Early Recurrence of an Intracranial Epidermoid Cyst Due to Low-Grade Infection: Case Report

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ABSTRACT

Intracranial epidermoid cysts are slow-growing lesions, which may recur after incomplete resection, but do so over many years. The authors present the case of an epidermoid that repeatedly recurred over a short period, which was discovered to be secondary to a low-grade bacterial infection. A 30-year-old woman presented with signs and symptoms related to brainstem and cranial nerve compromise from a large cerebellopontine angle epidermoid cyst. She underwent a subtotal excision of a macroscopically and histologically typical epidermoid. The lesion recurred within 1 year of surgery, but with atypical radiological appearances. No systemic or local evidence of infection was found during a second resection. A further large recurrence with the same atypical features occurred after another 6 months, necessitating a third surgical resection. On this occasion, the atypical cyst contents grew coagulase-negative *Staphylococcus* after prolonged culture in an enrichment medium. Following a course of appropriate antibiotics, the residual cyst contents completely resolved. This case highlights an unusual complication of an epidermoid cyst. Early recurrence of an epidermoid, even in the absence of overt evidence of infection, should produce a high index of suspicion that there may be a low-grade infective cause. Surgical excision coupled with antibiotics resulted in a symptomatic and radiological recovery.

KEYWORDS: Epidermoid cyst, infection, recurrence

Epidermoid cysts occurring at various positions within the cranial cavity are benign, very slow-

growing tumors.¹⁻³ They respond well to surgical excision, although it is recognized that complete

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excision of the tumor capsule is often not possible due to the high risk of damaging adherent neural or vascular structures.^{2,4,5} As a consequence, there are a number of these lesions that recur, usually many years after the original surgery.³ This case describes a remarkably early symptomatic recurrence of an epidermoid cyst, along with imaging characteristics that were very atypical for an epidermoid. This led to the diagnosis of a low-grade bacterial infection within the residual cyst, a condition that has not been previously reported. We present the patient's subsequent management and clinical course, as well as discuss various aspects of epidermoid cysts pertinent to this case.

CASE REPORT

A 30-year-old woman initially presented to her general practitioner with slurring of speech, a feeling of excessive salivation, and disturbed balance for a preceding period of 6 months. She was seen some months later by a neurologist, and during this interim period she had become pregnant. The neurologist also documented the presence of a headache, but examination at this stage was entirely normal. Due to the pregnancy and the lack of physical signs, imaging was delayed until she was postpartum. Over the course of the next 6 months she developed some worsening of her balance, and by the time she was admitted to neurosurgical care, she had nystagmus, mild right limb ataxia, a diminished right corneal reflex, and an impaired gag reflex.

A magnetic resonance (MR) scan demonstrated an extremely large extra-axial mass anterior and to the right of the brain stem, causing marked distortion of the brain stem and effacement of the fourth ventricle. The lesion extended through the tentorial hiatus with compression of the posterior part of the third ventricle. The signal characteristics were consistent with an epidermoid cyst. No contrast was given for this initial scan (Fig. 1).

The patient underwent excision of the lesion shortly thereafter via a combined middle fossa

Figure 1 T1-weighted axial nonenhanced MR scan of the epidermoid cyst at presentation. It shows the slightly heterogeneous hypointense cyst exerting dramatic mass effect on the brain stem.

and posterior fossa approach with splitting of the tentorium. It was confirmed to be an epidermoid cyst by virtue of the pearly-white desquamated keratin flakes that were present within it and histological examination of the capsule that showed stratified squamous epithelium. A subtotal removal of the cyst contents was achieved because the middle fossa component was difficult to access. Similarly, some of the capsule was excised, but capsule that was densely adherent to the brain stem was left in place. Postoperatively the patient had a new right-sided third nerve palsy despite anatomical continuity of the nerve. She otherwise made an unremarkable recovery with no wound leaks or infections and no clinical evidence of meningism in her early postoperative course.

Three weeks after her discharge, the patient was reviewed due to headaches and a pseudomeningocele underlying her wound. The wound did not appear inflamed, but a wound swab sent at this time grew coagulase-negative *Staphylococcus*. The meningocele and headaches subsided shortly afterwards.

Two months later the patient was readmitted with a recurrence of headaches, intermittent vomiting, and neck stiffness. An MR scan showed a small

Figure 2 T1-weighted axial MR scans with gadolinium enhancement of the enlarging recurrent epidermoid cyst. The cyst is seen to extend superiorly with a large component in the middle fossa (right). There is widespread enhancement of the walls of the lesion, and the cyst contents are more hyperintense relative to cerebrospinal fluid than they had originally been.

residuum of cyst, particularly in her middle fossa. The patient was apyrexial throughout her admission, and serum inflammatory markers (C-reactive protein and peripheral white cell count) were entirely normal. For this reason, an infective cause was excluded, and a presumptive diagnosis of chemical meningitis was made. She was commenced on a short course of steroids to which she responded well, and she was discharged asymptomatic.

A year later she returned with worsening visual acuity, increasing balance difficulties, and a mild left-sided weakness. Further MR imaging confirmed progressive enlargement of the residual cyst, causing renewed brainstem compression as well as anterior extension to the suprasellar region and presumed compromise of the optic apparatus. The scan also showed a change in signal characteristics of the cyst contents and prominent enhancement around the margins of the lesion with enhancement also seen internally (Fig. 2). She underwent a repeat excision, but on this occasion the cyst was approached through an orbitofrontal craniotomy with a sylvian fissure split due to its

predominantly middle fossa location. On breaching the capsule, the main component of the cyst was found to be thin straw-colored fluid with some admixed solid keratinous components. A catheter with an Ommaya reservoir was left within the cyst cavity.

The patient's preoperative visual deterioration and limb weakness recovered promptly after surgery, but her complete third nerve palsy dating from the original surgery was unaltered. Microscopy and culture of the cyst fluid demonstrated a white cell count of $13/\text{mm}^3$ with no bacterial growth. As a result, it was concluded that this was an aseptic inflammatory response, and no antibiotics were prescribed.

After a 6-month period in which she was minimally symptomatic, she re-presented with progressive headaches and vomiting. These complaints were temporarily relieved by aspiration of her cyst contents via the Ommaya reservoir. Once again, this produced yellowy-brown, slightly turbid fluid. A repeat MR scan showed a slight reduction in the cyst size, but there remained prominent

Figure 3 T2-weighted axial MR scan of the recurrent cyst demonstrating marked edema of adjacent temporal lobe white matter which extends up into the capsular region.

enhancement around the margins of the lesion. A further development was striking reactive edema extending superiorly into the capsular areas (Fig. 3). The scan appearances were becoming ever more suggestive of an infection, despite the persistent lack of raised inflammatory markers and negative culture of the aspirated cyst fluid.

She returned to theater several days later for an extended middle fossa approach including a mastoidectomy and presigmoid approach to the posterior fossa. Aspiration of turbid yellow fluid and squamous material was again performed, and specimens were sent for microbiological examination. On this occasion, initial cultures were negative, but coagulase-negative *Staphylococcus* was obtained on prolonged enrichment culture of both the fluid and solid components. The relevance of this culture result was questioned, but in the clinical setting of rapid recurrence, we felt it was significant. She was therefore commenced on meropenem, rifampicin, and linezolid. In total she was given 2 weeks of intravenous meropenem and oral rifampicin, and 10 days of linezolid. Unfortunately her treatment was complicated by the development of

Figure 4 T1-weighted axial MR scans with gadolinium enhancement of the cyst after the third operation and completion of the course of antibiotics. This shows a marked reduction of the size of the cyst, but with continued enhancement of the margins of the lesion.

Figure 5 T1-weighted axial MR scans with gadolinium enhancement a further 5 months after the scan in Fig. 4. The lesion has almost completely resolved, with only minimal residual enhancement in the cerebellopontine angle.

profound neutropenia secondary to the antibiotics. The regime was subsequently changed to teicoplanin, and rifampicin was reintroduced when her neutropenia had recovered. She remained on intravenous teicoplanin for a further 3 weeks and was discharged thereafter. She had no change in her neurological condition following this third operation.

An MR scan 2 months postoperatively showed much-improved appearances. The cyst was significantly reduced in size, although a small element remained in the cerebellopontine (CP) angle, and its border continued to enhance (Fig. 4). A further scan after another interval of 5 months revealed the most dramatic changes: the residual cyst had decreased in size and the peripheral enhancement had almost completely resolved (Fig. 5). Clinically the patient is currently asymptomatic, although her third nerve palsy has remained.

DISCUSSION

This case is unusual from the simple perspective of it being the first described occurrence of a confirmed postoperative low-grade infection in an epidermoid cyst. There are, however, several salient aspects to this case that are worth highlighting.

The natural history of epidermoid cysts is well described. They are benign tumors of embryonal origin, usually occur in isolation, and constitute ~1% of all intracranial tumors.^{3,6} Depending on their location, they can have a long duration of symptoms prior to presentation, and this is particularly true of CP angle cysts.^{2,3,6-8} The implication of this particularly indolent pattern of growth is that symptomatic recurrence of a cyst is usually described many years or even decades after the original surgery.^{1,3,5,9} The extent of initial surgery is obviously an important determinant of how soon they recur, but even with subtotal excision, a mean interval of 8 years has been reported between original surgery and second operation.¹ There have been varying opinions expressed as to the

ideal strategy for surgical management: the most popular view is to resect as much of the capsule as possible, although it is recognized that it can be densely adherent to vital neural or vascular structures, and an aggressive approach needs to be tempered by the risk of severe deficits.¹⁻⁶ Although we recognize that a subtotal removal of the tumor was achieved in our patient's first operation, the rapid recurrence of symptoms was entirely unexpected. Such a rapid recurrence should be a warning sign of something more sinister than a simple reaccumulation of cyst contents.

We have emphasized the lack of clinical evidence of infection in this case. Although the patient did complain of meningitic symptoms at a relatively early stage in her course, it was easily ascribed to the well-documented phenomenon of aseptic chemical meningitis.^{1-3,6} It has been remarked that this is particularly prevalent in patients who have had an incomplete excision^{5,6} and has even been reported to occur spontaneously in unoperated cysts.¹⁰⁻¹² This assertion was further supported by her response to steroids on her first readmission. While we cannot disprove that this early symptom recurrence was due to chemical meningitis, it seems likely in the light of subsequent events that it was a low-grade bacterial meningitis. This should serve as a caution against indiscriminate labeling of meningism as a reaction to chemical irritation.

This case also presented us with difficulty in interpreting postoperative MR scan appearances. The appearances of unoperated epidermoid cysts are widely reported: they are usually lesions displaying a hypointense signal on T1-weighted sequences and a heterogeneous hyperintense signal on T2-weighted sequences. They may very occasionally vary from this rule, showing reversed signal intensities to the above, a so-called "white epidermoid."^{13,14} A better way of assessing their signal characteristics is a comparison with cerebrospinal fluid (CSF) signal intensity. The majority are isointense to slightly hyperintense to CSF on T1, and similarly isointense to hyperintense relative to CSF on T2.^{13,15,16} A variety of other sequences have

been described to better characterize these tumors and thereby eliminate diagnostic uncertainty.^{15,17} Of greater relevance to this case is whether they enhance following intravenous contrast injection. There are some conflicting reports in the literature as to this point: the predominant opinion is that they do not enhance, presumably due to minimal vascularity.^{3,13,14,18} However, there are two reports describing rim enhancement in a minority of cases.^{1,15} These papers do go on to explain that the enhancement was subtle and not completely circumferential. The one well-described situation in which an epidermoid cyst will enhance is following malignant degeneration to a squamous cell carcinoma.^{3,12,19,20} These malignant tumors demonstrate irregular contrast enhancement, in comparison to this lesion which showed uniform enhancement around its periphery. Although it has been surmised that some epidermoid cysts display chronic inflammation secondary to repeated cyst rupture,¹² this in itself does not seem to cause the cyst wall to enhance. As regards edema in the adjacent brain, most publications do not mention this as a feature, and the only reference reporting a parenchymal edematous reaction describes it as unusual and limited in extent.¹⁵

Our patient underwent two redo operations, both of which followed deterioration in symptoms secondary to mass effect of the lesion. Residual cyst was demonstrated early in her course, but we elected not to undertake further surgery because her symptoms at this time (presumed chemical meningitis) responded to a brief course of steroids. The timing of repeat surgery with epidermoids is debated; the literature advocates either waiting for symptom recurrence or using unequivocal evidence of radiological progression.¹⁻³

There are reports of infection occurring in relation to an epidermoid cyst, but they are all different in character to this case. One small series describes a patient with an infratentorial epidermoid developing a fulminating infection within 3 months of surgery.²¹ There are several reported cases of epidermoid cysts occurring within the bones of the skull and presenting primarily with an in-

fection.^{22,23} There is understandably a propensity to develop infections in either intracranial epidermoid or dermoid cysts if they occur in association with a dermal sinus.²⁴ However, the development of a low-grade infection in a tumor without a bony or dermal component is not described. The organism responsible for the infection was coagulase-negative *Staphylococcus*, a skin commensal that typically results in low-grade infections. The protracted but rather benign course that resulted from this infection would not be expected with a more virulent organism. The converse to this is the resultant difficulty in diagnosis: culture of an indolent bacterium can present a considerable challenge, and it was only on the second occasion that culture of the cyst contents yielded the causative organism. Coagulase-negative *Staphylococcus* is not uncommonly identified as a contaminant in microbiological samples, given its status as a ubiquitous skin commensal. However, any initial doubt as to the significance of the culture was dispelled following the dramatic radiological response to appropriate antibiotics.

CONCLUSIONS

Intracranial epidermoid cysts are rare, slow-growing tumors, which even with subtotal resection have a very good prognosis in terms of gradual tumor regrowth. This report describes a unique case where rapid recurrence occurred secondary to a low-grade infection within the residual cyst cavity. Repeated surgical removal together with appropriate antibiotics produced an excellent clinical and radiological improvement. We would propose that in a rapidly recurring and contrast-enhancing epidermoid it should be assumed that there is a low-grade infective cause, even if there is a lack of confirmatory evidence.

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