Rare disease

An unusual cure for acromegaly

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Summary

The authors present the case of a 30-year-old female patient with acromegaly whose disease had not been cured after transcranial neurosurgery, two transsphenoidal surgeries and stereotactic radiosurgery. She required treatment with octreotide and pegvisomant to normalise growth hormone levels. Seven years after the diagnosis of acromegaly, she noticed acute vision loss in her left eye and presented with meningism. She had an intrasellar abscess which was confirmed and treated by surgical drainage. As a result of the abscess, she was cured of acromegaly and able to discontinue both octreotide and pegvisomant.

BACKGROUND

Pituitary abscess and acromegaly are both rare conditions. A combination of both in one patient is remarkable, even more so when a pituitary abscess results in the cure of an hormonally active pituitary tumour. In a review of the literature, we could not find any other description of acromegaly cured by a pituitary abscess.

CASE PRESENTATION

The patient presented at the age of 23 years with homonymous haemianopia. At that time, the diagnosis of acromegaly was made and a massive tumour was found, extending to the lateral fissure. Neurosurgery using a fronto-basal approach allowed partial removal of the tumour. Postoperative MRI showed intra and suprasellar tumour remnants with infiltration of the cavernous sinus bilaterally. Sellar tumour remnants were partially removed using a transsphenoidal approach 3 months after the initial surgery. As growth hormone (GH) and insulin like growth factor 1 (IGF-1) remained elevated, treatment with octreotide LAR (20 mg intramuscularly once monthly) was started. GH and IGF-1 remained high, and pegvisomant (15 mg subcutaneously once daily) was added 1.5 years later. Despite combination treatment, GH and IGF-1 could not be normalised. In an attempt to further reduce the intra and suprasellar tumour remnants, a second transsphenoidal surgery and fronto-basal craniotomy were performed in the same year, followed by stereotactic radiosurgery the following year. Tumour remnants persisted in the cavernous sinuses bilaterally, especially on the left, but with ongoing octreotide and pegvisomant treatment, IGF-1 levels were maintained within the normal range. The time course of IGF-1 levels and interventions are summarised in figure 1A. Central hypothyroidism developed after initial neurosurgery and was treated with levothyroxine, the other pituitary hormone axes remained intact.

At the age of 30 (ie, 7 years after the diagnosis of acromegaly and 4 years after radiosurgery) the patient noticed an acute deterioration of sight in her left eye and a sudden onset of back pain. Infiltration of her cervical spine with

a local anaesthetic (lidocain) had been performed 2 weeks previously due to chronic cervical pain.

INVESTIGATIONS

She presented to the emergency department of the local hospital and was found to have meningism on examination, a temperature of 38.5°C and a C reactive protein of 135 mg/l (normal <5 mg/l). A CT of the brain showed an ill-defined sellar mass without evidence of an intracranial bleed. On MRI, the mass was suspicious for an intrasellar abscess invading the cavernous sinus on the left (figure 1B). A lumbar puncture showed elevated mono-(527/μl) and polynuclear leucocytes (1774/μl) an increased protein level (2972 mg/l) and decreased glucose (2.2 mmol/l in cerebral spinal fluid, 5.9 mmol/l in plasma). Liquor and blood were sent for culture.

TREATMENT

An empiric antibiotic therapy consisting of ceftriaxone and amoxicillin was begun. On the following day, abducens paresis and haemianopia of the left eye developed and vancomycin was added to the antibiotic regimen. Because of clinical deterioration, the patient was referred to our institution, and surgical drainage of the abscess was performed, 5 days after the patients' initial presentation. Gram positive cocci of the *Streptococcus milleri* group (SMG) were cultured from the abscess (*S intermedius* and *S constellatus*). The antibiotic regimen was adapted to ceftriaxone and metronidazole.

OUTCOME AND FOLLOW-UP

Postoperatively, sight in the left eye improved. Hypocortisolism and hypogonadism were diagnosed and substitution therapy with glucocorticoids commenced (initially dexamethasone, followed by hydrocortisone). The patient developed marked polyuria because of new onset central diabetes insipidus. Desmopressin 10 μg twice daily led to complete resolution of polydipsia and polyuria.

During treatment of the intrasellar abscess, the patient continued pegvisomant 15 mg subcutaneously once daily

Intrasellar abscess as unusual cure for acromegaly.

A. Time course of IGF-1 before (years) and after (months) admission. Interventions are depicted by arrowheads (S: transsphenoidal surgery; RT: stereotactic radiotherapy) and medical treatment by horizontal bars (O: octreotide; P: pegvisomant). Grey area represents IGF-1 reference range.

B. Pituitary, T2-weighted MRI on admission. Arrowhead: intrasellar, cystic mass with enhanced rim suspicious for abscess invading the cavernous sinus on the left.

Figure 1 (A, B) Intrasellar abscess as unusual cure for acromegaly.

but her monthly octreotide injection was withheld. An IGF-1 level measured on admission was 262 µg/l (normal range 115–307). One month after surgery IGF-1 had decreased to 208 µg/l, 5 months after surgery IGF-1 had further decreased to 151 µg/l. Thirteen months after surgery IGF-1 was 60 µg/l and GH 0.12 µg/l. At this point, a treatment decision to discontinue pegvisomant was made. Two months after discontinuation of pegvisomant, IGF-1 remained stable at 67 µg/l and GH was 0.23 µg/l, 7 months later (5 years after radiosurgery) IGF-1 was 53 µg/l and GH 0.1 µg/l (figure 1A).

DISCUSSION

Pituitary abscess is a very rare condition that accounts for less than 1% of all pituitary diseases. Although pituitary abscesses are rare, they can be potentially lethal and require prompt diagnosis. Presenting symptoms are headache (90%), visual disturbances (50%–75%, including loss of visual acuity or of the visual field and optomotor palsies) and diabetes insipidus, which occur because of hypothalamic or pituitary stalk compression in up to 50% patients.¹ Clinical signs of infection such as meningism and fever may be present, but are infrequent (25–30%). There is no unique symptom to distinguish pituitary abscess from another mass lesion of the pituitary.

On T2-weighted MRI, pituitary abscess usually presents as a sellar enlargement with moderate to high intrasellar signal levels, suggestive of a fluid-containing cyst. On T1-weighted MRI, the sellar mass can be hypointense to mildly hyperintense. Peripheral or rim enhancement is seen in only a minority of cases.² The signal intensity of an abscess is affected by its protein content or the presence of haemorrhage, making contrast enhancement variable and difficult to interpret. Because of this, pituitary abscesses are often radiologically indistinguishable from other pituitary lesions. The differential diagnosis of a fluid sellar lesion includes cystic pituitary adenoma, craniopharyngioma,

Rathke's cleft cyst, epidermoid tumour and rarely arachnoid or colloid cysts.

Pituitary abscesses can occur in a pre-existing pituitary lesion such as an adenoma or a Rathke's cleft cyst, which account for approximately 40% of all pituitary abscesses³ or may be the result of direct extension or haematogenous spread of sphenoid sinusitis, meningitis, cavernous sinus thrombosis or osteomyelitis of the sella floor (30% of reported cases).⁴ Rarely complications of transsphenoidal surgery are the source of an abscess (liquorrhoea). In approximately 30% of patients no obvious underlying infection or pre-existing pituitary disease is found. Risk factors for pituitary abscess are immunosuppression, previous pituitary surgery or irradiation of the pituitary gland,⁵ as in our patient.

In previously reported cases, a wide spectrum of microbiological agents have been found in pituitary abscesses, including Gram positive cocci, Gram negative bacilli, fungi, amoebae and yeasts.⁶ Often, no organisms are cultured, probably due to preoperative antibiotic therapy or inadequate bacteriological material. The most common infective agents are bacteria, mainly *Staphylococci* and *Streptococci*, as in our patient. The Gram positive cocci of the SMG that were cultured in this case are bacteria commonly found in paranasal sinuses, the oral cavity, facial soft tissue, deep neck spaces or the peritonsillar region.⁷ SMG bacteria include *S intermedius*, *S anginosus* and *S constellatus* and are aggressive pathogens of the head and neck region with a propensity for abscess formation and local extension. The exact source of SMG in our patient remained unclear, cervical abscess after infiltration of the spine was considered (performed 2 weeks before admission) but could be ruled out by MRI.

When a pituitary/sellar abscess is suspected, transsphenoidal surgical drainage followed by appropriate antibiotic therapy is the treatment of choice. The abscess contents should be cultured to isolate the offending organism (including fungal and anaerobic cultures) and broad-

spectrum antibiotics given. Although pituitary abscesses have been treated successfully with antibiotics alone, this is controversial⁸ and not generally recommended. After combined surgical and medical treatment, most patients recover fully (60%), while the remaining patients recover with hormonal or visual impairment.¹

Our patient developed panhypopituitarism but was in turn cured of acromegaly. It could be argued that the long-term effect of the radiotherapy she received 4 years previously led to resolution of her acromegaly, rather than the pituitary abscess. However, she required two drugs to control her levels of GH (octreotide and pegvisomant) before her presentation. Immediately after diagnosis of the pituitary abscess, octreotide could be discontinued. GH and IGF-1 levels decreased rapidly, pegvisomant was discontinued 13 months after abscess surgery. Treatment with pegvisomant could probably have been suspended earlier, if the patient had had more frequent follow-up appointments. The close temporal relationship between the diagnosis of the pituitary abscess and the decrease in GH levels strongly suggests a causal relationship between the abscess and resolution of acromegaly. In a review of the literature, we could not find any description of a similar case.

Learning points

- ▶ Pituitary abscess is a rare and potentially lethal condition.
- ▶ Pituitary abscess frequently manifests with headache, visual impairment and diabetes insipidus rather than with clinical signs of infection.
- ▶ Pituitary abscess is one of the differential diagnoses of a fluid-containing cyst on cranial imaging, especially when meningism or fever is present.
- ▶ Transsphenoidal surgery and broad-spectrum antibiotics are the treatment of choice.

Competing interests None.

Patient consent Obtained.

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