SHORT REPORT

Symptomatic Rathke’s cleft cyst with hypophysitis

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Abstract
We report a case of symptomatic Rathke’s cleft cyst (RCC) with associated chronic hypophysitis. Symptomatic RCCs are rare and an associated inflammatory reaction is even rarer. The clinical and pathological findings are discussed in the light of previous published reports, together with the problems involved in making a preoperative diagnosis in such cases.

Key words: CT, inflammation, MRI, Rathke’s cleft cyst.

Introduction
Rathke’s cleft cysts (RCCs) are benign intrasellar cysts containing mucoid material and lined by epithelium which is generally of cuboidal or columnar type, but may also be pseudostratified or squamous. The most widely accepted theory is that they originate from remnants of Rathke’s pouch,¹⁻⁵ an embryonic diverticulum which arises from the roof of the stomodeum (primitive mouth cavity) at around 24 days embryonic age and extends dorsally to eventually come into contact with the infundibulum, a vertical downgrowth of the diencephalon.

Asymptomatic RCCs are relatively common and have been found in up to 23% of unselected autopsies.⁴ It is, however, rare for them to become large enough to cause symptoms by compression of intrasellar or suprasellar structures. Even with modern neuroimaging technology, a recent review only found 147 symptomatic cases of RCCs recorded in the literature.⁵ We report here a case of a symptomatic RCC with the further unusual pathological feature of an associated chronic hypophysitis.

Case report
A 19-year-old woman was admitted to the Midland Centre for Neurology and Neurosurgery on 3 July 1989 with severe bifrontal headaches of 9 months duration. Episodes of pain typically lasted a few days and were associated with nausea, vomiting and general malaise. There were no other symptoms other than that she had missed two consecutive menstrual periods prior to admission. She had been taking an oral contraceptive pill for dysmenorrhoea since the age of 17. There was no other significant past medical or surgical history.

Physical examination was unremarkable, including full visual fields by confrontation. All routine biochemical and haematological tests were within normal limits except for a serum prolactin of 1200 mU/l (normal range 80–460 mU/l in premenopausal females) and an
When reviewed in November 1989 the patient reported worsening headaches, normal periods in August and September, but a missed period in October. She was referred to the Queen Elizabeth Hospital, Birmingham for an endocrinological opinion. Repeat CT at this time revealed no change in the size or other features of the pituitary mass lesion. In January 1990 whilst undergoing further pituitary function tests, the patient continued to have intermittent headaches and amenorrhoea, but now also admitted to having galactorrhoea. Thyroid function remained within normal limits, but the low oestradiol persisted and a flat growth hormone response was demonstrated. No abnormality of visual fields was detected by perimetry. The symptoms and results were felt to be consistent with a non-functioning pituitary adenoma.

In March 1990 the patient underwent a transethmoidal hypophysectomy. Perioper-

oestradiol of 74 pmol/l (normal range [follicular] 160–1310 pmol/l). The short synacthen test (baseline serum cortisol 180 nmol/l, 30 min serum cortisol 490 nmol/l) and thyroid function tests [thyroid stimulating hormone 0.2 mU/l (normal female 0–7.5 mU/l), free thyroxine 9.1 pmol/l (normal 9–23 pmol/l)] showed borderline abnormalities.

Plain radiographs of the skull revealed a minimally abnormal sella turcica and perimetry was normal. Computed tomography (CT) with contrast showed a rim enhancing isodense mass within the pituitary fossa. (Fig. 1). A right carotid angiogram failed to demonstrate an aneurysm or tumour blush. Magnetic resonance imaging (MRI) revealed the lesion to be 1.8 by 1.4 cm and in contact with the optic chiasm. However, the latter was not compressed or displaced. These features were regarded as being a physiological variant and a diagnosis of common migraine was made. The high prolactin level was attributed to the oral contraceptive pill which was stopped.

Fig. 1. CT scan with contrast at the time of initial investigation, interpreted as a physiological variant (see text).

Fig. 2. Low power photomicrograph of tissue taken from pituitary fossa showing a central cavity lined by compressed, atrophic pituitary tissue containing many small inflammatory cells and bounded by a fibrous capsule. Haematoxylin and eosin, scale bar = 200 μm.
compressed and atrophic anterior pituitary tissue, one of which contained a central cavity (Fig. 2), with considerable fibrosis in some areas, and infiltrated by a diffuse mixed chronic inflammatory cell population, including many plasma cells, moderate numbers of lymphocytes and scattered polymorphs (Figs 3 and 4). There was no evidence of germinal centre formation. Some fragments of tissue were lined by epithelium composed mostly of cuboidal, ciliated cells resembling respiratory epithelial cells (Fig. 4) with squamous differentiation in one area (Fig. 4). However, in many regions the epithelium was denuded, with a thin layer of fibrin on the surface. Stains and cultures for bacterial and fungal organisms were negative. The appearances were interpreted as an intrasellar RCC with an associated chronic hypophysitis.

One month postoperatively the patient felt well with resolution of her headaches. There was a transient diabetes insipidus, probably due to minor damage to the pituitary stalk. Replacement therapy at three months was hydrocortisone 20 mg daily, thyroxine 100 μg daily and marvelon oral contraceptive cyclically for persisting amenorrhoea. CT at 6 months after operation showed residual tissue in the pituitary fossa which was felt to represent the muscle graft inserted, and a further scan 1 year postoperatively was of a similar appearance.

Discussion

The histological findings of fragments of atrophic and fibrotic anterior pituitary tissue lined by ciliated, cuboidal epithelium, with some evidence of squamous metaplasia, were interpreted as a RCC and are similar to previous descriptions in the literature. In addition, our case showed a heavy, mixed chronic inflammatory cell infiltrate in the cyst wall. Inflammatory lesions of the pituitary gland are rare, but various forms have been reported. A predominantly lymphocytic hypophysitis can occur either during or immediately after pregnancy, or in association with
autoimmune disorder, such as Hashimoto’s disease,8 pernicious anaemia,8 and lymphoid thyroiditis.10 Other inflammatory lesions are characterised by a chronic granulomatous process containing multinucleated giant cells: such a picture can occur in cases of syphilis, tuberculosis and sarcoidosis.11

In the case presented no organisms were demonstrated in the inflamed tissue, and there were no histological or clinical features to suggest an autoimmune type of hypophysitis. The inflammation was therefore interpreted as a reactive process in response to the cyst contents. Previous series disagree as to whether such reactive inflammation associated with a RCC is unusual or common. Many reports do not specifically mention inflammation. However, it is clear that in a few unusual cases, rupture with the release of cyst contents may stimulate an aseptic meningitis. There have also been rare cases reported of abscess formation in a RCC, due to infection by pyogenic bacteria.12

The hypopituitarism associated with these cases may be due to a mass effect or tissue destruction by the inflammatory process. It has been suggested that, when the primary lesion producing adenohypophyseal insufficiency is in the adenohypophysis itself, no symptoms are detectable unless approximately 70% of the gland is ablated.13

Symptomatic RCCs usually present with pituitary hypofunction (with or without raised prolactin), visual disturbances (temporal field defects) and headaches (often bifrontal). In this respect the present case was fairly typical. Raised prolactin levels are due to loss of inhibitory control by the hypothalamus, and generally levels associated with RCC do not reach as high as those associated with prolactin-secreting adenomas.14 More rarely there may be diabetes insipidus or obstructive hydrocephalus, and one or two case reports document isolated episodes of sudden haemorrhage into a cyst, producing pituitary apoplexy15 or cyst rupture, with the contents giving rise to an aseptic meningitis.

The common presentation of RCC is thus closely similar to that of other slowly enlarging, non-endocrinologically-active mass lesions in and around the sellar turcica. Radiology may help by demonstrating the cystic nature of the lesion. CT generally shows a hypodense, non-calcified, non-enhancing cystic mass within the sella. However, some may be isodense or hyperdense enhancing and, rarely, show calcification. They can thus appear similar to many other cystic sellar lesions including cystic pituitary adenoma, cystic craniopharyngioma, arachnoid cyst, epidermoid cyst, intrasellar aneurysm and mucocele.5 In our case, the isodense CT appearance was thought to make a cystic lesion unlikely; although isodense RCCs have been reported,16 they are rare. It may be that the partially fibrous nature and/or viscous contents of the cyst contributed to the non-cystic CT appearance.

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References
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