Endocrinol Nutr. 2015;62(4):200–206

ENDOCRINOLOGÍA Y NUTRICIÓN

www.elsevier.es/endo

SCIENTIFIC LETTERS

Pituitary apoplexy in a pregnant woman with cystic microprolactinoma☆

Apoplejía hipofisaria en gestante con microprolactinoma quístico

We report the case of a 37-year-old female patient who two years previously had been diagnosed with a 3-mm cystic microprolactinoma after routine laboratory tests revealed a prolactin level of 68 ng/mL (normal, 2.4–25 ng/mL). The patient had not experienced any prior menstrual changes, galactorrhea, or neurological symptoms. Cabergoline (0.5 mg/week) was administered with a good biochemical response. However, tumor size increased in the first six months of treatment to 7.9 mm × 5 mm × 5 mm, and then remained stable for the following six months. Some months after this last radiographic control, cabergoline was discontinued due to pregnancy, and levothyroxine (50 μg/day) was added for secondary hypothyroidism (TSH 1.74 mU/L [normal: 0.35–4.9 mU/L] and free T4 0.65 ng/dL [normal: 0.7–1.5 ng/dL]).

The patient attended the emergency room of our hospital at 24 weeks of pregnancy complaining of continuous retro-orbital headache and decreased visual acuity in the right eye for approximately 10 days. Pituitary MRI performed based on a clinical suspicion of pituitary apoplexy (PA) showed a cystic pituitary lesion 15 mm × 15 mm × 22 mm in size with serohematic content and an extrasellar component compressing the central portion of the optic chiasm (Fig. 1). The results of a complete blood count, general chemistry, and coagulation tests were normal, and the serum PRL level was 64.5 ng/mL. The ophthalmology department confirmed the decrease in visual acuity in the right eye (0.4/1), and also detected inferior temporal quadrantanopia in the same eye. Treatment was restarted with dopamine agonists (bromocriptine 2.5 mg/day), and surgery was decided in agreement with the neurosurgery department and based on the decision taken by the patient herself. Surgery was performed through an endoscopic transsphenoidal approach with no complications. The histological report confirmed that the tumor was a pituitary adenoma with densely granulated cells secreting PRL.

After surgery, drug treatment with bromocriptine, hydrocortisone, and levothyroxine was maintained until the end of pregnancy. Visual acuity and campimetry findings normalized. During the remainder of her pregnancy, the patient was jointly monitored by the departments of obstetrics, neurosurgery, and endocrinology and nutrition. An elective cesarean section was performed at 37 weeks of pregnancy, and a healthy male infant was delivered (Apgar 10/10). Hormone replacement therapy was discontinued after delivery based on a normalization of pituitary function. MRI has not shown tumor remnants since then.

Drug therapy is the treatment of choice for prolactinomas.[1,2] Bromocriptine is recommended during pregnancy because of the wide experience that has been accumulated in using this drug. When women with prolactinoma want to become pregnant, PRL levels in the normal range and a tumor size less than 10 mm are recommended to prevent complications. In the event of a microprolactinoma, when pregnancy is confirmed, a discontinuation of drug treatment is recommended because of the estimated 2.2–5% risk of growth during pregnancy. Drug maintenance is however advised in macroprolactinoma, particularly in invasive tumors or tumors close to the optic chiasm.

In the reported cases, prolactinoma size a few months before pregnancy was less than 10 mm, and PRL levels were normal. It could therefore be considered an adequate response to discontinue dopamine agonists once pregnancy had been confirmed. However, the following factors should have been taken into account before a decision was reached as to whether to continue or discontinue drug treatment:

1. the tumor was a cystic microprolactinoma, a type of adenoma related to a lower response to treatment with dopamine agonists.[1,3]
2. Adenoma size had increased despite treatment with dopamine agonists, although its growth had subsequently stabilized.[1,3]

☆ Please cite this article as: Querol Ripoll R, Cámara Gómez R, del Olmo García M, Simal Julián JA, Merino Torres JF. Apoplejía hipofisaria en gestante con microprolactinoma quístico. Endocrinol Nutr. 2015;62:200–202.

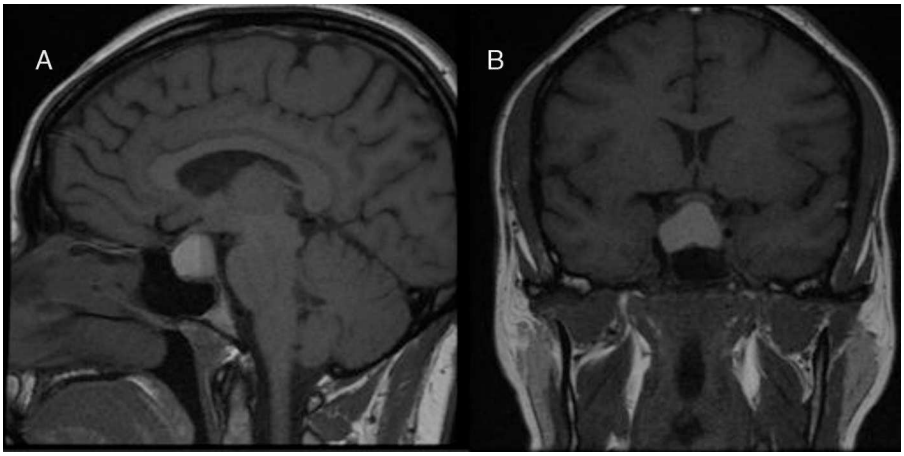

Figure 1 (A) T1-weighted sagittal MRI image showing a sellar lesion with suprasellar extension with a fluid-fluid level suggesting bleeding in different evolutionary stages. (B) T1-weighted coronal MRI image showing a markedly hyperintense sellar lesion with suprasellar extension related to bleeding in contact with the optic chiasm.

3. *De novo* TSH deficiency was diagnosed at the start of pregnancy, and should have raised the alert of a potential tumor growth.

PA results from bleeding or hemorrhagic infarction in a pituitary tumor, and is a potentially serious condition. It may represent the first manifestation of a macroadenoma or microadenoma, and occurs in both functioning and non-functioning tumors. PA has been related to diabetes mellitus, intracranial hypertension, functional pituitary tests, and the use of bromocriptine and anticoagulants. The occurrence of PA is very rare in pregnancy, and few cases have been reported in patients with microprolactinomas.[4–8]

Treatment of PA should be individualized.[9,10] The few cases of PA reported during pregnancy have been treated both conservatively and with surgery, with good results irrespective of the option selected.[11,12] In the case reported, because of visual symptoms and patient desire, as well as the availability of a team of experienced neurosurgeons, surgery was performed with an excellent result.

In conclusion, we think that in cases similar to the one reported (women with cystic microprolactinoma and/or with no adequate tumor size reduction despite treatment with dopamine agonists), the continuation of drug treatment during pregnancy and monitoring similar to that recommended for pregnant women with macroprolactinoma should be considered. If PA occurs during pregnancy, given the lack of consensus regarding its treatment, this should be decided upon only after the evidence provided by the series reported, the tolerability of oral medication, the opinion of patients and relatives, and the surgical experience of neurosurgeons at the hospital have all been taken into consideration.

Funding

None.

Conflicts of interest

None of the authors has conflicts of interest.

Acknowledgements

We thank the departments of neurosurgery, obstetrics, and endocrinology and nutrition.

References

1. Imran SA, Ur E, Clarke DB. Managing prolactin-secreting adenomas during pregnancy. Can Fam Physician. 2007;53:653–8.
2. Halperin I, Cámara R, García M, Ollero D. Guía clínica de diagnóstico y tratamiento del prolactinoma y la hiperprolactinemia. Endocrinol Nutr. 2013;60:308–19.
3. Iglesias P, Díez JJ. Macroprolactinoma: a diagnostic and therapeutic update. Q J Med. 2013;106:495–504.
4. Corkill G, Hanson FW, Sobel RA, Keller TM. Apoplexy in a prolactin microadenoma leading to remission of galactorrhea and amenorrhea. Surg Neurol. 1981;15:114–5.
5. Couture N, Aris-Jilwan N, Serri O. Apoplexy of a microprolactinoma during pregnancy: case report and review of literature. Endocr Pract. 2012;18:e147–50.
6. Janssen N, Dreyer K, van der Weiden R. Management of pituitary tumour apoplexy with bromocriptine in pregnangy. J R Soc Med Sh Rep. 2012;3:43.
7. Tandon A, Alzate J, LaSala P, Fried MP. Endoscopic endonasal transsphenoidal resection for pituitary apoplexy during the third trimester of pregnancy. Surg Res Pract. 2014;2014, http://dx.doi.org/10.1155/2014/397131. Article ID: 397131.
8. Chegour J, El Ansari N. Pituitary apoplexy during pregnancy. Pan Afr Med J. 2014;17, http://dx.doi.org/10.11604/pamj.2014.17.211.4133. Article ID: 211.
9. Serramito R, García A, Arcos AN, Castro D, Santín JM, Gelabert M. Apoplejía pituitaria. Revisión del tema. Neurocirugia. 2011;22:44–9.
10. Vicente A, Lecumberri B, Gálvez MA. Guía de práctica clínica para el diagnóstico y tratamiento de la apoplejía hipofisaria. Endocrinol Nutr. 2013;60:e1–12.
11. de Heide LJ, van Tol KM, Doorenbos B. Pituitary apoplexy presenting during pregnangy. Neth J Med. 2004;62:393–5.
12. Janssen NM, Dreyer K, van der Weiden RMF. Management of pituitary tumour apoplexy with bromocriptine in pregnancy. JR Soc Med Sh Rep. 2012;3:43.

Roser Querol Ripoll[a,*], Rosa Cámara Gómez[a], Maribel del Olmo García[a], Juan Antonio Simal Julián[b], Juan Francisco Merino Torres[a]

[a] *Department of Endocrinology and Nutrition, Hospital Universitario y Politécnico La Fe, Valencia, Spain*

[b] *Department of Neurosurgery, Hospital Universitario y Politécnico La Fe, Valencia, Spain*

[*] Corresponding author.
E-mail address: Roserquerol86@gmail.com
(R. Querol Ripoll).

18F-DOPA vs. 18F-FDG PET/CT in the ectopic ACTH syndrome due to pulmonary carcinoid tumor

18F-DOPA vs. 18F-FDG PET/TC en el síndrome de producción ectópica de ACTH por tumor carcinoide pulmonar

Overproduction of corticotropin by the pituitary gland or extrapituitary tumors leads to ACTH-dependent Cushing's syndrome; 10% of these are due to ectopic production. These tumors often suppose a difficult diagnostic challenge because of their small size and multiplicity.

The pulmonary neuroendocrine-tumors (NET) originate from the enterochromaffin-cells which are diffusely distributed in the body. Their incidence has increased significantly in recent decades due to the available diagnostic resources; they represent about 1–2% of all lung tumors and 20–30% of all NET.[1]

6-Fluoro-(18F)-L-3,4-dihydroxyphenylalanine (18F-DOPA) is an aminoacid-analog for positron emission-tomography (PET) imaging which has been registered since 2006 in several European Union countries and by several pharmaceutical firms. NET imaging is part of its registered indications.

18F-DOPA offers distinct advantage over fluorodeoxyglucose (18F-FDG) for the detection of carcinoids especially since many of these tumors are indolent with low proliferation activity and good differentiation. Furthermore, 18F-DOPA was able to detect more lesions, more positive regions, and more lesions per region than combined somatostatin receptor scintigraphy (SRS) and CT.[2]

We present the case of a 33-years-old male with a history of *ACTH*-dependent Cushing's syndrome. Dynamic testing of hypothalamo–pituitary–adrenal axis and high levels of ACTH (131 pg/ml) led to diagnosis of ectopic ACTH secretion. Chest X-ray showed a solitary pulmonary nodule in the anterior-segment of the right-upper-lobe. First PET/CT was performed after injection of 259 MBq of 18F-FDG, and revealed a pulmonary nodule located in the right-upper-lobe (Fig. 1a). The maximum standardized uptake value (SUVmax) measured was 1.9. Furthermore, a second pleural-based pulmonary nodule was observed in the left-upper-lobe with SUVmax 10.3 (Fig. 1b). According to these findings, contralateral or pleural involvement could not be dismissed. In order to better characterize the areas of increased radiopharmaceutical uptake, the patient underwent an 18F-DOPA-PET/CT after the injection of 233 MBq of radiotracer, which revealed a solitary pulmonary node in the right-upper-lobe (Fig. 1d) with SUVmax 1.1. 18F-DOPA-PET/CT allowed discarding the contralateral and pleural involvement (Fig. 1e).

An atypical resection of the left-upper-nodule was performed by minithoracotomy approach. Lobectomy was discouraged after histopathology revealed alveolar hemorrhage, organizing pneumonia and areas of necrotizing granulomatous inflammation. Right-upper-lobectomy including video-assisted mediastinal lymphadenectomy was performed at a second time. Histology demonstrated a low grade well-differentiated ACTH-producing pulmonary NET with low mitotic and proliferative indices (<2 mitoses per 10 high power fields and Ki67 < 1%, respectively), cromogranine/sinaptophysine/CD56 and ACTH positive; TTF1 negative; pT1aN2 stage according to TNM classification. Only 1/8 mediastinal lymph nodes were affected.

The patient recovered rapidly, with normalization of serum ACTH levels. The symptoms of hypercortisolism were resolved 6 months after lobectomy.

Functional imaging based on radiolabeled-analogs targeting overexpressed receptors and transporters is playing a pivotal role in imaging of cancer. SRS, (123)I-metaiodobenzylguanidine (MIBG) scintigraphy and 18F-FDG-PET/CT remain the 3 molecular imaging techniques most widely available and with the most comprehensive clinical experience for NET.[3]

Published results indicated that 18F-FDG-PET/CT could be valuable for selecting treatment, monitoring therapy and determining prognosis, especially in poorly differentiated NET.[4] On the other hand, 18F-DOPA has been used for PET imaging in humans for more than two decades, initially for Parkinson's syndrome, and later in oncology for brain tumors or NET; it has proved to be an excellent tool for staging and restaging patients with documented carcinoid tumor.

The efficacy of 18F-DOPA-PET imaging in identifying carcinoid tumors depends on the ability of tumor cells to uptake, decarboxylate, and store aminoacids. 18F-FDOPA offers distinct advantages over 18F-FDG for detection of carcinoids, especially since many of these tumors are indolent, with low proliferation activity and good differentiation.[5]

18F-DOPA-PET is useful for detecting primary and metastatic neoplasia with neuroendocrine differentiation, such as carcinoid, gastroenteropancreatic tumors, glomus tumors, medullary thyroid cancer, small cell lung cancer, and pheochromocytoma/paraganglioma.[6,7]

When compared with other available functional imaging, 18F-DOPA-PET/CT was able to detect more lesions, more positive regions, and more lesions per region than combined SRS and CT in catecholamine-producing tumors with a low aggressiveness and in well-differentiated tumors.[2,8]

While the practice of 18F-FDG-PET/CT is fully standardized, up to now this has not been accomplished for