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CSF Rhinorrhea – A Rivulet from the Skull Base – Otolaryngologist's Perspective in Endoscopic Repair – Role of Tissue Glue in 'Titanic Trickles'

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ABSTRACT

Introduction: Endonasal endoscopic CSF leak repair has now become the primary modality of management for patients with CSF rhinorrhea. The aim of this article is to emphasise on the factors responsible for the success of the surgery and the advantages of using fibrin/tissue glue in closure CSF leak defects.

Materials & Methods: A retrospective study was done on a group of 10 patients diagnosed with CSF rhinorrhea who have been surgically managed with endonasal endoscopic multilayered CSF leak repair with the help of tissue glue (fibrin glue/sealant). All 10 patients were reviewed regularly post-operatively over a period of 1 year, in order to assess the success in closure of the defect and to assess the recurrence rate in case of failed closure.

Results: Out of 10 patients, 7 had CSF leakage from left nasal cavity, 2 from right nasal cavity, 1 from both nasal cavities. 90 % of the study population was female, 10 % male. Among the 10 patients, 7 had spontaneous CSF leaks (1 associated with idiopathic intracranial hypertension) and 3 were post traumatic. Multilayered leak repair approach was utilized in all the cases which significantly reduces the chances of recurrences and fibrin glue expresses adhesive sealant property that is one of the most important factors contributing to the success of surgery, especially in cases with leaks associated with idiopathic intracranial hypertension.

Conclusion: Multilayered closure involving 3 or more layers and the usage of fibrin glue proves to be an excellent augmentative adhesive sealant especially in cases with multiple sites of leak and/or in spontaneous leak with idiopathic intracranial hypertension.

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Introduction

Cerebrospinal fluid is a clear, colorless, transparent, alkaline, ultrafiltrate of the plasma flowing through the brain, subarachnoid space and central canal of the spinal cord. It is produced from the choroid plexus present in the ventricles, brain interstitial fluid and circumventricular organs. Cerebrospinal fluid leakage is not as uncommon as we like to contemplate. With an average incidence of 44 percent in the Indian population, Cerebrospinal fluid rhinorrhea is the leakage of cerebrospinal fluid through the nasal cavity via a defect in the skull base. Among the plethora of causes classified under traumatic and non-traumatic, CSF rhinorrhea most frequently occurs post trauma. However non-traumatic causes include idiopathic/spontaneous (being the most common), neoplasms, congenital defects and following infections.

Spontaneous/Idiopathic leaks are infamous for the highest rate of recurrences as they are associated with multiple subdural defects, high lumbar opening pressure and presence of meningoceles / meningo-encephalocele. The most common sites of leak of CSF in spontaneous leaks are cribriform plate, roof of ethmoid sinuses, olfactory groove and posterior wall of sphenoid sinus in decreasing order of frequency.

Pioneered by Wigand in the year 1981, trans-nasal endoscopic CSF leak repair has transformed the field of skull base surgeries. Endoscopic CSF leak repair has a huge advantage when compared to conventional craniotomy and leak repair methods wherein the hazards of intracranial abscess, pneumocephalus are foregone, and also has a higher success rate. However, the success of endoscopic repair depends on multiple factors, including the size and etiology of the defect, intracranial pressure, surgical technique including the number of layers and their properties used for closure, CSF pressure control after the surgery, such as, head elevation and bed rest, cough suppressants and stool softeners and the usage of lumbar drainage.

Additionally, the utilization of fibrin glue gives an added advantage in providing strong cohesion to the multilayered flap closing the defect. We in our study aim at identifying the various factors required for a successful closure of CSF leak with emphasis on the importance of tissue glue in difficult cases.

Materials and Methods

A retrospective analysis of 10 patients of CSF rhinorrhea, who were diagnosed and operated in the department of Otorhinolaryngology at Government Thanjavur Medical College for a period of one year (May2024 to May 2025), was done. The Patients details were collected, along with the possible factors that could potentially impact the repair outcome, such as, patient's age, sex, etiology, comorbidities, investigations, operative findings, and localization of the CSF leak site, size of the defect, method of repair, usage of tissue glue, opening lumber pressure and usage of lumbar drain.

From the collected data, it was noted that the diagnosis was made based on the history of unilateral watery nasal discharge which increases especially with head tilt and investigations like nasal discharge analysis for Beta2 transferrin levels, High resolution Computed Tomogram with or without cisternography and Magnetic Resonance Imaging of skull base. All the patients irrespective of the etiology of leak, were started on prophylactic antibiotics and in cases of spontaneous CSF rhinorrhea, Oral Acetazolamide was started accordingly.

Patients underwent Endoscopic CSF leak repair surgery under hypotensive general anesthesia using Storz HD endoscopy system wherein the sinuses are opened and the entire length of skull base from frontal recess to clivus was exposed and site of leak was identified and repaired. The size of the defect, which was categorized as defects less than 3mm, 3-5mm and more than 5mm (based on pre-op CT scan), was used as an important factor to decide the number and type of layers used to close the defect intra-operatively. High opening lumbar pressure and identifying multiple defects became an important factor for usage of tissue glue and lumbar drainage. Several factors which have a potential to contribute or affect the surgical outcomes are considered in this study for each of the 10 cases.

Results

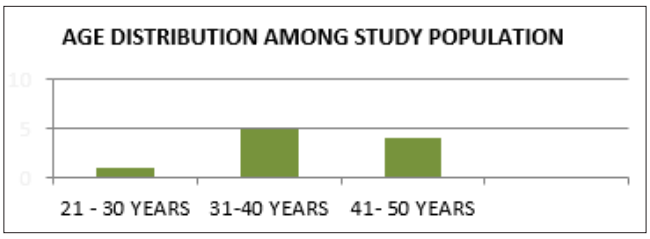

Figure 1: Graphical Representation of Age Distribution of Study Population

The incidence of spontaneous leaks was high in obese middle-aged women whereas post-traumatic CSF leaks were found more common to be in young males (21 – 30 years) majorly involved in road traffic accidents and post endoscopic sinus surgery for chronic rhinosinusitis. The mean age of the patients included in our study was 35.5 ±8.803. and the mean body mass index of the patients included in the study was 33.7 ± 3.33.

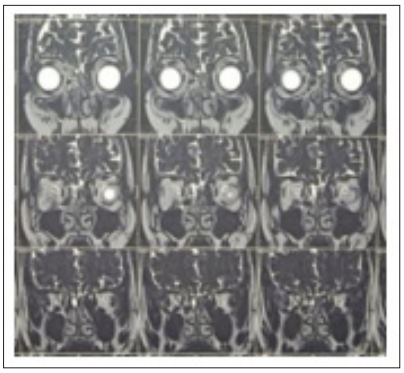

Figure 2: A Coronal View of MR Cisternogram showing T2 Hyperintense Fluid Leak from the Right Cribriform Plate

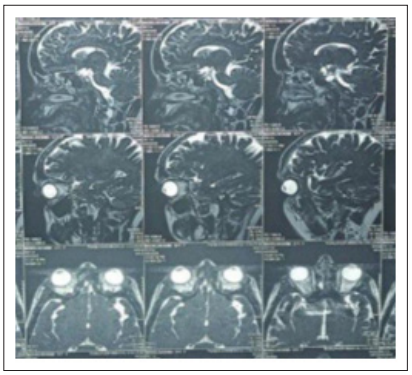

Figure 3: A Sagittal View of MR Cisternogramtaken for the patient with IIH with Meckel's Cave and Peri-Optic CSF Space Widening, Optic Nerve Tortuosity and Empty Sella

1. Symptoms and signs of raised intracranial pressure.
2. No localizing signs in the neurological examination (except abducens nerve palsy).
3. Normal neuroimaging (except empty sella).
4. Opening pressure of lumbar puncture of greater than 250 mm water, with normal CSF
5. Alert and awake patient
6. No other cause of raised intracranial pressure

Figure 4: Modified Dandy Criteria for the Diagnosis of Idiopathic Intracranial Hypertension

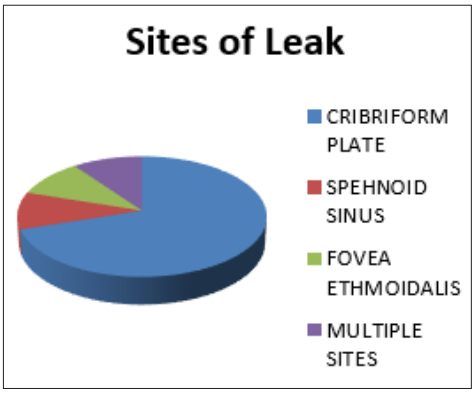

Figure 5: Distribution of Patients Based on Sites of CSF Leak

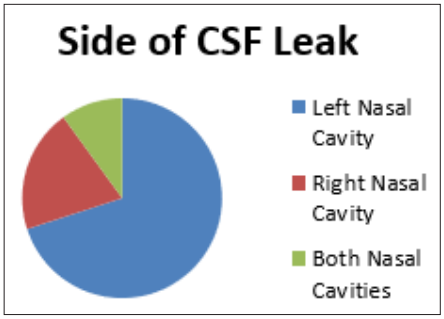

Figure 6: Distribution of Patients based on Side of Leak

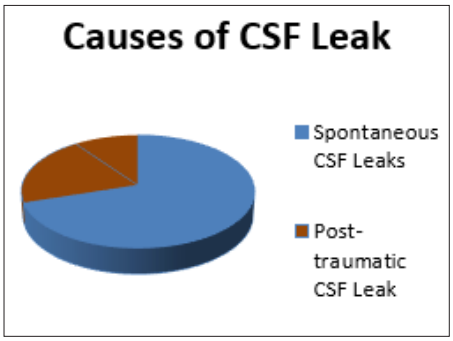

Figure 7: Distribution of Patients Based on Causes of CSF Leak

90% of the patients were females and only 10% males.70% of patients had spontaneous leaks while 30 percent of patients presented with history of trauma (2 patients with history of endoscopic sinus surgery and 1 patient with history of road traffic accident causing the leak) The size of the defect was 1-3 mm in most of the patients and greater than 5 mm in just 1 patient (wherein the defect measured 5.7 mm antero-posteriorly and 2.3 mm mediolaterally), whereas in all the other patients the size of the defect ranged between 3.5±1.65 mm.

Patients were assessed post-operatively with diagnostic nasal endoscopy 4 weeks, 8 weeks, 6 months and 1 year after discharge and all the patients achieved successful defect closure following primary endoscopic repair.

Table 1: Compiled Data of All Patients

AGE GROUP	NUMBER OF PATIENTS
21-30 years	1
31-40 years	5
41-50 years	4
SIDE OF LEAK	NUMBER OF PATIENTS
Left nasal cavity	7
Right nasal cavity	2
Both nasal cavities	1
SITE OF LEAK	NUMBER OF PATIENTS
Cribriform plate	7
Sphenoid sinus	1
Fovea ethmoidalis	1
Multiple sites	1
CAUSES OF LEAK	NUMBER OF PATIENTS
Spontaneous/idiopathic	7
Post endoscopic sinus surgery	2
Post road traffic accident	1
SIZE OF DEFECT	NUMBER OF PATIENTS
1-3 mm	6
3-5 mm	3
More than 5 mm	1
OPENING LUMBAR PRESSURE	NUMBER OF PATIENTS
High (> 180 mm of water)	1
Low (< 180 mm of water)	9
SELLA STATUS	NUMBER OF PATIENTS
Empty sella	1
Normal sella	9
MEAN BODY MASS INDEX	33.7 ± 3.33

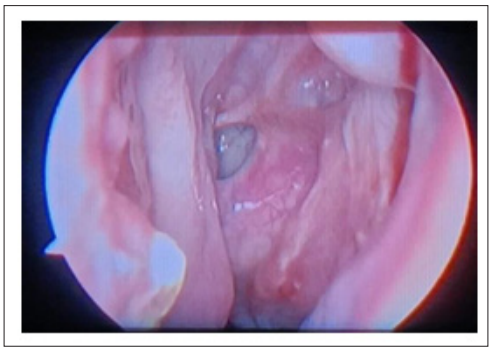

Figure 8: Post operative diagnostic nasal endoscopic image

In our case series, CSF leaks were largely spontaneous/idiopathic with a predilection to the female sex whereas post-traumatic leaks were predominantly seen in males [1]. The most common site involved in both post-traumatic and spontaneous CSF leaks was the cribriform plate, however multiple sites were involved in post-traumatic leak patients such as sphenoid sinus and fovea ethmoidalis [2].

Discussion

Transnasal Endoscopic repair of CSF fistula is a well-established surgical technique with a high success rate. A relative low incidence of these cases and a non-availability of a standard technique makes it difficult to access the factors affecting the success rate in these cases. However, based on various studies done in the past, the success depends on several factors, which includes host factors (such as Age, sex, BMI, etiology, number and size of the defect, CSF pressure etc.,), surgical factors such as, the nature and number of layers used for the closure of the defect, usage of tissue sealant and usage of lumbar drainage) and post operative care [3].

Spontaneous leaks associated with intracranial hypertension was found in 1 female in our study who had a body mass index of 35 and with a defect of size more than 5mm and with high opening lumbar pressure and also with the presence of meningocele – patient was managed with a lumbar drain (both pre-opertively and post-operatively) and a multilayered closure approach with inert layer of autologous fat (in this case, fat graft from thigh and fascia lata was harvested), Hadad (naso-septal) flap reinforced with surgical with tisseel and supported with anterior nasal packing. Post-operatively, patient was kept on strict bed rest till post-operative day 5, stool softeners, cough suppressants, acetazolamide were prescribed to avoid a raise in intracranial pressure and was

advised mild aerobic exercises to encourage weight loss. Thus, we concluded by the end of 1 year follow-up that the patient was symptomatically better and there were no recurrence of symptoms such as watery nasal discharge, headache, nasal obstruction as before. In patients with leaks from multiple sites with defect sizes ranging from 1-5mm, were managed accordingly.

With the above procedure, we could conclude that more than the site of leak, size of the leak prevails as an important prognostic factor. Along with size of defect,

i) Clinical obesity (body mass index of more than 25) played an important role in the development of idiopathic intracranial hypertension, thus an important prognostic factor deciding the success of surgery.
ii) Presence of empty sella – is a sign of idiopathic intracranial hypertension, which warrants a multilayered closure of the defect, failing which recurrence is imminent
iii) In our study we mainly aim at studying the intra-op factors favouring success of an endoscopic CSF leak repair

i) **Nature and number of layers used during closure:**

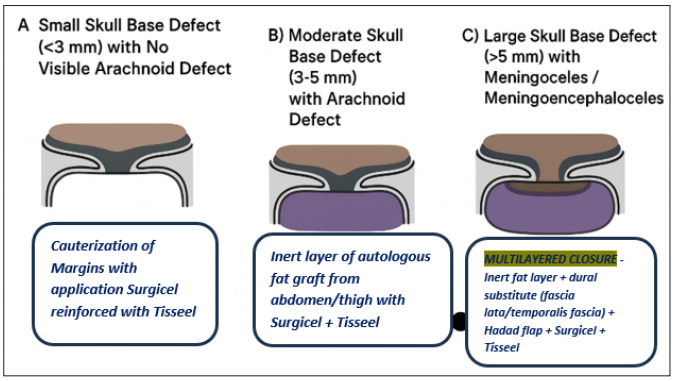

Figure 9: showing different types of defects based on CT scan and their closure. A) Small defect <3mm with no visible arachnoid defect – requires adequate cauterization of the margins with applying a surgicel reinforced with tissue sealant. B) Moderate defect 3-5mm with arachnoid defect-requires an inert layer of autologous fat graft from abdomen or thigh reinforced with surgicel and tissue sealant. C) Large defect >5mm usually associated with meningoceles / meningo-encephalocele – requires multilayer closure with an inert fat layer, a dural substitute (fascia lata / temporalis fascia), a hadad flap, finally reinforcing with surgicel and tissue sealant with a proper nasal packing to hold the layers in place using PVA sponge.

Based on previous studies, the layers used to close a skull base defect includes, first, a layer of inert sealant material to plug the arachnoid defect and prevent further leak and second, a layer to reinforce the defect in the dura, to close the intracranial part [4]. The Third layer may require a cartilage or bone graft to close the skull base defect to prevent post operative meningocele formation. This is required mainly in cases of post skull base tumor excision which leaves very large skull base defects and can be bypassed in defects due to traumatic and spontaneous CSF leaks. Fourth layer always includes a vascularized mucosal flap, which is required for vascularity of rest of the layers and that portion of the skull base. Finally, the layers should be reinforced with a layer of surgicel and tissue sealant. The layers are held together with a good buttress type nasal pack at the end. Different studies have shown good results and reduced recurrence rates with such multilayered closure of the defect [4]. Since in our study we encountered most defects, either post traumatic or spontaneous, with one case with idiopathic intracranial hypertension. Hence, we followed a multilayered closure similar to what is discussed thus far, except the usage of a cartilage or bone graft.

ii) Usage of Lumbar drainage

Lumbar drain was inserted pre-operatively in patients with high opening lumbar pressure based on advocation by Hegazy et al meta-analysis that directly correlated with the success of repair and largely decreased need for a revision repair surgery [1]. The indications for lumbar drain placement were presence of active CSF leak or multiple areas of CSF leak noted intraoperatively, dural defect, encephalocele/ meningocele and bone defect in the skull base > 1 cm [5]. In our study we had used lumbar drain in one such case of Idiopathic intracranial hypertension.

iii) Usage of Fibrin tissue sealants (fibrin glue / TISSEAL)

Fibrin glue/Tissue glue is a two-component sealant system which comprises of the:

a) Sealer protein solution - synthetic aprotinin, factor XIII, fibrinogen (along with excipients such as human albumin, histidine, nicotinamide, sodium citrate, polysorbate 80, water for injections)
b) Thrombin solution - thrombin and calcium chloride dehydrate (excipients such as human albumin, sodium chloride, water for injection)

Fibrin sealant is a concentrated protein solution. Upon application, fibrinogen is coagulated by mixing with a thrombin-calcium chloride solution, following which the rigidity of the adhesives increases further as a consequence of fibrin crosslinking. The formation of fibrin and its crosslinking by factor XIIIa are essential for wound healing. The fibrin network produced under physiological conditions provides a platform for the ingrowth of fibroblasts and the formation of collagen fibers, thereby allowing for robust wound healing. The advantages of using tissue glue are

a) Improves hemostasis and encourages wound healing
b) Provides excellent adhesiveness
c) Musters polymorphonuclear cells which in turn lead to fibroblasts proliferation
d) Promotes vascular proliferation

However, it contains the risk of anaphylaxis/allergic reactions, transfer of viral particles/prions etc. have been documented earlier. Therefore, necessary precautions must be taken care of prior to the utilization of fibrin glue.

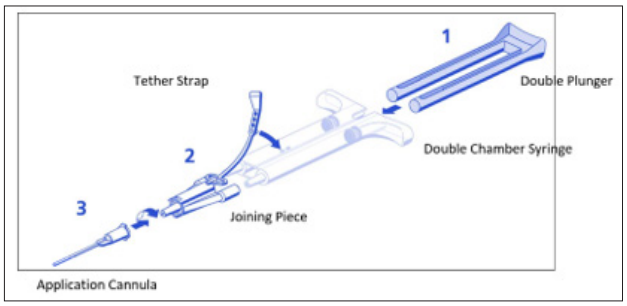

Figure 10: Duo Set (AST Syringe) used for Fibrin Glue Application

Prescribing tablet acetazolamide also played a crucial role in the lowering of CSF pressure by reducing CSF production both pre-operatively and post-operatively. Supplementary medications such as cough suppressants, anti-emetics, and stool softeners played a

vital role in the post-operative management [6].

Intra-operative cauterization of meningocele with bipolar diathermy was done leading to the retraction of meningocele in order to obtain a better visualization of the site of defect [2]. Intra-operative usage of fibrin glue and post-operative management drastically reduces recurrence rates as spontaneous CSF leaks poses the highest risk of recurrence [7-14].

Conclusion

Multilayered repair of CSF leaks with the help of tissue glue has proven to successfully obliterate the defect after the very first attempt. It also shows better and faster healing due to fibroblast proliferation induced by the inflammatory mediators that is stimulated by the tissue glue. Moreover, the augmenting sealant action of fibrin glue gives a sturdy closure and support to the skull base defects especially in cases of high-pressure leaks (associated with idiopathic intracranial hypertension) and leaks from multiple sites. Lumbar drainage must also be considered in such cases for adequate control on CSF pressure both during surgery and post operatively, to prevent recurrence.

Human Ethics and Consent to Participate Declarations

Not applicable to our study.

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