CASE REPORT

Just another case of bacterial meningitis... or... is it?

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SUMMARY

Non-traumatic cerebrospinal fluid (CSF) rhinorrhoea is a rare condition. We describe a case of a 62-year-old woman with pneumococcal bacterial meningitis who later was found to have CSF rhinorrhoea secondary to an eroding skull base tumour, which was proven to be pituitary macroadenoma on biopsy. She recovered well from meningitis without any neurological sequelae and underwent trans-sphenoidal surgery for tumour removal as well as dural repair.

BACKGROUND

We present a rare case of bacterial meningitis who later was found to have cerebrospinal fluid (CSF) rhinorrhoea for a few months prior to presentation in the context of eroding pituitary macroadenoma. Ascending bacterial meningitis is a rare but important complication of CSF rhinorrhoea. Prompt recognition of CSF rhinorrhoea and early involvement of neurosurgeons is warranted to prevent complications as well as associated morbidity and mortality.

CASE PRESENTATION

A 62-year-old woman presented around mid-day with severe frontal headache and vomiting since waking up that morning and a progressively decreasing conscious level. Her medical history included a hysterectomy, osteoporosis and carcinoma breast for which she had wide local excision and radiotherapy 3 years ago. She was on a non-steroidal aromatase inhibitor (anastrozole 1 mg once a day), alendronic acid 70 mg once a week, calcichew D3 forte one tablet once a day and mometasone nasal spray once a day. Her most recent mammogram 4 months previously was normal. She worked as a pharmacy assistant and lived with her husband. She was a non-smoker and drank alcohol occasionally. There was no h/o drug allergies or usage of illicit drugs. There was no relevant family history.

On admission, her Glasgow Coma Scale (GCS) score was 8–9/15 (E2, M5, V1–2). She was febrile (37.9°C) but normotensive (140/85). Her respiratory rate was 17/min and saturations on air were 96%. Tachycardia was noted (pulse rate: 108/min, regular). Her capillary blood glucose was 9.1 mmol/L. Her pupils were equal and reactive to light. She was drowsy but agitated. There was no evidence of rash or photophobia. She was moving all four limbs. There was an element of neck stiffness, but systemic examination otherwise was normal. She was started on broad-spectrum antibiotics given the nature of the presentation.

INVESTIGATIONS

She was intubated and ventilated. CT of brain, neck, abdomen and pelvis with contrast revealed a large skull base tumour within the pituitary fossa (25×18×19 mm) eroding through the anterior and posterior bony parts of the sella. There was no evidence of pneumocephalus on CT brain (figure 1). Her bloods showed neutrophilia and raised C reactive protein (59 mg/L). Kidney and liver function tests as well as calcium were normal. A venous blood gas revealed normal pH, normal pCO₂ (5.35 kPa) and slightly elevated lactate (2.7 mmol/L). Lumbar puncture (which was performed nearly 20 hours after the initial dose of antibiotics) showed cloudy/turbid CSF with high opening pressure at 24.5 cm of water. There was very high CSF protein (4.59 g/L; range 0.15–0.45), decreased glucose levels (<0.6 mmol/L; range 2.2–3.9) and raised white cells (12 480×10⁶/L) with predominant polymorphs (95%) and few lymphocytes (5%). CSF gram stain was negative. CSF culture later came back as negative. Blood cultures showed no growth after 5 days. However, molecular testing of CSF as well as blood were positive for *Streptococcus pneumoniae* (pneumococcus) PCR DNA but negative for meningococcus and herpes simplex types 1 and 2.

TREATMENT

She improved well with the antibiotics (ceftriaxone 2 g twice a day), was extubated on day 8 and discharged to the medical ward (Endocrine) on day 11. She was afebrile with stable vitals and GCS score of 15/15. At this point, on reviewing the history, she had occasional minor headaches for a few months but had no history suggestive of visual field defects. On direct questioning, she reported a 'runny nose' for 3–4 months prior to admission for which she had seen her general practitioner and was prescribed mometasone nasal spray as it was thought that she had allergic rhinitis. She did not report sneezing or itchiness. Her symptoms did not improve with mometasone.

It was clear fluid rhinorrhoea, provoked by bending forward. A sample of nasal fluid was immediately collected into a universal container and the fluid was clear like water. Beta-2-transferrin analysis, following liaison with the biochemist, was positive, confirming the clinical suspicion of CSF rhinorrhoea. Her anterior pituitary function testing including prolactin levels were normal. Visual field testing revealed non-specific upper left nasal defect. A dedicated pituitary MRI confirmed large enhancing central skull base tumour within the pituitary fossa, extending into both cavernous sinuses, the sphenoid sinus, clivus and along the pituitary stalk. It surrounded and encased both carotid

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Figure 1 CT brain, bone window, sagittal section showing no e/o pneumocephalus.

arteries and abutted the optic chiasm. The pituitary gland could be seen separately to the tumour (figures 2 and 3).

A diagnosis of ascending bacterial meningitis due to CSF rhinorrhoea secondary to eroding skull base tumour was made.

OUTCOME AND FOLLOW-UP

Patient was referred to the affiliated tertiary neurosurgical centre and discussed in the regional skull base and pituitary multidisciplinary team meetings. The appearance of the tumour was felt to be unusual and there was not a clear radiological diagnosis. Given the history of breast cancer, the main differential diagnosis was a metastasis and a PET-CT was arranged to exclude metastases elsewhere. A trans-sphenoidal biopsy of the lesion via the dural defect was therefore performed. The defect was repaired. Histology revealed a null cell pituitary adenoma. Significant

Figure 2 MRI brain, sagittal section; large pituitary adenoma extending forward and downward (highlighted by arrow).

Figure 3 MRI brain, coronal section; arrow showing pituitary macroadenoma abutting chiasma superiorly and extending laterally towards cavernous sinuses.

tumour remains in the cavernous sinuses, which is not surgically resectable. She remains under close follow-up of endocrinologist and neurosurgeon. Patient's general practitioner was advised to ensure patient had vaccinations against *Haemophilus influenzae* and *Streptococcus pneumoniae*. When last reviewed (at 12 months from initial presentation), she was stable with no long-term neurological sequelae.

There has been debate regarding whether residual tumour should be treated with radiotherapy or not, as this could promote further CSF leak and make future repairs more challenging.

DISCUSSION

The most common cause of CSF rhinorrhoea is trauma (90% of cases). It can also occur due to congenital skull base/dural defects, postsurgical (neurosurgery or ear-nose-throat surgery) or with tumours. Primary spontaneous CSF rhinorrhoea is reported in patients with idiopathic intracranial hypertension usually in middle-aged obese women.¹ The potential leak sites include the cribriform plate, ethmoid, sphenoid and frontal sinuses.

It is a common complication of trans-sphenoidal surgery for pituitary and parasellar lesions with quoted incidence of 2.3% to 13%.² In a large retrospective analysis of 1002 patients who underwent endoscopic trans-sphenoidal pituitary surgery, it was noted that almost half of the patients who developed postoperative CSF rhinorrhoea had no evidence of intraoperative CSF leak. Authors felt that empirical sellar reconstruction in the absence of intraoperative CSF leak may be of benefit following resection of large pituitary tumours, especially if the arachnoid is thinned out and herniated into the sella.³

CSF rhinorrhoea in the context of pituitary tumours has been reported with medical therapy as well, including dopamine agonists for prolactinomas^{4,5} and somatostatin analogue treatment.^{4,6} CSF leak has also been reported after gamma knife radiosurgery although early leaks are more common than delayed (after 1 year).⁷ Tumour shrinkage with these therapies exposes the pre-existing dural defects resulting in CSF rhinorrhoea. It

is also reported rarely due to either direct tumour invasion or enzymatic destruction of the bone and dura.

Beta-2 transferrin is a protein that is produced by neuraminidase activity and unique to CSF, perilymph of inner ear and aqueous humour. It is very sensitive and specific for CSF.^{8 9}

Complications of CSF rhinorrhoea are ascending meningitis, encephalitis, brain abscess and pneumocephalus, which can be life changing/life threatening. Henceforth, it is important to involve neurosurgeons as soon as possible in patients with CSF rhinorrhoea.

Significantly lower incidence of meningitis has been reported with primary spontaneous (PS) CSF rhinorrhoea compared with the secondary group (annual incidence of 0.12 vs 1.22 episodes), which may be explained by an elevated intracranial pressure that hinders the ascension of bacteria in PS CSF rhinorrhoea.¹⁰

Meningitis cases almost halved in the UK since the introduction of vaccination against *H. influenzae*, meningococcal C and 13 strains of pneumococcus in 1989. The incidence of bacterial meningitis in adults is 1–2 cases per 100 000 people per year in the UK and Western Europe. *S. pneumoniae* (pneumococcus) is the most common cause of bacterial meningitis in adults in majority of the world.¹¹ Reported mortality with meningitis in adults is up to 30%. Long-term neurological sequelae are more common in pneumococcal meningitis when compared with meningococcal meningitis (approximately 25%).

Learning points

- ▶ Suspect cerebrospinal fluid (CSF) rhinorrhoea in patients with clear nasal discharge.
- ▶ Beta-2-transferrin analysis of the fluid is extremely sensitive and specific for CSF.
- ▶ If CSF rhinorrhoea is confirmed, be aware of the possible complications including ascending meningitis.
- ▶ Intracranial tumours (mainly pituitary) account for the majority of cases of non-traumatic CSF rhinorrhoea.
- ▶ It is important that patients with CSF leak are vaccinated against *Streptococcus pneumoniae*.

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