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Role of Intrathecal Fluorescein in Identification of CSF Leak During Transsphenoidal Pitutary Surgery

Tarek Hassan Abd el-Bary [1], Essam Mohammed Elsayed Youssef [1], Ahmed Massoud Hassanien Mohamed [1], Hassan Ahmed Abaza [1]

[1]Neurosurgery Department, Faculty of Medicine, Zagazig University, Egypt

Corresponding author: Ahmed Massoud Hassanien Mohamed

Email: meseoozil@gmail.com , Mobile: +201012153589

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Abstract:

Effective management of cerebrospinal fluid (CSF) leaks can reduce significant associated morbidity. Intrathecal fluorescein (IF) may be a valuable intra-operative adjunct to localise leak sites.

Keywords:Intrathecal fluorescein, CSF, leak.

Introduction:

CSF rhinorrhea and meningitis are among the more common serious complications associated with transsphenoidal surgery. The incidence of CSF leak in the United States National Survey (USNS) ranged between 1.5% for the most experienced to 4.2% for the least experienced group **(1).**

One of the major measures of success in any endoscopic skull base procedure is rate of CSF leak. Failure to complete a watertight closure of dura and arachnoid can predispose to post-operative CSF leak with a subsequent increased risk of meningitis, pneumocephalus and other intracranial complications **(2).**

Careful identification of intra-operative defects is paramount in ensuring a satisfactory result by influencing decision making in surgical repair **(2).**

Grading of intraoperative CSF leak

Table (1): Cerebrospinal Fluid Leak Grading System and Repair Protocol

Grade of Leak	Description of Leak	Repair Method
0	No leak observed	No packing or absorbable hemostatic gauze
1	Small cerebrospinal fluid leak without a visible diaphragmatic defect	1) Intrasellar fat graft 2) Artificial dura over sellar dura
2	Moderate leak with diaphragmatic definite defect	1) Intrasellar fat graft 2) Artificial dura over sellar dura
3	Large diaphragmatic defect with or without a third ventricular cerebrospinal fluid leak	1) Fascial graft over sellar dura 2) Fat graft in sphenoid sinus 3) Pedicled nasoseptal flap covered on the surface of fat graft

CSF leakage repair techniques

After tumor removal, a careful examination for CSF leakage is undertaken. Surgeons generally close the sella in one of three ways. If there is no evidence of CSF leak, a small piece of Gelfoam is placed in the resection cavity for hemostasis and the floor of the sella is reconstructed with vomeric bone harvested during the approach. **(3)**

If CSF leakage is observed and the approach has been transsellar only, then we harvest abdominal fat and fill but do not overpack the sella. The floor of the sella is then reconstructed with vomeric bone**.** If the mucosa over the sphenoid has been preserved, this can be reapproximated over the floor of the sella. **(Fig. 1) (4)**

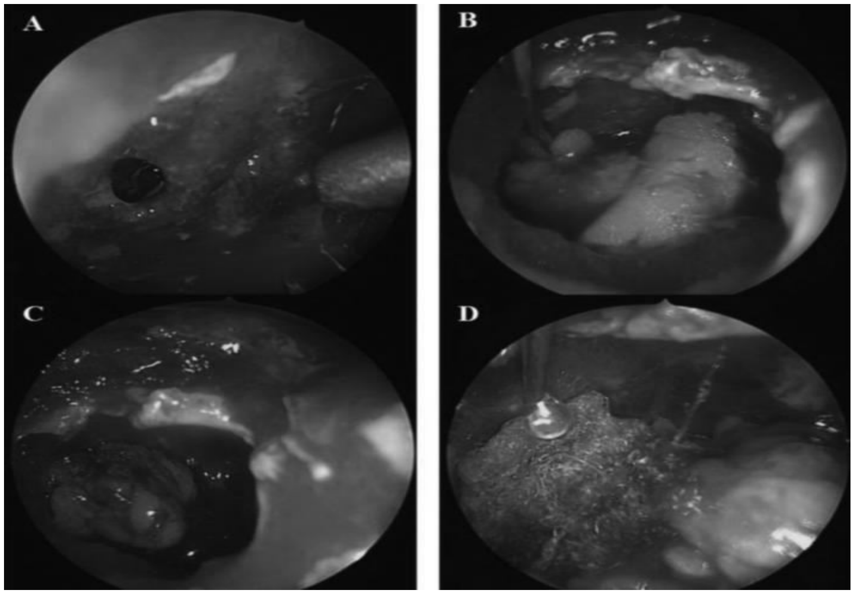

Figure (1): A) Identify the arachnoid defect laceration. B, C) Embed the dumbdell- shaped autologous fat in the defect. D) The fat graft was covered immediately with fibrin glue and surgical **(4).**

If there has been a large opening in the skull base, use either a "gasket seal" method or pack the sella with fat followed by a nasoseptal flap **(5).**

Briefly, a piece of fascia lata, larger than the defect, is first centered over the opening in the skull base. Then a piece of vomeric bone, the same size as the defect, is centered over the tissue graft and countersunk into the bony defect. This draws the tissue graft into the bony defect to form a gasket seal around the rigid graft. Recently surgeons have begun also placing an additional nasoseptal flap on top of the gasket seal. Finally, a thin layer of fibrin matrix or polymerized hydrogel (Duraseal) can be placed over the closure to obtain a watertight closure**.** The latter substance is preferred **(6).**

Thrombin-infused gelatin matrix (FloSeal) is used to fill the sphenoid sinus, to aid in hemostasis. Lumbar drainage is not routinely used during transsellar surgery because the risk of CSF leak is so small and patients often go home soon after surgery. A small piece of Telfa is placed in each nostril overnight to absorb any drainage and is removed in the morning **(7).**

Sodium Fluorescein

Many substances give off light when excited by heat energy or electromagnetic radiation. When a substance emits light during excitation of its atoms by light energy, i.e., the atoms absorb the energy of the light, and stops the release of light when the excitation ceases, the light emitted from the substance is called fluorescence. The fluorescein dye molecules during an angiogram absorb the incoming blue light energy, raising the electrons to a higher energy level. Immediately after the exciting light ceases, the electrons release the extra energy absorbed and drop back to their original energy level **(8).**

Fluorescein is an orange–red powder with the molecular formula C20H12O5 and a molecular weight of 332.31 Da. It is widely used in the scientific and medical industries as fluorescein isothiocyanate-1 (FITC), Alexa 488 fluorophore, and other variants **(9).**

Fluorescein sodium, or sodium fluorescein, is also known as uranine or resorcinolphthalein, is a dye made principally from two petroleum products called resorcinol and phthalic anhydride **(8).**

Petroleum is an oily substance, naturally occurring, composed mainly of a mixture of gaseous, liquid, and solid hydrocarbons. Resorcinol is a member of the phenol group of chemicals extracted from this mixture. The dye is manufactured by mixing seven parts of resorcinol with five parts of phthalic anhydride at 195 degrees Celcius. It is boiled, filtered, precipitated, refiltered, dissolved, reprecipitated and purified, a process done in several steps and with several solutions, most notably sodium hydroxide, so that at the end of the process it is a pure substance that may be used to make the injectable solution, a topical solution, or dye-impregnated paper strips. Water, sodium hydroxide, and/or hydrochloric acid, are added to the dye powder to make the injectable form **(8).**

Since it was discovered in 1871, The uses of fluorescein (FL) as a contrast dye and fluorophore in technical chemistry have an astonishingly broad spectrum in different applications. During World War II, air force pilots carried small bottles of FL, and in case of having to parachute into water, a vivid green marking was produced that can be seen from long distances. Also FL aids in detecting subsea oil and gas pipelines leak **(10).**

Fluorescein metabolism and excretion

Fluorescein undergoes rapid metabolism to fluorescein monoglucuronide after a period of 1 hour post dose, indicating relatively rapid conjugation. Fluorescein and its metabolites are mainly eliminated via renal excretion. After administration, the urine remains slightly fluorescent for 24 to 36 hours. The systemic clearance of fluorescein was essentially complete by 48 to 72 hours after administration depending on the dose **(11).**

In medicine, the fluorescein sodium (FL) salt is used as a marker of BBB disruption differentiating it from perilesional edema in a cortical lesion in rats. Tumor boundaries observed using fluorescein correlate well with preoperative gadolinium contrast-enhanced boundaries. However, fluorescein has no particular interaction with the tumor cells itself, and may not show fluorescence in diffuse, low-density tumor cell infiltrates **(12).**

Role of intrathecal fluorescein in identification of CSF leak:

Because CSF is translucent and the operative field is often blurred with small pools of blood or mucosal secretions, it may be difficult to recognize small CSF leaks. One technique for identifying such leaks is the intrathecal administration of fluorescein, a green fluorescent compound, which imparts its fluorescence properties to CSF and facilitates its identification **(13).**

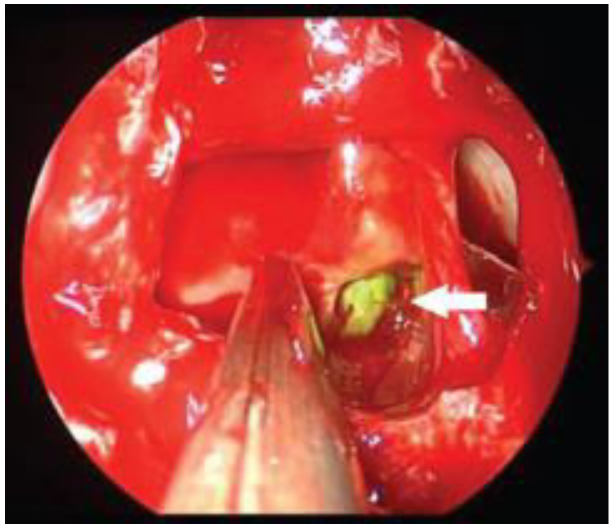

Figure (2): Intraoperative endoscopic photograph. Fluorescein-stained cerebrospinal fluid (CSF; arrow) can be seen extruding from the skull base defect.**(14).**

Its use has been well documented since the 1960s for its value in localising CSF leaks due to its fluorescent properties that allow detection of translucent CSF when exposed to a white or fluorescent illumination **(13).**

Despite not being FDA or MHRA approved, many studies have demonstrated IF to be safe at low doses (<50mg) **(15).**

In a paper recently published in WORLD NEUROSURGERY, the group led by Dr Schwartz and Anand reports on their extensive experience with the use of fluorescein in pituitary surgery. This report follows a previous one by the same group, in which they reported the low rate of complications associated with the use of intratechal fluorescein **(2).**

The authors underline that fluorescein increases the sensitivity of CSF detection .in clinical practice, it is difficult to detect small CSF leaks; typically, maneuvers such as a Valsalva increase the chance of detection, but they imply that a systematic search for a small CSF leak is performed (grade 1) but larger CSF leaks are usually obvious. As stated by the authors, the endoscope most probably increases our sensitivity for detecting CSF leaks, as long as a clear operative field is maintained. If we accept this reasoning, then fluorescein has a clinical role if a minor CSF leak leads to a different reconstruction technique as to when no CSF leak is evident **(16).**

There is no general consensus as to what is the best way to avoid postoperative leak during transsphenoidal surgery. (**17).**asserted that sellar reconstruction is not necessary if an intraoperative CSF leak is not evident, but their study considered a small number of patients and lacked a comparison group; (**3**) also reported satisfactory results with no sellar reconstruction when no CSF leak was evident intraoperatively.

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