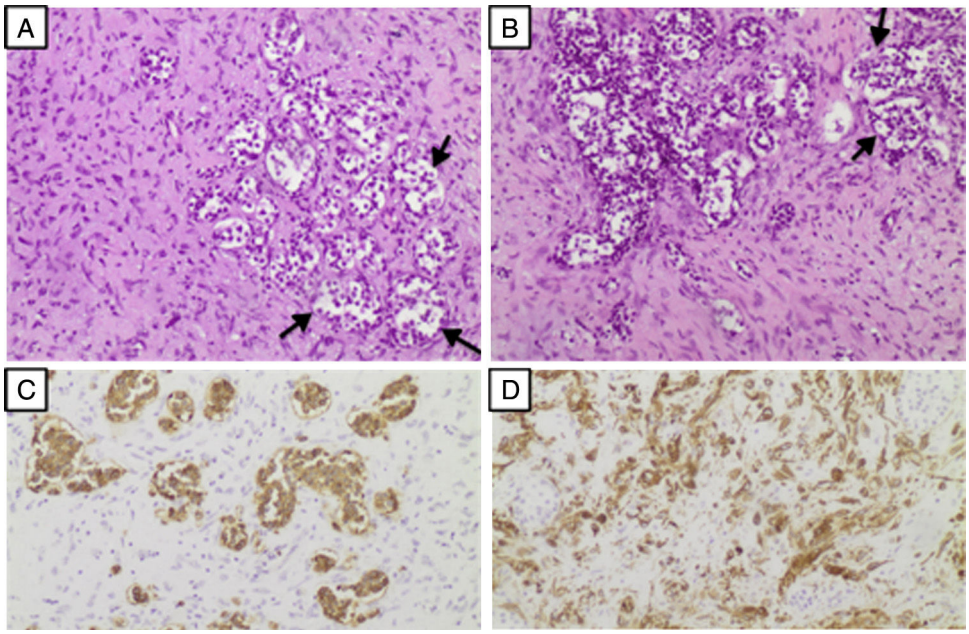

Figure 1 Histopathology of collision sellar tumor. Hematoxylin-eosin stained sections (10×) show a proliferation of fusiform cells in a lax stroma, intermixed with islands of epithelial appearance (arrows) (A, B). Chromogranin expression by epithelial cells (C). Mesenchymal cells present vimentin immunophenotype and positive smooth muscle actin (SMA) (D).

is an extremely rare event. To date, only 18 cases of primary sarcomas of the sellar region have been reported; of these, six were fibrosarcomas, with only one case of neoplasm with biphasic or collision pattern.[7] To our knowledge, this case is only the second ever report of a collision pituitary tumor involving a primary fibrosarcoma. Moro et al. reported the first case, which consisted of combined sellar fibrosarcoma and prolactinoma in a patient who had not undergone previous radiotherapy. The patient presented a thymic carcinoma with metastatic disease, which was treated by administering etoposide, and a subsequent prolactinoma treated with bromocriptine without radiotherapy. Eight years later, radiological examination revealed a large pituitary mass, which on histological examination was compatible with fibrosarcoma in close association with a pituitary adenoma.[8] Moro argues that etoposide tends to cause fibrosis in the pituitary stroma. In contrast to Moro's report, no adjuvant treatment was administered in the present case.

The low incidence of these tumors is largely conditioned by the difficulty of pre-operative diagnosis since most cases present clinically and radiologically as pituitary adenomas.[6] This was true of the present case, in which clinical examination accompanied by a suggestive radiographic image led to an initial diagnosis of pituitary macroadenoma. The definitive diagnosis of a collision sellar lesion can only be determined by histological study because of the difficulty of distinguishing between these entities in clinical or radiological examination.

To date, no proven pathogenetic mechanism has been identified that might explain the relationship between a pituitary adenoma and a second sellar lesion. Regarding the etiology of the present case's fibrosarcomatous component, the literature hypothesizes two possibilities: metaplastic transformation from pituitary adenoma, or independent collision tumors.[6,7] Unfortunately, distinguishing between these two possibilities on the basis of morphology alone is not possible.

Conflict of interest

The authors have no conflicts of interest to disclose.

References

1. Prevedello DM, Thomas A, Gardner P, Snyderman CH, Carrau RL, Kassam AB. Endoscopic endonasal resection of a synchronous pituitary adenoma and a tuberculum sellae meningioma: technical case report. Neurosurgery. 2007;60:E401.
2. Kontogeorgos G, Scheithauer BW, Horvath E, Kovacs K, Lloyd RV, Smyth HS, et al. Double adenomas of the pituitary: a clinicopathological study of 11 tumors. Neurosurgery. 1992;31:840–9.
3. Sano T, Horiguchi H, Xu B, Li C, Hino A, Sakaki M, et al. Double pituitary adenomas: six surgical cases. Pituitary. 1999;1:243–50.
4. Nishio S, Mizuno J, Barrow DL, Takei Y, Tindall GT. Pituitary tumors composed of adenohypophyseal adenoma and Rathke's cleft cyst elements: a clinicopathological study. Neurosurgery. 1987;21:371–7.
5. Cossu G, Daniel RT, Messerer M. Gangliocytomas of the sellar region: a challenging diagnosis. Clin Neurol Neurosurg. 2016;149:122–35.
6. Koutourousiou M, Kontogeorgos G, Wesseling P, Grotenhuis AJ, Seretis A. Collision sellar lesions: experience with eight cases and review of the literature. Pituitary. 2010;13:8–17.
7. De Silva AC, Rodriguez FJ, Aldecoa I, McDonald W, Ribalta T. Compound gonadotrophic pituitary adenoma and rhabdomyosarcoma. Histopathology. 2016;68:1111–4.
8. Moro M, Giannini C, Scheithauer BW, Lloyd RV, Restall P, Eagleton C, et al. Combined sellar fibrosarcoma and prolactinoma with neuronal metaplasia: report of a case unassociated with radiotherapy. Endocr Pathol. 2004;15:149–58.

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Dolor abdominal y crisis hipertensiva como manifestación inicial de un feocromocitoma maligno

Abdominal pain and hipertensive crisis as initial manifestation of a malignant pheocromocytoma

Varón de 42 años, sin antecedentes familiares ni personales de interés que acudió a urgencias por cefalea intensa, náuseas y vómitos; se objetivó tensión arterial de 220/100 mmHg e hiperglucemia. La TAC cerebral fue normal. Posteriormente inició dolor en hipocondrio derecho; la ecografía abdominal mostró una masa retroperitoneal derecha, y la TAC toraco-abdominal confirmó una lesión suprarrenal derecha (16 × 13 × 15 cm) sugestiva de carcinoma suprarrenal, más un conglomerado adenopático mediastínico.

Ingresó en urología y en colaboración con endocrinología se completó el perfil analítico: hemoglobina, PTH, calcitonina, cortisol basal, ACTH, DHEAS y androstendiona normales; transaminasas elevadas, enolasa 226 ng/ml (0-16,3), cromogranina A 1.004 ng/ml (< 450); en orina de 24 h se objetivó metanefrinas 4.748,85 μg/24 h (20-374), normetanefrinas 80.233,96 μg/24 h (30-778) y ácido vanilmandélico 10,1 mg/24 h (1-7,3).

La gammagrafía y SPEC-TAC con metayodobencilguanidina (I^{131}-MIBG) mostró aumento de captación en glándula suprarrenal derecha y enfermedad diseminada ganglionar (cérvico-mediastínica e interaorto-cava), hepática y ósea, planteándose diagnóstico diferencial entre metástasis de feocromocitoma y paragangliomas múltiples.

La biopsia de un ganglio linfático interaorto-cava, en la que se observó la presencia de cuerpos de Zellballen con amplios citoplasmas basófilos y granulares y extensa infiltración capsular y vascular, fue informada como metástasis de feocromocitoma[1].

Dada la elevación de tanto normetanefrinas como metanefrinas, y la utilidad de la información genética para orientar el manejo y tratamiento dirigido se realizó estudio genético de SDHx[1,2], VHL y RET, que fue negativo[2–5].

El paciente fue intervenido quirúrgicamente, previo bloqueo alfa-adrenérgico con doxazosina (4 mg/24 h) 27 días antes, más bloqueo beta-adrenérgico con propranolol (10 mg/8 h) los últimos 7 días por taquicardia sinusal[1,6]. Se realizó adrenalectomía y nefrectomía derecha, asociando exéresis de un nódulo hepático para estudio histológico. La cirugía resultó hemorrágica, con tendencia inicial a hipertensión arterial y posterior hipotensión refractaria a relleno vascular. En el postoperatorio inmediato descendieron los valores de metanefrinas (2.472,5 μg/24 h) y normetanefrinas (23.775,6 μg/24 h).

La histología de la masa suprarrenal fue compatible con feocromocitoma con infiltración de cápsula suprarrenal, vascular y de tejido adiposo periadrenal, con necrosis y pleomorfismo, con comportamiento agresivo. El nódulo hepático resecado era metastásico de feocromocitoma (este hallazgo que en tejido no cromafín es criterio de malignidad)[5]. El estudio anatomopatológico suprarrenal y hepático mostró un índice mitótico < 1 mitosis/10 CGA, Ki-67 del 3% y tinción inmunohistoquímica de sinaptofisina y cromogranina positiva.

La enfermedad progresó, por lo que 4 meses después se practicó cirugía citorreductora de metástasis con resección de masa mediastínica (19 cm) y nódulo en lóbulo superior del pulmón izquierdo (1,5 cm). Posteriormente, una TAC toraco-abdominal constató evolución de la enfermedad. Destacaba conglomerado adenopático supraclavicular izquierdo, adenopatías mediastínicas paraaórticas izquierdas, nódulos pulmonares, metástasis hepáticas, voluminosa masa interaortocava y nódulo heterogéneo (3 cm) en lecho quirúrgico de adrenalectomía.

Se administraron 2 dosis fraccionadas de 100 mCi de I^{131}-MIBG[7], con un intervalo de 2 meses, con buena tolerancia. En el rastreo corporal total (RCT) tras la primera se detectó progresión de enfermedad, con lesiones de alta afinidad por el radiotrazador (fig. 1). Por el contrario, tras la segunda disminuyó la captación en algunas lesiones, con ligera reducción del tamaño, especialmente las pulmonares, sin nuevas adenopatías ni metástasis a distancia. Los valores de metanefrinas y normetanefrinas se redujeron notablemente 3 meses después de la segunda dosis (metanefrinas: 677,29 μg/24 h, normetanefrinas: 11.215,51 μg/24 h), sin cambios en el tamaño de las lesiones en la TAC.

Seis meses después, ante la persistencia de enfermedad se inició tratamiento con quimioterapia sistémica (ciclofosfamida-vincristina-dacarbacina)[7], que fue retirada por toxicidad (emesis, insuficiencia renal y pancitopenia). Finalmente se pautó sunitinib (inhibidor de tirosina kinasa), 50 mg/día, suspendido por empeoramiento clínico a los 4 días [7]. El paciente falleció tras una crisis catecolaminérgica en el contexto de feocromocitoma maligno esporádico en estadio IV, con una supervivencia global de 17 meses.