The Journal of Laryngology & Otology
June 2000, Vol. **114,** pp. 462–464

Rhinorrhoea feigning cerebrospinal fluid leak: nine illustrative cases

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Abstract

Before contemplating surgery for cerebrospinal fluid (CSF) rhinorrhoea it is vital that the correct diagnosis is established. This can be done using immunofixation of beta-2-transferrin, that is nearly always positive in cases of CSF rhinorrhoea. Fluorescein lumbar puncture is useful in establishing the exact site of a leak and also in confirming the absence of a leak where the clinical suspicion is high but the beta-2-transferrin is negative. High resolution computed tomography (CT) scanning is a useful radiological investigation for identifying a bony defect. We present nine patients who presented with clear rhinorrhoea that was clinically highly suggestive of a CSF leak. Three of these patients had undergone previous craniotomies for presumed CSF rhinorrhoea. The diagnosis of CSF rhinorrhoea was excluded in all patients using beta-2-transferrin with or without fluorescein lumbar puncture. The authors believe that measurement of beta-2-transferrin should be mandatory before surgery for CSF rhinorrhoea.

Key words: Cerebrospinal fluid; Nose; Endoscopy

Introduction

The surgical treatment of cerebrospinal fluid (CSF) rhinorrhoea has traditionally been undertaken by both neurosurgeons and otorhinolaryngologists. Over the last 30 years the extracranial approach has increasingly found favour over the intracranial approach. The extracranial option is associated with less morbidity and has become the preferred approach.[1] The advent of endoscopic sinus surgery has led to further advances in this field and recently this has been advocated as the approach of choice where access allows.[2–8]

The diagnosis of unilateral clear rhinorrhoea lies between a CSF leak and unilateral vasomotor rhinitis. It is important to establish the correct diagnosis before surgery, in order to avoid unnecessary surgery, particularly if intracranial surgery is contemplated.

If the diagnosis is uncertain two tests are of use in distinguishing CSF leaks from clear nasal mucus. Immunofixation of beta-2-transferrin is nearly always positive in patients with CSF rhinorrhoea.[9] Fluorescein injected intrathecally is a valuable test for determining the site of the leak and also to confirm the absence of a leak when the beta-2-transferrin is negative.

Radiological assessment in the form of high resolution CT and magnetic resonance imaging may be of use in identifying a bony defect or the nature of a soft tissue lesion but is not diagnostic in isolation.

We present nine cases referred to our unit with a presumptive diagnosis of CSF rhinorrhoea. Three of these patients had had unsuccessful attempts at intracranial repair. The diagnosis of CSF rhinorrhoea was excluded in all these patients and their rhinitis was successfully managed medically.

Case reports

Case 1

A 65-year-old lady was seen by a neurosurgeon and underwent two craniotomies for a suspected CSF leak. The site was not defined and there was no clear history of unilateral rhinorrhoea. Ten years later she presented with left-sided unilateral rhinorrhoea and underwent a left-sided extracranial approach, again no defect was found. Five years later she again presented with unilateral clear rhinorrhoea and underwent a further craniotomy. At surgery there was thought to be a right-sided defect. Post-operatively her rhinorrhoea persisted.

On referral to our unit the fluid was tested on three separate occasions for beta-2-transferrin and was found to be negative. Attempts at medical treatment of her presumed rhinitis with ipratropium bromide spray were partially successful but she still had unilateral rhinorrhoea. She underwent fluorescein lumbar puncture and endoscopic examination of her anterior skull base under anaesthetic. Even when the CSF pressure was raised no leak was identified. Post-operatively her rhinorrhoea stopped and she has had no recurrence for the last 17 months.

Case 2

A 22-year-old lady underwent a transphenoidal hypophysectomy for acromegaly. One week post-operatively she reported clear rhinorrhoea from the left nostril. Surgery was contemplated but the decision was made to refer to this unit. The fluid was tested twice for beta-2-transferrin and on both occasions this was negative. Endoscopic examination of her nasal cavity revealed diffuse clear

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Accepted for publication: 27 January 2000.

mucus production and a diagnosis of unilateral vasomotor rhinitis was made. The patient's symptoms subsided over the following months.

Case 3

A 47-year-old man suffered an anterior skull base fracture with a consequent CSF leak. This was repaired successfully using a craniotomy. Sixteen years later he presented to a neurosurgeon with headaches and left-sided episodic unilateral rhinorrhoea. He underwent attempted repair via a craniotomy but the rhinorrhoea persisted. Post-operatively the fluid was tested for beta-2-transferrin and this was found to be negative. A fluorescein lumbar puncture was performed pre-operatively and endoscopic examination of the nasal cavity intra-operatively revealed no leak. The only finding on endoscopy of the nasal cavity was pooling of mucus in his ethmoid air cells. Following intra-operative opening of his ethmoidal sinuses his episodic rhinorrhoea stopped.

Case 4

A 51-year-old lady presented with headaches and bilateral rhinorrhoea. She underwent craniotomy and fascia lata grafting of her anterior skull base but post-operatively the headaches and rhinorrhoea persisted. CT scanning showed a retention cyst in the sphenoid sinus. Beta-2-transferrin was negative. She underwent fluorescein lumbar puncture and endoscopic examination of the nasal cavity under general anaesthesia with sphenoidotomy. No leak was identified at the time of surgery. Her symptoms remain unchanged.

Case 5

A 60-year-old man underwent transphenoidal hypophysectomy for acromegaly. Eighteen months later he presented with clear unilateral rhinorrhoea and was referred to our unit for management of his presumed CSF leak. Beta-2-transferrin was negative. Out-patient examination with a rigid nasal endoscope revealed only clear mucus tracking out of the paranasal sinuses. Fluorescein lumbar puncture followed by endoscopic examination with sphenoidotomy showed no leak. He was successfully treated with a topical nasal steroid.

Case 6

An 84-year-old lady presented following a head injury with unilateral clear rhinorrhoea. She was referred with a strong clinical suspicion of a CSF leak. Out-patient endoscopy revealed a clear, moist nasal airway. Analysis of the fluid for beta-2-transferrin was negative. Fluorescein lumbar puncture performed without surgery showed no leak. Four months after the injury the rhinorrhoea had cleared.

Case 7

A 23-year-old lady was referred from an otorhinolaryngological colleague with unilateral left-sided rhinorrhoea. A presumptive diagnosis of CSF rhinorrhoea was made. Analysis of the fluid for beta-2-transferrin was negative. Out-patient endoscopy revealed unilateral excessive mucus production. CT and magnetic resonance image (MRI) scans were normal. The patient was treated with ipratropium bromide nasal spray which resulted in an improvement in her symptoms.

Case 8

A 44-year-old lady who was referred to a neurosurgeon having consulted an otolaryngologist with a 16-year history of bilateral clear profuse rhinorrhoea. A presumptive diagnosis of cerebrospinal fluid rhinorrhoea was made. Coronal CT scans of the anterior skull base showed no anterior cranial fossa defect but did show fluid in her sphenoid, ethmoid and frontal sinuses. On this basis arrangements were made for an intracranial exploration of the anterior skull base. Concerned as to the potential complications of intracranial surgery the patient sought a second opinion and was referred to the senior author. Out-patient examination of the nasal cavities with the nasal endoscope revealed a diffuse rhinitis. The skin prick test was positive for house dust mite antigen. Immunofixation of beta-2-transferrin was negative. A diagnosis of perennial allergic rhinitis was made and she was treated appropriately with topical nasal steroids, systemic antihistamines and advice with regard to allergen avoidance. These measures resulted in an improvement in her symptoms.

Case 9

A 50-year-old man was referred by a neurosurgeon who had undertaken a frontolateral approach to excise a large arachnoid cyst. Post-operatively he developed bilateral rhinorrhoea and it was thought that he had developed a CSF leak. The fluid was twice tested for beta-2-transferrin and was negative. Nasal endoscopy showed diffuse rhinitis. Skin prick tests were negative. A high definition CT scan of the anterior skull base showed no bony defect other than that from the craniotomy. His rhinorrhoea subsided over the course of the following three months.

Discussion

It is important that unnecessary intracranial procedures are avoided. Three of our series had had an incorrect diagnosis of CSF rhinorrhoea followed by a craniotomy and this is unacceptable in modern clinical practice.

Beta-2-transferrin is a protein produced by neuramidase activity in the brain. It is found only in cerebrospinal fluid, aqueous humour and perilymph and this fact makes it an invaluable test in the investigation of suspected CSF rhinorrhoea.[10,11] It is the first line investigation of choice when CSF rhinorrhoea is suspected.[9] It can be detected in a sample of fluid by immunofixation electrophoresis. Some authors have claimed 100 per cent sensitivity and specificity using this.[12] Others have noted the possibility of false positive results in patients with chronic liver disease, inborn errors of glycoprotein metabolism or genetic variants of transferrin.[13] It is for this reason that it has been proposed that venous blood be sampled at that same time as the fluid. This has not been the practice of other workers in the field[14] and is not the practice in this unit. It is a sensitive, specific, inexpensive test that requires only a small amount of fluid and we would suggest that it should be mandatory for each patient where surgery is contemplated.

The fluorescein lumbar puncture technique compliments the immunofixation of beta-2-transferrin in ensuring that there is no CSF leak. Two to three hours after fluorescein is injected into the intrathecal space it can be seen leaking from the nose as a brilliant yellow colour. The fluorescein is injected using a standard lumbar puncture technique and this technique is well documented.[15] After injection the patient is kept in a 10-degree head down position for three hours. The patient can then be observed for yellow fluid coming out of the nose. Nasal endoscopy thus allows very precise localization of the site of the leak at the time of surgery. When the endoscope is used a blue filter allows

https://doi.org/10.1258/0022215001905850 Published online by Cambridge University Press

very small concentrations of fluorescein to be easily detected (up to 1:10 000 000).[16] The experience in this unit has been that this is rarely necessary.

When repairing CSF leaks endoscopically the senior author has found on several occasions that fluid may not be seen leaking from a genuine fistula until the patient's CSF pressure is raised. It has, therefore, been his practice to ensure that before the diagnosis is ruled out the patient is made to cough against a closed glottis either by a simple request if the patient is awake or, if the patient is anaesthetized, by lightening their state until they strain on a cuffed endotracheal tube.

Radiology has a potentially useful role to play in the investigation of CSF rhinorrhoea, although it cannot alone confirm or refute the diagnosis. High resolution CT scanning of the anterior skull base can identify a bony defect and has been proposed as the only necessary imaging test necessary in identifying the site of a leak.[17] This has also been the experience in this unit. MRI may identify an associated soft tissue lesion e.g. tumour, meningocoele etc. It has been suggested in the past that the radiological investigation of choice for these patients is CT cisternography. This is however an invasive investigation requiring an intrathecal injection of radio-opaque contrast material. It has been the experience of this unit that a combination of CT scanning and an intrathecal injection of fluorescein has allowed accurate location of a leak where one exists and we feel that this supersedes the use of CT cisternography.

Four of our patients presented with spontaneous rhinorrhoea, three were post-surgery and two presented following head injury. Six patients presented with unilateral clear rhinorrhoea, three with bilateral clear rhinorrhoea. Three had had craniotomies for the attempted repair of their presumed CSF rhinorrhoea. These patients had not had Beta-2-transferrin measured prior to surgery and none had genuine CSF rhinorrhoea.

Our findings in these patients not only highlight the importance of a reliable diagnosis prior to surgery but would also suggest that unilateral vasomotor rhinitis is a distinct clinical entity which may follow surgery, or trauma, or may occur spontaneously. This may cause confusion when it may feign CSF rhinorrhoea. The majority of our cases settled spontaneously or responded to a topical ipratropium bromide spray or a topical nasal steroid.

Conclusion

We would suggest that in order to avoid unnecessary procedures designed to repair presumptive dural defects that it should be considered mandatory that beta-2-transferrin is measured as a first line investigation on any patient in whom a CSF leak is considered. No patient should undergo a surgical procedure without a positive result. When the result is negative but there remains strong clinical suspicion then we have found the use of fluorescein lumbar puncture, especially combined with the use of the nasal endoscope, a useful technique in excluding the presence of CSF rhinorrhoea.

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N. S. Jones takes responsibility for the integrity of the content of the paper.
Competing interests: None declared