Letters to the Editor

Small-Cell Lung Cancer Presenting as Hypopituitarism

**Hipopituitarismo como forma de inicio de un carcinoma microcítico de pulmón**

To the Editor,

Bronchogenic carcinoma can present metastases in any territory during its evolution, and occasionally the symptoms derived from the organ in which they settle may be the presenting form. Metastases in the pituitary gland are an uncommon presentation of carcinomas; bronchogenic carcinoma is one of the potential tumours that can cause them, resulting in panhypopituitarism.

We present the case of a patient with bronchogenic carcinoma who presented with panhypopituitarism due to a single pituitary gland metastasis three months before diagnosis of the primary tumour. To the best of our knowledge, this has not been previously described in Spanish medical literature.

A 77-year-old male ex-smoker (102 packs/year), diagnosed with chronic obstructive pulmonary disease, was admitted to neurology for symptoms of asthenia, hyporeflexia, generalised weakness and hyponatraemia. On admission he was conscious and oriented, with arterial blood pressure 100/50 mmHg, respiratory rate 18 breaths/min and heart rate 80 beats/min. Cardiac auscultation was normal; pulmonary auscultation detected crackles in the lower third of the left hemithorax and expiratory wheezing. Bilateral malleolar oedema was noted during the rest of the examination. Neurological examination revealed that the upper cognitive functions were normal, as were the cranial pairs, with cautious gait and normal static balance.

Complete blood count and coagulation were normal. Biochemistry tests revealed sodium of 120 mmol/l and C reactive protein of 2.6 mg/dl. A prolactin of 52.25 ng/ml (normal values: 2.6–19) was notable in the hormone study. Tumour markers, blood and urine protein electrophoresis and immunofixation, urinary sediment and 24-h urinary protein were normal. The electrocardiogram showed sinus rhythm, with no conduction or repolarisation abnormalities. Hyperinflation, with increased hila of vascular appearance, was observed on the chest X-ray.

Cranial computed axial tomography (CT) revealed a 1 cm suprasellar nodular lesion with well-defined borders in the upper part of the pituitary stalk, with moderate contrast enhancement (Fig. 1a). The first possibility raised was that it was in the pituitary stalk, infundibulum or adjacent meningeal structures. Brain magnetic resonance imaging (MRI) showed a 1 cm suprasellar nodule, attached to the pituitary stalk that affected the hypothalamus and optic chiasm, consistent with an adenoma. There were no findings of interest on the magnetic resonance angiography of the circle of Willis. A 1.5 cm × 1 cm × 1.8 cm mass was observed on the pituitary gland MRI, affecting the pituitary stalk and the hypothalamic region, consistent with metastasis. Bone scintigraphy was normal.

The patient was discharged from neurology and followed-up in outpatients. Three months later, he was readmitted due to fever and bloody sputum, for which he was referred to Respiratory Medicine.

The chest X-ray did not show any significant changes with respect to the previous one. On the chest–abdominal–pelvic CT

![Fig. 1. (a) Cranial CT scan: pituitary lesion. (b) Chest CT scan: lesion in the left lower lobe indicative of malignancy.](image)

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scan, a soft tissue density infiltrative lesion was noted which surrounded the left hilum and extended to the basal pyramid, with a slight decrease in volume in the left lower lobe and bilateral pleural effusion (Fig. 1b). Bronchoscopy revealed a tumour in the left sixth segment; the biopsy was consistent with undifferentiated small cell carcinoma. Spirometry showed a severe obstructive disorder, with a negative bronchodilator test. With the diagnosis of pituitary metastasis with hypopituitarism secondary to undifferentiated small cell carcinoma (stage IV), the patient began chemotherapy. He remained stable and tumour size was reduced in the first six months. However, he died one year later due to disease progression.

Pituitary gland metastases are an uncommon presentation of carcinomas, because the pituitary gland does not receive a direct systemic blood supply. Its incidence is 3.6% in 500 autopsies. A review from 1966 to 2004 found only 249 patients with metastatic involvement of the pituitary gland; breast and lung cancer were the most common primary tumours, occurring in two thirds of cases. At diagnosis, most had generalised disease, usually associated with five or more metastatic sites, especially bone; rarely, as in our case, was it the first manifestation of an occult primary carcinoma as the only site of metastasis. Cases secondary to bronchogenic carcinoma as a presenting form have been reported occasionally. Since metastatic lesions in the pituitary gland are very rare, it is difficult to distinguish them from adenomas. In fact, CT is of limited use in distinguishing benign tumours; MRI has better diagnostic specificity.

The most common clinical symptoms of pituitary gland metastases are diabetes insipidus when they occur in the posterior lobe, and hypopituitarism when they occur in the anterior lobe, as in our patient. Pituitary gland metastases are symptomatic in only 7% of patients. Diabetes insipidus, anterior pituitary dysfunction, visual field defects, headaches and ophthalmoplegia are the most commonly reported symptoms. Branch and Laws proposed that the triad of headache, ophthalmoplegia and diabetes insipidus was very indicative of metastases, even if the patient did not have confirmed cancer. Our patient did not present headache or ocular impairment. His presenting symptoms were derived from hyponatraemia secondary to hypopituitarism. Hyperprolactinaemia has been found in only 6.3% of reported cases, but very high levels generally indicate prolactinoma rather than metastases. The mean survival of these patients is 6–22 months.

References

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Reply to Letter to the Editor “Infections by Gram-Negative Bacilli in Patients with Pulmonary Arterial Hypertension Treated with Intravenous Prostacyclin”

Réplica a la Carta al Director “Infecciones por gram negativos(BGN) en pacientes con hipertensión arterial pulmonartratados con prostaciclina intravenosas”

To the Editor,

We would like to thank Dr Gómez Sánchez for his close reading and comments of our article on catheter-associated bloodstream infection in patients with pulmonary hypertension receiving intravenous treprostinil. In this letter, we would like to mention the article by Kitterman et al., which was published after our manuscript was accepted for publication by Archivos de Bronconeumología. Some conclusions have been drawn from the analysis of this registry that coincide with those of our study and with the results of previous studies carried out in the United States, which we cite in our article. In all of these papers, a significantly greater risk of bacteremia is observed in patients receiving intravenous infusions of treprostinil, particularly bacteremia due to gram-negative bacilli, than in patients treated with epoprostenol.

In our series, the distribution over time of the 5 episodes of bloodstream infection detected during the study period (1991–2011) in patients receiving intravenous treprostinil was as follows: 2 episodes in 2008 and 3 episodes in 2010. To this we can add that outside the follow-up period, between January and September 2012, four patients in our hospital received intravenous treprostinil of which one developed Pseudomonas aeruginosa subcutaneous tunnel infection, associated with the vascular catheter for drug delivery, and another developed vascular catheter-related bacteremia, also caused by Pseudomonas aeruginosa. The small number of patients receiving treprostinil (10 in total), the limited number of episodes of bacteremia and the short follow-up period make us cautious about drawing conclusions regarding a trend over time in the incidence of this complication.

The experience that we reported, together with other studies performed in North America, can be regarded as yet another element to be taken into consideration when making decisions on the use of prostanooids in the treatment of patients with pulmonary arterial hypertension.

We fully agree with Dr Gómez Sánchez in emphasising the use of strict aseptic methods in the insertion and handling of venous access catheters for the infusion of prostanooids. The complications associated with the intravenous infusion of prostanooids have led to the development of alternative forms of delivery, including a subcutaneous continuous infusion pump. Of the 85 patients followed in our hospital in whom this alternative method of infusion was used, no significant episodes of local or systemic infection have been recorded to date, so we currently consider this to be the method of choice for the administration of treprostinil.