SELF ASSESSMENT ANSWERS

Nausea and vomiting in a patient with increasing thirst

Q1: Describe the finding on computed tomography and MRI and give a differential diagnosis

Enhanced axial computed tomography of the brain with iodine based contrast (iodine 300 mg I/ml) demonstrates a 1.5 cm diameter enhancing lesion in the suprasellar cistern involving the pituitary stalk.

The supplementary T_1 weighted MRI scan with gadolinium DPTA enhancement shows this lesion to be based in the pituitary stalk with involvement of the floor of the hypothalmamus. There was preservation of the normal high signal in the posterior pituitary gland.

In a patient with known breast carcinoma this would represent a pituitary stalk metastasis. For radiological differential diagnoses see table 1.[1]

Q2: What three simple biochemical tests would you perform, and what result would you expect and why?

The simple biochemical tests would be a serum urea and electrolytes, a corrected serum calcium, and osmolality of the serum and urine. The anticipated finding on the serum urea and electrolytes would be a raised sodium, because of the dehydration of the polyuria. You may have expected the serum calcium to be raised from the history of breast cancer due to either skeletal metastases or secondary to chemotherapy. The raised calcium could contribute to a potential nephrogenic diabetes insipidus.

On the osmolality testing you would have suspected a normal to high serum osmolality and a low urine osmolality.[2]

A serum fasting blood glucose would be another reasonable biochemical investigation. For biochemical results in our patient see table 2.

Q3: What special biochemical test would you perform, and what result would you expect and why?

To confirm the clinical diagnosis of cranial diabetes insipidus you should perform a water deprivation test, demonstrating that the urine does not become more concentrated as serum becomes more concentrated. When desmopressin 20 μg is given intranasally you would expect the urine osmolality to increase at least approximately 1.5 times, confirming a cranial cause for the diabetes insipidus. If it does not increase after desmopresssin one's suspicion of a nephrogenic cause is strengthened considerably. For causes of diabetes inspidius see table 3.[1 3 4]

This was not performed in our patient as the imaging demonstrated a lesion in an appropriate site for a cause of cranial diabetes insipidus.

Q4: How does the anatomical location succinctly explain the symptoms?

The pituitary stalk lesion extends from the hypothalamus and floor of the third ventricle. The stalk lesion will cause pressure effects on axons coursing from the supraoptic nucleus and paraventricular nucleus of the hypothalamus to the posterior pituitary. This will interfere in the axonal flow of antidiuretic hormone and its carrier protein to the posterior pituitary, hence explaining in part the diabetes insipidus despite a normal appearing posterior pituitary gland on MRI. As the lesion extends up into the hypothalamus, it will involve the suproptic nucleus directly.

Adjacent in the hypothalamic region are the satiety centre in the ventromedial nucleus and regulation of hunger from the dorsomedial nucleus. The blood supply to the pituitary stalk and pituitary is different from the rest of the brain, it has a portal circulation from the hypothalamus (particularly the arcuate nucleus) that is essential for the neuroendocrine regulation of the anterior pituitary, with a systemic arterial supply the inferior, middle, and superior hypophyseal arteries from the cavernous and supraclinoid portions of the internal carotid artery. Thus metastases are more common here, particularly the pituitary stalk and posterior pituitary.[5] Because of the neuroendocrine function of the pituitary and its stalk, there is an absence of the blood-brain barrier, hence explaining why metastases can present here earlier than the remainder of the brain.[3 5]

Final diagnosis

Cranial diabetes insipidus.

Acknowledgements

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Table 1 Radiological differential of a suprasellar mass

- Meningoma
- Craniopharyngioma
- Chiasmal and optic nerve glioma
- Hypothalamic glioma
- Hamartoma of tuber cinereum
- Infundibular tumour/pituitary stalk metastasis and primary
- Germinoma
- Suprasellar internal carotid aneurysm

Table 2 Biochemical results in patient studied

Substance measured	Result
Urea and electrolytes	
Sodium	140 mmol/l
Potassium	4.1 mmol/l
Urea	2.5 mmol/l
Creatinine	77 mmol/l
Calcium	
Corrected	2.76 mmol/l
Osmolality	
Serum	292 mosmol/l
Urine	139 mosmol/l
Urine	
Sodium	15 mmol/l
Potassium	16 mmol/l
Urea	87 mmol/l
Creatinine	1.7 mmol/l
Random blood glucose	6.1 mmol/l

Table 3 Causes of cranial diabetes insipidus

- Head injury
- Surgery
- Infiltrative disorders:
  - Langerhan's cell histocytosis
  - Sarcoid
  - Wegener's granulomatosis
- Primary and secondary pituitary neoplasia
- Postpartum pituitary necrosis
- Pituitary apoplexy
- Amyloid
- Tuberculosis

References

1 **Chaudhuri R**, Twelves C, Cox TCS, *et al*. MRI in diabetes insipidus due to metastatic breast carcinoma. *Clin Radiol* 1992;**46**:184–8.
2 **Imura H**. Lymphocytic infundibuloneurohypophysitis as a cause of central diabetes insipidus. *N Engl J Med* 1993;**329**:683–9.
3 **Nelson PB**, Robinson AG, Martinez AJ. Metastatic tumor of the pituitary gland. *Neurosurgery* 1987;**21**:941–4.
4 **Gorczyca W**, Hardy J. Arterial supply of the human anterior pituitary gland. *Neurosurgery* 1987;**20**:369–78.
5 **Koshimoto Y**, Maeda M, Naiki H, *et al*. MR of pituitary metastasis in a patient with diabetes insipidus. *AJNR* 1995;**16**:971–4.

A rare cause of empyema in a non-immunocompromised case and successful combined treatment

Q1: What abnormality was seen on the thoracic computed tomogram?

Thoracic computed tomography demonstrated an irregular and thick walled cavity, 3 cm in diameter and a left pleural loculated collection including draining catheter on the right hand side image.

Q2: What was the diagnostic procedure?

The diagnostic procedure was thoracentesis. This yielded a highly viscous, purulent fluid, with 28 000 neutrophils $\times 10^6$/l and hyphae on the smear. The culture was positive for *Aspergillus fumigatus*. The precipitating antibodies in the serum and the weal flare cutaneous reaction for aspergillus was positive. Based on these findings a diagnosis of aspergillus empyema was established.

Q3: What additional tests were/should be performed?

All other microbiological cultures and serological tests including mycobacteria were negative. Tuberculin test was positive (16 mm). Blood cultures were negative, sputum culture yielded a normal throat flora, and there was no evidence of an immunocompromised state. The bronchoscopic examination was normal. Abdominal ultrasonography was unremarkable.

Q4: What is the treatment?

The patient was started on intravenous liposomal amphotericin B (amph-B) (Fungizone, Bristol-Myers Squibb) therapy (50 mg/day) immediately after the microscopic examination of the pleural fluid. The

pleural cavity was drained and irrigated with normal saline and povidone iodine solution through an intercostal drain every other day. A dose of 25 mg liposomal amph-B was also administered into the pleural cavity on the 10th day of intravenous therapy.

Outcome

The patient improved considerably after three weeks of intravenous amph-B therapy. The intercostal drain was removed on the 20th day and treatment was changed to itraconazole 400 mg/day orally during the next nine weeks. A satisfactory improvement in both clinical symptoms and radiological findings were achieved. Six months after, control computed tomography was normal except for minimal residual pleural thickness. The patient remained well over the next year.

DISCUSSION

Aspergillus empyema is a rare clinical entity that predominantly affects patients with previous tuberculous infection, who have had thoracic surgery, or are taking cytotoxic therapy.[1] Pleural invasion by *Aspergillus* species occurs most commonly as a late complication of thoracoplasty for tuberculosis, often in association with a bronchopleural fistula or as a complication of surgical resection.[2 3] An increase in the number of critically ill or immunocompromised patients made aspergillus empyema a common manifestation of invasive pulmonary aspergillosis.[4] Rarely the rupture of cavitary aspergillosis into the pleural space can produce aspergillus empyema.[5] Interestingly, our patient had no history of pulmonary disease, operation, or evidence of an immunocompromised state, including HIV seropositivity, diabetes mellitus, and T or B cell abnormalities that were excluded by positive skin tests and normal immunoglobulin levels. Although he had an odontogenic infection, no pathogenic micro-organism could be grown on culture. Existence of a thick walled cavity on computed tomography suggested that empyema was a consequence of rupture of the aspergilloma cavity into the pleural space.

The treatment of aspergillus empyema differs among centres. Early administration of antifungal agents and pleural drainage are thought to be helpful in improving the outcome of patients.[6] Highly viscous or purulent fluids require drainage via a chest tube.[7]

Amphotericin is the main drug for the treatment of most fungal infections. In 1959, it was first used systemically to treat a case of aspergillus empyema developing in a patient previously treated by pneumothorax for pulmonary tuberculosis.[8] The major limitation of amph-B is its toxicity (nephrotoxicity, phlebitis, hypokalaemia, hypomagnesaemia, and anaemia) seen in nearly 80% of patients.[9] Liposomal amph-B offers the potential of a less toxic intravenous alternative to amph-B. Local administration of this drug is also mentioned in the literature when the infection appears to be local like a mycetoma rather than an invasive disease.[3]

Itraconazole is an orally active triazole compound against *Aspergillus* species. Variable absorption and interpatient variation of serum levels are the main problems. The role for itraconazole in prophylaxis, primary treatment, and salvage therapy of invasive aspergillosis needs further controlled studies but seems promising.[1] Preliminary uncontrolled studies showed itraconazole to be effective in the treatment of disseminated fungal infections in immunocompromised hosts.[10 11] Itraconazole may also be used as maintenance therapy for susceptible strains of aspergillus after the initial treatment and clinical response to amph-B.[11] Concomitant use with amph-B has a potential for antagonism and adverse drug interactions.[12]

A successful management with remarkable clinical and radiological improvement was achieved by pleural drainage and irrigation, intrapleural and intravenous amph-B followed by oral itraconazole therapy. Therefore, we recommend combined treatment using mechanical drainage and systemic and topical administration of antifungal agents.

Final diagnosis

Aspergillus empyema.

References

1 **Denning DW**, Stevens DA. Antifungal and surgical treatment of invasive aspergillosis: review of 2121 published cases. *Rev Infect Dis* 1990;**12**:1147–201.
2 **Hillerdal G**. Pulmonary aspergillus infection invading the pleura. *Thorax* 1981;**36**:745–51.
3 **Parry MF**, Coughlin FR, Zambetti X. Aspergillus empyema. *Chest* 1982;**81**:768–70.
4 **Conant MA**. Fungal infections in immunocompromised individuals. *Cutan Mycol* 1996;**14**:155–92.
5 **Irani FA**, Dolovich J, Newhouse MT. Bronchopulmonary and pleural aspergillosis. *Am Rev Respir Dis* 1971;**103**:552–6.
6 **Ko SC**, Chen KY, Hsueh PR, *et al*. Fungal empyema thoracis, an emerging clinical entity. *Chest* 2000;**117**:1672–8.
7 **Orringer MB**. Thoracic empyema: back to basics. *Chest* 1988;**93**:901–2.
8 **Kelmenson VA**. Treatment of pulmonary aspergillosis. *Dis Chest* 1959;**36**:442–3.
9 **Gallis H**, Drew R, Pickard W. Amphotericin B: 30 years of clinical experience. *Rev Infect Dis* 1990;**12**:308–28.
10 **Viviani MA**, Tortorano AM, Pagano A, *et al*. European experience with itraconazole in systemic mycoses. *J Am Acad Dermatol* 1990;**23**:587–93.
11 **Nucci M**, Pulcheri W, Bacha PC, *et al*. Amphotericin B followed by itraconazole in the treatment of disseminated fungal infections in neutropenic patients. *Mycoses* 1994;**37**:433–7.
12 **Polak A**. Combination therapy for systemic mycosis. *Infection* 1989;**4**:203–9.