Unusual association of diseases/symptoms

Metastatic haematological malignancy presenting as a sellar mass

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Summary

A man in his 60s with a history of multiple myeloma diagnosed 6 months previously was referred with a diagnosis of a sellar mass. He reported a 3-month history of headaches associated with double vision which appeared to improve with corticosteroid treatment. An MRI scan revealed a 3.7 cm×3 cm×2.6 cm sellar mass with erosion into the sphenoid sinus and extending to the right cavernous sinus. Pituitary function tests were normal apart from hypogonadotrophic hypogonadism. A diagnosis of plasmacytoma was considered and so transphenoidal biopsy of the sellar lesion was organised, which revealed sheets of mature appearing plasma cells, staining exclusively for κ-light chain immunoglobulins. He was to be started on chemotherapy for the myeloma and radiotherapy for the plasmacytoma. The patient's clinical course was complicated by community-acquired pneumonia and renal failure resulting in his death a month after the diagnosis of plasmacytoma.

BACKGROUND

This case highlights the importance of the differential diagnosis of sellar-based lesions and the rare association of an intrasellar plasmacytoma with multiple myeloma. It is important to appreciate that the clinical presentation, radiological features and light microscopic features may be indistinguishable from a non-functional pituitary adenoma, so a high index of suspicion is required to initiate the correct diagnostic strategy.

CASE PRESENTATION

A man in his 60s presented with a 12-week history of severe right-sided throbbing headaches which was episodic in nature (5–6 episodes per day) associated with lacrimation and conjunctival injection in his right eye, double vision and rhinorrhoea. The headaches were not associated with neck stiffness or photophobia. Neurological examination at initial presentation was documented as being normal. As a consequence of these symptoms, a CT head scan was organised which revealed a mass located in the pituitary fossa. Blood tests showed normochromic anaemia (haemoglobin 9.1, mean corpuscular volume (MCV) 80 fl) with normal liver function and renal function tests.

His headaches were diagnosed as cluster headaches and he was initially treated with non-steroidal anti-inflammatories (Ibuprofen) and paracetamol, followed by sumatriptan subcutaneously with moderate relief of his headaches. He was started prophylactically on a tapering dose of corticosteroids (Prednisolone 60 mg/day reduced by 10 mg every 3 days) by the admitting physician for a period of 3 weeks and referred to the tertiary endocrine centre.

He had been diagnosed with multiple myeloma 6 months previously on the basis of normochromic

anaemia (haemoglobin of 9.7 g/dl, MCV 80 fl) and positive serum protein electrophoresis (compact band in gamma region with IgG κ-paraproteinaemia) for which he was under regular review by haematology, although he had not received any specific chemotherapy due to the patient's concern with side effects of chemotherapy. His medical history included a diagnosis of retinal detachment 7 years ago with a residual visual field deficit in the left inferior-temporal quadrant.

At the initial endocrine consultation after 4 weeks of his presentation, his headaches and double vision appeared to have improved which he attributed to the corticosteroids but he complained of severe left-sided chest pain and upper back pain which did not respond to analgesics (Ibuprofen and paracetamol) prescribed by his family physician. He denied symptoms of dizzy spells, nasal discharge, polyuria and polydipsia but reported a 12-month history of loss of libido with reduced frequency of erections. Examination revealed chest wall tenderness over the left 10th rib and lumbar vertebrae. Neurological examination revealed right sixth cranial nerve palsy with left inferior temporal quadrantanopia. An ECG done at admission was normal.

Due to his chest pain, he was admitted for pain management and further investigation of the sellar mass.

Pituitary function profile was normal apart from a low testosterone level (6 nmol/l) with normal follicle stimulating hormone (FSH) (3.6 IU/l) and luteinising hormone (LH) (6.2 IU/l) suggestive of hypogonadotrophic hypogonadism. A short synacthen test showed adequate adrenal reserve with 30 min cortisol at 644 nmol/l (adequate response defined as cortisol >450 nmol/l 30 min after intravenous injection of 250 µg of synthetic adrenocorticotrophic hormone (ACTH) (tetracosactrin).

INVESTIGATIONS

Laboratory findings on presentation	On presentation	Reference range
Haemoglobin (g/dl)	9.1	13.5–18
Platelets (per litre)	252×10^9	$150\text{--}450 \times 10^9$
Total protein (g/l)	87	60–80
Albumin (g/l)	37	35–50
CRP	32	<5
Calcium (mmol/l)	2.51	2.2–2.6
Sodium (mmol/l)	136	133–146
Potassium (mmol/l)	3.7	3.5–5.3
Urea (mmol/l)	5.8	2.5–5.8
Creatinine ($\mu\text{mol/l}$)	96	62–105
Thyroid stimulating hormone (mU/l)	1.56	0.3–4.2
T4 (pmol/l)	12.3	12–22
Cortisol (nmol/l)	413 (9 am)	170–450
Cortisol (30 min post-ACTH) (nmol/l)	644	>450
Prolactin (mIU/l)	362	100–350
FSH (IU/l)	3.6	1.5–12
LH (IU/l)	6.2	1.6–8.6
IGF-1 (nmol/l)	18	6–30
Testosterone (nmol/l)	6	9–24

Chest x-ray showed fracture of the left 10th rib (figure 1) and x-ray of the lumbar spine showed wedge fracture of L1 vertebra (figure 2). ECG showed normal sinus rhythm.

CT scan of brain showed air fluid levels in both sphenoid sinuses with erosion of planum sphenoidale (right side) and a sellar mass (figure 3). An MRI scan of the pituitary confirmed a uniformly enhancing soft tissue mass measuring 37.3 mm×30 mm×26 mm with features of erosion into the sphenoid and right cavernous sinus, partial destruction of the dorsum sellae with displacement of the pituitary gland superiorly (figure 4). There was also erosion of a portion of the clivus (a shallow depression formed of the sphenoid bone located posteriorly to the dorsum sellae) suggesting an invasive tumour (figure 5). The overall appearances suggested a tumour centred on the clivus with a differential diagnosis of a chordoma, plasmacytoma or metastasis.

Based on the previous diagnosis of multiple myeloma, a trans-sphenoidal biopsy of the sellar mass was performed.

Figure 1 x-Ray chest showing fracture of left 10th rib laterally.

Figure 2 x-Ray lumbar spine showing wedge fracture of L1 vertebra.

Histopathological analysis of the specimen showed fragments of bone and fibrous tissue with sheets of mature appearing plasma cells and cells with plasmablastic morphology. Tumour cells showed widespread immunoreactivity for CD43, CD138, CD79a, MUM-1, CD56 and Bcl2. Histological staining was positive for immunoglobulin, κ -light chains confirming a diagnosis of a plasmacytoma.

Figure 3 CT scan head showing erosion of sphenoid bone (right) with air fluid levels and a sellar mass.

Figure 4 MRI pituitary: coronal section showing a uniformly enhancing soft tissue mass eroding into the right sphenoid bone and cavernous sinus.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis is

- ▶ Atypical pituitary tumour
- ▶ Pituitary carcinoma
- ▶ Chordoma
- ▶ Metastasis
- ▶ Histiocytosis X
- ▶ Plasmacytoma

TREATMENT

The patient was referred to oncology for consideration of radiotherapy as the most appropriate approach to treating the plasmacytoma. With regard to his multiple myeloma, he was to be started on chemotherapy.

Figure 5 RI pituitary: sagittal section showing intrasellar mass centred on the clivus and displacing the pituitary gland superiorly.

OUTCOME AND FOLLOW-UP

An assessment of his pituitary hormonal profile posttrans-sphenoidal biopsy was normal. Prior to him being started on any definitive treatment, his clinical course was complicated by the development of community acquired pneumonia and acute renal failure necessitating his admission to hospital and leading to his untimely death.

DISCUSSION

Plasma cell neoplasms may present either as a solitary plasmacytoma which is a localised collection of plasma tumour cells or it may manifest as multiple myeloma (MM) which is a multifocal tumour primarily presenting as destructive plasma cell tumours involving the axial skeleton with features of osteolytic lesions, pathological fractures, hypercalcaemia, anaemia, bone pain and serum monoclonal protein levels. The bones most commonly affected (in descending order of frequency) are the vertebral column, ribs, skull, pelvis, femur, clavicle and scapula.¹ Intracranial involvement by myelomatous disease is rarely seen (3% of 273 cases of MM) as described by Silverstein and Doniger.²

Metastasis to the pituitary gland is a rare event. The most common primary neoplasms metastasising to the pituitary are breast (40%) and lung cancer (24%)³ which are typically seen in elderly patients with diffuse malignant disease. Diagnosis can often be difficult as the lesion may be too small and be entirely asymptomatic.

There have been 26 reported cases of patients in whom solitary plasmacytoma (no prior evidence of systemic disease) or MM presented as a mass involving the intrasellar region.^{4–6} Plasma cell tumours involving the sellar region are exceedingly rare and may mimic non-functioning pituitary adenomas in clinical presentation and imaging. It is believed that the origin of the tumour cells in a plasmacytoma is the surrounding bone or the mucosa within the petrous or the sphenoid bone.⁷

There seems to be a slight female preponderance (60%).^{4,5} As noted in our patient, extraocular muscle palsies are commonly noted in most cases of metastatic lesions involving the sella.⁸ The most common cranial nerves involved were the abducent, trochlear and oculomotor nerves. In our case, anterior pituitary function was preserved except for hypogonadotropic hypogonadism which may have been a consequence of compression of the pituitary gland by the sellar mass. Indeed, most reports of sellar plasmacytomas suggest well-preserved or minimally disturbed anterior pituitary function.^{9–10} The preservation of pituitary function may be a consequence of the development of the plasmacytoma outside the pituitary fossa resulting in a presentation with symptoms other than those of pituitary dysfunction. This is supported by the imaging characteristics in our patient, revealing erosion of the floor of the pituitary fossa with displacement of the pituitary gland superiorly.

Differentiating between a pituitary adenoma and a plasmacytoma can often be difficult in the absence of systemic features or biochemical data suggestive of MM. Five cases were identified where myelomatous intrasellar masses were incorrectly diagnosed as benign adenomas on histology but were later revised after clinical expression of occult disease or following use of immunohistochemical stains or electron microscopy.^{11–15} Clearly, a biopsy in our

patient confirmed the diagnosis of plasmacytoma which obviated the need for transsphenoidal hypophysectomy.

Treatment for sellar plasmacytomas (either for local or residual disease) is most commonly radiotherapy and chemotherapy for systemic myelomatous disease.^{5 6 15–18} Case reviews in 2007⁵ and a recent review⁶ on intrasellar plasmacytoma showed that majority of patients were diagnosed at pathology following transphenoidal resection. Subsequent treatment regimens included radiotherapy (upto 80%) and chemotherapy (42%) of patients. Recently quoted data support treatment with autologous bone-marrow stem cell transplantation in addition to conventional treatment.¹⁹

Patients diagnosed initially with a solitary intrasellar plasmacytoma in the absence of occult disease showed a variable time frame to the development of systemic manifestations (0–22 months).^{5 6} Over 50% will develop multiple myeloma within a decade and 10% develop a local recurrence of the plasmacytoma or another solitary plasmacytoma.²⁰ The size of the lesion, total serum protein levels and presence of a monoclonal spike on serum electrophoresis may be of prognostic significance in identifying patients likely to develop myeloma.

The presence of extraocular muscle palsies in a patient presenting with an aggressive sellar mass on imaging and minimal, or no evidence of, anterior pituitary hormonal deficiency should alert to a possible diagnosis of a plasmacytoma.

Learning points

Features of myelomatous disease involving the pituitary fossa:

- ▶ Myeloma may present as a solitary plasmacytoma or as a metastatic lesion which can mimic a non-functional invasive pituitary macroadenoma in clinical presentation as well as imaging studies.
- ▶ The presence of cranial nerve palsies may help to distinguish it from a benign adenoma.
- ▶ Anterior pituitary function is often preserved despite significant sellar destruction.
- ▶ Immunohistochemical stains and electron microscopy should be applied to biopsy specimens from pituitary adenomas with atypical features as it may be indistinguishable from a chromophobe pituitary adenoma on light microscopy.
- ▶ It is important to differentiate between pituitary adenomas and plasma cell tumours involving the sellar region as the management and prognosis are different.

Competing interests None.

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