Extramedullary Multiple Myeloma Presenting as a Pituitary Mass Lesion

Authors: C. Dimopoulou[1, 2], S. Ormanns[3], S. Eigenbrod[3], U. Müller-Lisse[1], B. Emmerich[1], M. Reincke[1]

Affiliations:
[1] Medizinische Klinik Campus Innenstadt, Klinikum der LMU, Munich, Germany
[2] Department of Neuroendocrinology, Max-Planck-Institute of Psychiatry, Munich, Germany
[3] Department of Pathology, Ludwig-Maximilians-Universität (LMU), Munich, Germany

Key words
- extramedullary multiple myeloma
- pituitary mass
- case report

Abstract

Introduction: A plasmocytoma involving the pituitary gland is an extremely rare entity, with approximately 22 cases of solitary myeloma or multiple myeloma presenting with sellar mass reported in the literature so far.

Case report: Here, we report the case of a 71-year-old female patient affected by an extramedullary IgG-lambda multiple myeloma presenting as a pituitary mass lesion. We summarize the diagnostic approaches that confirmed the diagnosis of multiple myeloma and describe treatment outcome after therapy.

Discussion: Intrasellar plasmocytoma though rare, should be considered in the differential diagnosis of a pituitary mass lesion, since associated with different therapeutic and prognostic implications. Physicians should be alert for intrasellar plasma cell tumors in case of well preserved anterior pituitary function in combination with cranial nerve neuropathies and sellar destruction.

received 31.10.2011
first decision 03.04.2012
accepted 28.06.2012

Bibliography
DOI http://dx.doi.org/10.1055/s-0032-1321810
Published online: July 31, 2012
Exp Clin Endocrinol Diabetes

ISSN 0947-7349

Correspondence
C. Dimopoulou, MD
Medizinische Klinik Campus Innenstadt
Klinikum der LMU
Ziemssenstraße 1
80336 München
Tel.: +49/89/30 62 24 60
Fax: +49/89/30 62 27 46 0
dimopoulou@mpipsykl.mpg.de

Introduction

Multiple myeloma, a neoplastic disorder arising from plasma cells in the bone marrow, represents with 13% the second most common hematological malignancy and 1% of all malignancies [1]. A plasmocytoma involving the pituitary gland is an extremely rare clinical entity, with approximately 22 cases of solitary plasmocytoma or multiple myeloma presenting with sellar mass reported in the literature so far [2, 3].

We describe the case of a 71-year-old female patient affected by an extramedullary IgG-lambda multiple myeloma presenting as a pituitary mass lesion. Since extramedullary multiple myeloma can both clinically and radiologically mimic non-functioning pituitary adenomas, physicians should be aware of intrasellar plasma cell tumors in order to prevent misdiagnosis and determine appropriate therapeutic approach and individual treatment outcome.

Case Report

A 71-year-old female patient presented in our emergency department with horizontal diplopia since the previous day. The patient's medical history was positive for an IgG-lambda multiple myeloma, initially diagnosed 11 years ago. The patient had received autologous stem cell transplantation 4 years ago and had in the meantime been treated with numerous chemotherapy regimens, lastly 1 month prior to admission with bendamustine 110 mg/m^2 und prednisolone 100 mg. No evidence of intracranial plasmocytoma manifestation was apparent up to now.

Neurological examination was remarkable for an incomplete palsy of the left sixth cranial nerve. Other cranial nerves were intact. Cranial computed tomography (CCT) was unremarkable. Magnetic resonance imaging (MRI) showed a 1.2 × 1.3 × 1.4 cm pituitary mass without evidence of destroying the floor of the sella; the optic chiasm was intact. However, an infiltration into the cavernous sinus irritating the left sixth cranial nerve could not be excluded (**Fig. 1**).

Hormonal evaluation revealed a normal TSH level with low free thyroxine and triiodothyronine, inappropriately low LH for the postmenopausal state and a modestly elevated serum prolactin level, suggestive for a partial pituitary failure with secondary hypothyroidism, secondary hypogonadism as well as hyperprolactinaemia due to pituitary stalk compression (**Table 1**).

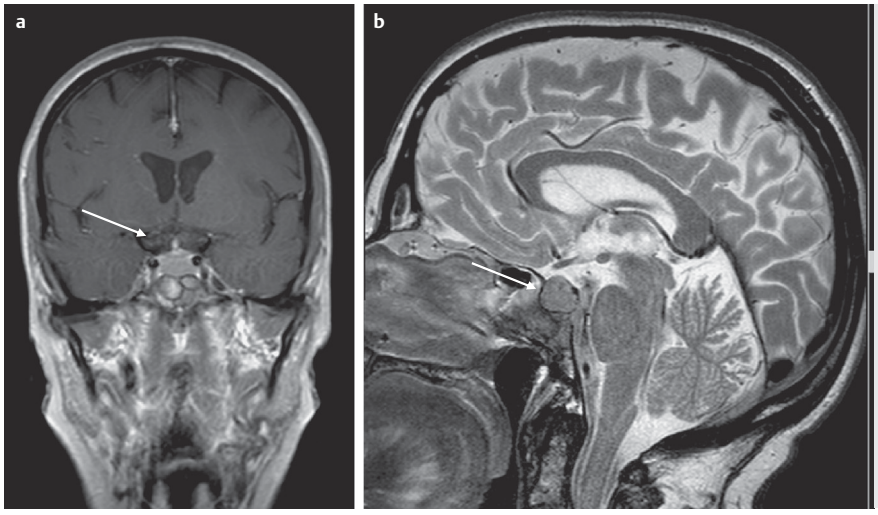

Fig. 1 Coronal **a** and sagittal **b** MRI scan on presentation showing a 1.2 × 1.3 × 1.4 cm pituitary mass lesion without evidence of destroying the floor of the sella; infiltration into the cavernous sinus irritating the left sixth cranial nerve could not be excluded. The optic chiasm was intact.

	Reference range	On presentation	Follow-up
TSH	0.30–4.00 µU/ml	0.93	–
TT4	0.80–1.80 ng/dl	0.89	–
TT3	2.30–4.30 pg/ml	1.93*	–
cortisol 0′	4.0–19.0 µg/dl	28.40	–
cortisol 30′	23.0–58.0 µg/dl	39.80	–
FSH	30.0–120.0 U/l	31.00	–
LH	16.0–64.0 U/l	9.1*	–
estradiol	< 30 pg/ml	< 10	–
prolactin	30–500 µU/ml	1 240*	–
total protein	6.0–8.5 g/dl	8.8*	–
albumin	3.5–5.0 g/dl	3.6	–
calcium	2.15–2.60 mmol/l	2.24	1.98
sodium/potassium	3.5–5.0 mmol/l/135–145 mmol/l	3.3*/136	4.2/
creatinine	0.5–1.0 mg/dl	0.9	1.09
Hb/Plts	12.0–16.0 g/dl/150–400 G/l	9.9/96*	10.2/144

Table 1 Laboratory findings on presentation and at follow-up.

Further endocrine and oncological evaluation took place as an outpatient. 2 weeks later, the patient presented clinically with persistence of the left sixth cranial nerve palsy. Sellar MRI demonstrated a constant in size pituitary mass lesion with left parasellar extension and extension to the clivus, complete infiltration of the sphenoid sinus and pituitary stalk thickening; the optic chiasm was not displaced.

Based on the radiological findings, the presumptive diagnosis was an extramedullary plasmocytoma originating from the sellar region presenting as a pituitary mass lesion and transsphenoidal biopsy of the sphenoid mass was performed. The histological appearance of the specimen showed a dense neoplastic cell population with plasmocytoid differentiation, considerably enhanced pleomorphic nuclei and focal mitotic activity. Immunohistochemical staining confirmed a mature-type plasmocytoma (**Fig. 2**).

Laboratory data summarized in **Table 1** including serum protein electrophoresis showed an elevation in IgG 4 032 mg/dl (700–1 600 mg/dl) and IgG lambda (λ) free light chains 1 200 mg/l (5.7–26.3 mg/l) in the serum. Beta 2 microglobulin level was 6.22 mg/l (0.7–1.8). Urine was not examined for Bence-Jones proteinuria. In addition, the patient had anemia with a haemoglobin level of 10.2 g/dl. No hypercalcaemia was detected. LDH was elevated as a tumor marker (354 U/l, reference range < 250 U/l).

Follow-up CT scan of the chest and abdomen revealed massive disease progress comprising multiple new soft-tissue metastases and among others a known metastatic lesion of the left 11^{th} and 12^{th} rib increasing in size from 4.5 × 6.5 up to currently 10 × 11.5 × 8 cm and infiltrating the skin. Due to the presence of systemic myelomatous disease, she underwent one cycle of chemotherapy with bortezomib 2.0 mg by subcutaneous injection, melphalan 9 mg/m^2 and dexamethasone 20 mg. Radiation therapy directed to the pituitary and the sphenoid sinus was administered for 3 sessions at a dose of 2 Gy per session; planned was a cumulative dose of 36 Gy over a 6-week period.

10 days later, the patient presented in our emergency department with severely reduced general condition, fever, productive cough and dyspnea due to critical neutropenia. Because of worsening respiratory failure due to pneumonia and septic shock, she was admitted to the Intensive Care Unit; the patient died despite intensive medical care.

Autopsy disclosed high-grade plasmacytic infiltration of the skeleton, mediastinal and retroperitoneal soft tissue and of the skin. Immunocytochemistry of the intrasellar mass was positive for CD 138, confirming that this tumor was a pituitary manifestation of a multiple myeloma. The cause of death was attributed to advanced terminal cancer; investigation for pneumonia was negative.

Discussion

Here, we report the case of a 71-year-old female patient affected by an extramedullary IgG-lambda multiple myeloma presenting as a

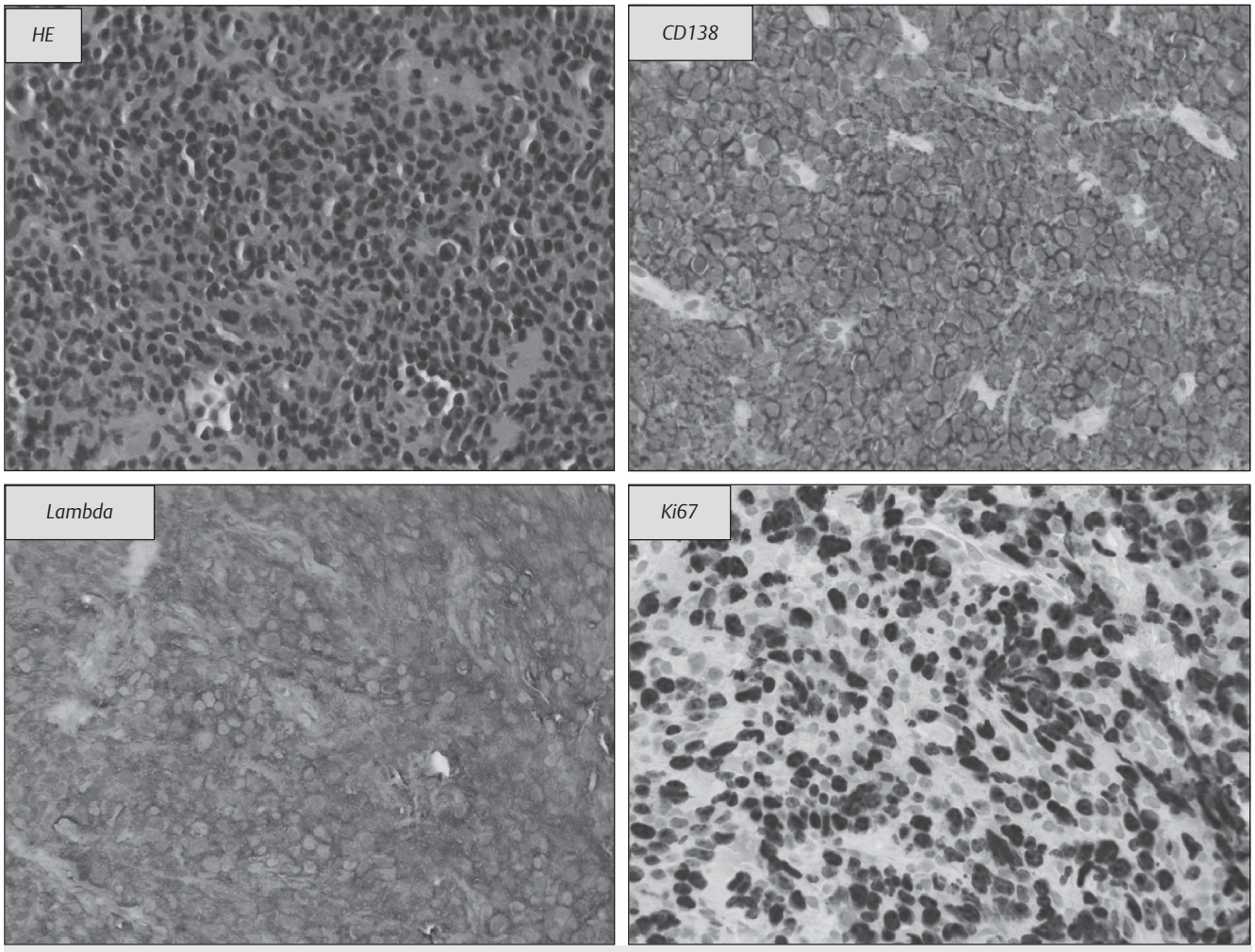

Fig. 2 HE: Dense infiltration by small, monomorphic tumor cells with chromatin rich, excentric nuclei. CD138: Strongly positive CD138 immunohistochemical staining identifies plasmocytoma cells. Ki67: Ki67 staining shows a high proliferative activity. Lambda: positive immunohistochemical staining for lambda light chain identifies lambda light chain plasmocytoma cells while a staining for kappa light chain remained negative (data not shown).

pituitary mass lesion. We summarize the diagnostic approaches that confirmed the diagnosis of multiple myeloma and describe treatment outcome after therapy.

Differential diagnosis of intrasellar masses masquering as pituitary adenomas is broad and complex as reported in the literature, comprising primary intracranial tumors and cysts e.g., craniopharyngeoma and pituitary carcinoma, primary cranial tumors e.g., chordoma and multiple myeloma, metastatic tumors, vascular anomalies, infectious and inflammatory disease e.g., lymphocytic hypophysitis [4].

A plasmocytoma involving the pituitary gland exhibits radiological and clinical similarities to a non-functioning pituitary adenoma (NFPA), possibly leading to misdiagnosis [2]. Radiological findings comprise evidence of sellar expansion in combination with destruction of the sellar floor [4].

Clinical presentation of the patients comprises headache, diplopia, as in our patient, visual loss, ptosis, facial numbness and different cranial nerve palsies including oculomotor, trochlear and abducent nerves [2]. Regarding hypopituitarism, the majority of the patients present with intact anterior pituitary function [4,5]. Normal or minimally disturbed anterior pituitary function is rather suggestive of a primary lesion lying outside the pituitary fossa [6]. In contrast to the published literature, our patient presented with a partial pituitary failure including secondary hypothyroidism, secondary hypogonadism and hyperprolactinaemia due to pituitary stalk compression. Evidence of impaired cortisol response after insulin induced hypoglycaemia has been reported in 1 case so far [6].

Definitive diagnosis for multiple myeloma with intracranial involvement is set by immunohistochemical analysis currently serving as “gold standard”. Tumor cells will exhibit positive staining with CD138 and/or kappa or lambda immunoglobulins [2]. Previously, interphase fluorescent in situ hybridization studies revealed chromosome abnormalities in multiple myeloma cells, possibly serving as adverse prognostic factors for patients’ treatment outcome [7,8].

The majority of the patients present with occult myelomatous disease prior to the development of cranial and intracranial involvement [4]. If not so, about 50% of the reported cases progress into multiple myeloma within 10 years time [9]. Solitary multiple myeloma progressing or not into multiple myeloma has also been reported [10]. Similar to our case, tumor cells are believed to originate from the surrounding bone e.g., the sellar region or the mucosa within the petrous or sphenoid bone [11].

Radiation therapy directed towards the sellar lesion as monotherapy or combined radio/chemotherapy in case of systemic myeloma represents the treatment of choice; autologous stem cell transplantation might be carried out in selected patients.

The patient described here is rare in that end stage disease lead to rapid tumor progression within 2 weeks and multifocal extramedullary growth comprising high-grade multiple plasmacytic infiltration of the skeleton, mediastinal and retroperitoneal soft tissue and of the skin. Lethal outcome was attributed to advanced terminal cancer despite initiation of combined radio/chemotherapy as currently recommended.

In conclusion, intrasellar plasmocytoma though rare, should be considered in the differential diagnosis of a pituitary mass lesion, since associated with different therapeutic and prognostic implications [2,4]. Preserved anterior pituitary function in combination with cranial nerve neuropathies and significant sellar destruction should alert physicians for intrasellar plasma cell tumors [4].

Conflict of Interest: The authors report no conflict of interest.

References

1 *Raab MS*, *Podar K*, *Breitkreutz I et al.* Multiple myeloma. Lancet 2009; 374: 324–339
2 *Yaman E*, *Benekli M*, *Coskun U et al.* Intrasellar plasmacytoma: an unusual presentation of multiple myeloma. Acta Neurochir (Wien) 2008; 150: 921–924; discussion 924
3 *Rivera J*, *Alves S*, *Bianchi CC et al.* An unusual collision tumor comprising a prolactinoma and a plasmocytoma originating from the sellar region. Pituitary 2010; 13: 189–193
4 *Sinnott BP*, *Hatipoglu B*, *Sarne DH.* Intrasellar plasmacytoma presenting as a non-functional invasive pituitary macro-adenoma: case report & literature review. Pituitary 2006; 9: 65–72
5 *McLaughlin DM*, *Gray WJ*, *Jones FG et al.* Plasmacytoma: an unusual cause of a pituitary mass lesion. A case report and a review of the literature. Pituitary 2004; 7: 179–181
6 *Evans PJ*, *Jones MK*, *Hall R et al.* Pituitary function with a solitary intrasellar plasmacytoma. Postgrad Med J 1985; 61: 513–514
7 *Huang SY*, *Yao M*, *Tang JL et al.* Clinical significance of cytogenetics and interphase fluorescence in situ hybridization analysis in newly diagnosed multiple myeloma in Taiwan. Ann Oncol 2005; 16: 1530–1538
8 *Chang H*, *Qi C*, *Yi QL et al.* p53 gene deletion detected by fluorescence in situ hybridization is an adverse prognostic factor for patients with multiple myeloma following autologous stem cell transplantation. Blood 2005; 105: 358–360
9 *Holland J*, *Trenkner DA*, *Wasserman TH et al.* Plasmacytoma. Treatment results and conversion to myeloma. Cancer 1992; 69: 1513–1517
10 *Pitini V*, *Arrigo C*, *Alafaci C et al.* Extramedullary plasmacytoma presented as a non-functional invasive pituitary macro-adenoma. J Neurooncol 2008; 88: 227–229
11 *Estopinan V*, *Riobo P*, *Fernandez G et al.* Intrasellar plasmacytoma simulating a pituitary adenoma. Med Clin (Barc) 1987; 89: 128