Eur. J. Oncol., vol. 16, n. 1, pp. 55-58, 2011

Occult lung adenocarcinoma mimicking diabetes insipidus due to single pituitary metastasis: case report and literature review

Un raro caso di diabete insipido da metastasi ipofisaria isolata come prima manifestazione di adenocarcinoma polmonare

Massimo Tonolini*, Sabrina Ferrario**

* Radiology Department, "Luigi Sacco" Hospital, Milan, Italy
** Oncology Unit, "Luigi Sacco" Hospital, Milan, Italy

Summary

We describe a 60-year-old female patient, with typical clinical and laboratory features of diabetes insipidus, treated with hormonal replacement. Subsequent investigations including head MR and total body CT imaging showed a lung adenocarcinoma with the pituitary gland as the only site of dissemination. The metastatic nature of the sellar lesion was confirmed by its rapid growth during chemotherapy along with progression of the primary tumor. Only a few similar cases have been reported in the literature. We discuss clinical and imaging features of pituitary metastases, usually diagnosed at autopsy or in advanced stages of neoplastic disease. Eur. J. Oncol., 16 (1), 55-58, 2011

Key words: **diabetes insipidus, pituitary, lung cancer**

Riassunto

Si descrive il caso di una donna di 60 anni presentatasi con un quadro clinico e laboratoristico tipico per una forma di diabete insipido e sottoposta a terapia ormonale sostitutiva. I successivi accertamenti diagnostici, tra cui l'imaging mediante RM dell'encefalo e TC del corpo intero, hanno portato al riscontro di un adenocarcinoma polmonare con l'ipofisi come unica sede di metastatizzazione. La natura secondaria della massa sellare è stata confermata dalla sua crescita in corso di chemioterapia, in parallelo con la progressione della neoplasia primitiva. In letteratura risultano riportati solo pochi casi simili. Vengono quindi discusse le caratteristiche cliniche e radiologiche delle metastasi ipofisarie, abitualmente diagnosticate autopticamente o in stadi avanzati di malattia neoplastica disseminata. Eur. J. Oncol., 16 (1), 55-58, 2011

Parole chiave: **diabete insipido, ipofisi, neoplasia polmonare**

Received/Pervenuto 11.10.2010 - Accepted/Accettato 9.2.2011
Address/Indirizzo: Dr. Massimo Tonolini, Servizio di Radiologia, Ospedale "Luigi Sacco", Via G.B. Grassi 74, 20157 Milano, Italy
Tel. 02/39043412 - Fax 02/39042560 - E-mail: mtonolini@sirm.org

Introduction

Neoplastic metastases involving the pituitary gland are rarely diagnosed during life in cancer patients, especially if compared with the incidence of brain metastases; they have been usually reported as sporadic cases, within a generalized metastatic dissemination, or in autopsy series. Breast and lung (usually non-small cell) cancers are the most common primary tumors (1-4).

We describe a very uncommon case of diabetes insipidus due to isolated pituitary metastasis as the presenting picture of a lung adenocarcinoma.

Case report

A 60-year-old female patient came to our attention because of polydipsia and polyuria (nearly 10 liters of urine output per day) for three weeks, and associated complaints of headaches, weakness and somnolence. She was a smoker and suffered from hypertensive cardiac disease.

Laboratory tests revealed raised Erythrocyte Sedimentation Rate (32 mm/hour), slight hypernatremia (147 mEq/l), renal function and plasmatic osmolality within normal limits; urinalysis reported: pH 6,5; density 1,004; concentration 260 mmol/kg. Ultrasound (not shown) did not discover disease in the abdominal and pelvic organs. The clinical picture improved during treatment with low-dose desmopressin, with normalization of diuresis.

Under clinical diagnosis of diabetes insipidus, the patient underwent Magnetic Resonance Imaging (MRI) focused on the diencephalic region that documented the presence of a solid, intensely enhancing sellar lesion with suprasellar extension and absence of the posterior pituitary (Fig. 1A-B).

Chest x-ray was obtained, and the finding of a right hilar solid mass lesion was confirmed by total-body contrast-enhanced Computed Tomography (Fig. 1C-D) and further investigated with fiberoptic bronchoscopy and percutaneous CT-guided aspiration biopsy. Final histological diagnosis was primary lung adenocarcinoma, without other detectable sites of metastatization apart from the pituitary lesion.

Serum tumor markers NSE, CEA and GICA were within normal limits, signs of pan-hypopituitarism included decreased ACTH, cortisol, GH, TSH, FT4, ADH and IGF1; hyperprolactinemia was present.

The patient was treated with systemic chemotherapy (consisting of cisplatin plus gemcitabine), and hormonal replacement with desmopressin, levothyroxine and corticosteroids. Clinical performance status worsening was observed during the treatment, with associated complaints of intense, progressive headaches and onset of diplopia.

After 6 months, follow-up body CT and cranial MRI examinations were obtained: the primary right hilar lung tumor was not significantly changed in size and shape; the pituitary lesion demonstrated significant growth particularly in its suprasellar portion with involvement of the hypothalamus and optic chiasm (Fig. 1 E-F), confirming its presumed metastatic nature. Whole-brain radiation and stereotactic radiosurgery were deemed not indicated by the consultant radiotherapist. Second-line chemotherapy with erlotinib was immediately stopped due to adverse event consisting in severe epidermolysis bullosa on the right arm, and replaced with palliative therapy with oral etoposide.

The patient passed away 10 months after initial presentation. Pathological investigation of the pituitary metastasis was not obtained since autopsy has not been performed, but increase in size paralleling the progression of primary tumor suggest its likeness.

Discussion

Diabetes insipidus is an uncommon yet characteristic medical condition consisting of polyuria, polydipsia and dehydration. The clinical manifestations and biochemical changes may result from either an impaired synthesis of antidiuretic hormone (the so-called “neurogenic” diabetes insipidus) or renal insensitivity (“nephrogenic”) to its effect (5). Lack of arginine-vasopressin, also known as antidiuretic hormone, may be idiopathic, or result from pathologic processes involving the hypothalamus including primary or secondary tumors, craniopharyngiomas, granulomatous lesions, rarely trauma and iatrogenic (postoperative) conditions (5, 6).

Metastatization may reach the sellar region through different routes including: hematogenous

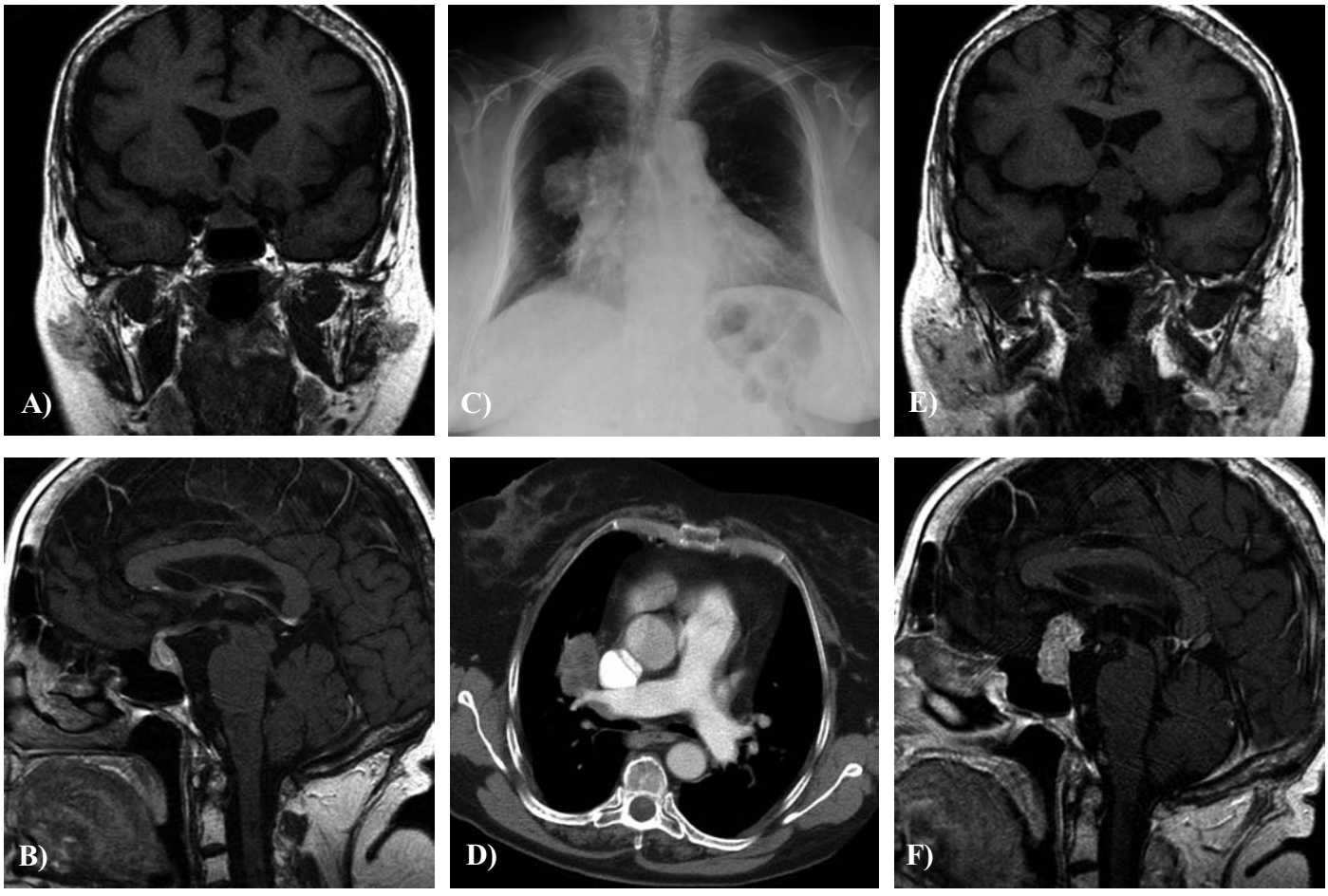

Fig. 1. At presentation, head MRI: an unenhanced coronal T1-weighted in (A) and a post-gadolinium sagittal T1-weighted image in (B) document a solid, intensely enhancing pituitary lesion with suprasellar extension and absence of the posterior pituitary. Chest radiograph (C) and contrast-enhanced CT (D) staging disclose a 5-cm right ilar solid mass consistent with primary lung tumor. Follow-up head MRI (E and F, same imaging sequences as in A-B) after 6 months, show significant progression of the pituitary lesion and of its suprasellar portion.

spread to the pituitary gland, direct extension from a hypothalamic lesion, extension from skull base metastases, and meningeal spread to the basal cisterns. Involvement of both pituitary lobes is common, with preferential or initial involvement of the posterior one whose blood supply comes from the systemic circulation (2, 7).

Symptoms related to pituitary involvement intermix with non-specific complaints occurring in end-stage cancer patients such as vomiting, weakness, weight loss and or other neurological signs. Visual loss, headache, cranial nerve deficits (particularly extraocular palsies), hyperprolactinemia, and signs of pan-hypopituitarism may be present (1-3). Diabetes insipidus is a characteristic feature, often in a highly suggestive clinical triad with headache and extraocular nerve deficits, and reflects the involvement of the posterior lobe, while most of the anterior pituitary has to be destroyed before hypopituitarism manifests (1, 2).

Similarly to our patient, very few reported cases describe the occurrence of a pituitary metastasis as the earliest manifestation of an occult primary cancer, or the initial site of dissemination: in most of these cases the primary tumor was a small-cell lung cancer (7-12).

From the diagnostic point of view, metastases only represent a small percentage of all pituitary lesions, but cannot be reliably differentiated from primary sellar tumors (particularly non-functioning pituitary adenoma) both on clinical grounds and on imaging features (4, 13).

MRI is the mainstay modality to image the sellar region: the usual appearance of a pituitary metastasis is a T1 hypo-isointense lesion, with absence of the high-signal posterior lobe on T1 precontrast images, intermediate- high T2 signal intensity, homogeneously enhancing post gadolinium. Pituitary masses usually respect the diaphragm sellae, and show an indentation at its level causing a dumb-bell shaped intrasellar and suprasellar tumor growth. Rapid progression or aggressive behaviour, infundibular invasion, edematous response in the adjacent portion of the brain, bone destruction, compression of neural tissue or vessels, leptomeningeal extensions and multiplicity of metastases should suggest the diagnosis of metastasis (2, 4).

Treatment of pituitary metastases is multimodal but almost always palliative, depending of the extent of the systemic neoplastic burden (2, 4). Complete resection is unlikely, surgical exploration with biopsy and decompression may be helpful if diagnostic clarification is needed and likely to affect therapeutic choice, or if causing progressive visual loss (3, 4, 13). Radiation is recommended as the initial and most amenable therapeutic option, plus hormone substitution therapy including exogenous vasopressin. Recently, stereotactic radiosurgery (Gamma-Knife) has been reported to be safe and effective for treating pituitary metastases and promptly improved patients' symptoms (14). Prognosis of patients with pituitary metastases is usually poor with a mean reported survival at 6-7 months, because of the spread and aggressiveness of the primary tumor (1-4, 7, 8).

In conclusion, the uncommon possibility of metastatization to the pituitary gland must be kept in mind when dealing with symptoms related to diabetes insipidus and hypopituitarism, particularly in patients with history of lung or breast cancer.

References

1. Sioutos P, Yen V, Arbit E. Pituitary gland metastases. Ann Surg Oncol 1996; 3: 94-9.
2. Komninos J, Vlassopoulou V, Protopapa D, *et al*. Tumors metastatic to the pituitary gland: case report and literature review. J Clin Endocrinol Metab 2004; 89: 574-80.
3. Morita A, Meyer FB, Laws ER Jr. Symptomatic pituitary metastases. J Neurosurg 1998; 89: 69-73.
4. Fassett DR, Couldwell WT. Metastases to the pituitary gland. Neurosurg Focus 2004; 16: E8.
5. Blevins LS Jr, Wand GS. Diabetes insipidus. Crit Care Med 1992; 20: 69-79.
6. Adam P. Evaluation and management of diabetes insipidus. Am Fam Physician 1997; 55: 2146-53.
7. Ito I, Ishida T, Hashimoto T, *et al*. Hypopituitarism due to pituitary metastasis of lung cancer: case of a 21-year-old man. Intern Med 2001; 40: 414-7.
8. Harzallah L, Migaw H, Harzallah F, *et al*. Diabetes insipidus and panhypopituitarism revealing pituitary metastasis of small cell lung carcinoma: a case report. Ann Endocrinol (Paris) 2005; 66: 117-20.
9. Alacacioglu A, Oztop I, Fidan F, *et al*. Diabetes insipidus caused by pituitary gland metastasis accompanied by iris metastasis of small cell lung cancer: case presentation and review of the literature. Tumori 2008; 94: 765-8.
10. Guillen Ponce C, Garrido Lopez MP, Molina Garrido MJ, *et al*. Panhypopituitarism as first manifestation of a lung cancer. Clin Transl Oncol 2007; 9: 53-5.
11. Granata A, Figura M, Gulisano S, *et al*. Central diabetes insipidus as a first manifestation of lung adenocarcinoma. Clin Ter 2007; 158: 519-22.
12. Ruelle A, Palladino M, Andrioli GC. Pituitary metastases as presenting lesions of malignancy. J Neurosurg Sci 1992; 36: 51-4.
13. Branch CL Jr, Laws ER Jr. Metastatic tumors of the sella turcica masquerading as primary pituitary tumors. J Clin Endocrinol Metab 1987; 65: 469-74.
14. Mori Y, Kobayashi T, Shibamoto Y. Stereotactic radiosurgery for metastatic tumors in the pituitary gland and the cavernous sinus. J Neurosurg 2006;105 Suppl: 37-42.