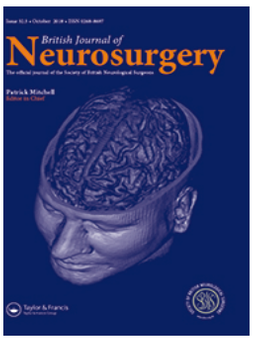

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ORIGINAL ARTICLE

Use of cyanoacrylate to prevent cerebrospinal fluid fistulas after cranial surgery

Ziya Asan[a] and Asuman Kilitci[b]

[a]Department of Neurosurgery, Faculty of Medicine, Ahi Evran University, Kırşehir, Turkey; [b]Department of Pathology, Faculty of Medicine, Ahi Evran University, Kırşehir, Turkey

ABSTRACT

Purpose: Cerebrospinal fluid (CSF) fistula is one of the most common complications encountered after cranial surgeries. In cases where CSF fistula frequently appears due to surgical technique, dural sealants are used as auxiliary preparations to prevent CSF fistula and provide convenience to the surgeon.

Materials and Methods: Data obtained from 128 number of cases where cyanoacrylate (CA) had been used for dural repair to prevent CSF fistula was evaluated, retrospectively. The cases of skull base and frontal sinus fractures where the primary repair had not been carried out were also included in the study.

Results: The mean follow-up of all cases was 9,7 months. CSF fistula was not encountered in 121 of 128 cases. 4 of the cases developed CSF fistula in the early period. 3 of the cases presented with CSF fistula in the late period after discharge. No side effects due to hypersensitivity or preparation were encountered.

Conclusion: CA can help dural repair against the development of CSF fistula by taking effect quickly. Also, it is a rapid anti-haemorrhagic agent. It can also be used after posterior fossa surgery, skull base surgery where dural repair is difficult, or during sinus repair.

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Cerebrospinal fluid fistula; complication; CSF fistula; cyanoacrylate; posterior fossa surgery

Introduction

Cerebrospinal fluid (CSF) fistula development is one of the most common complications encountered following intracranial surgery. In intradural surgery, care must be taken to open the dura with the appropriate method when reaching the target pathology and to close it in a way that it will be waterproof. Development of CSF fistula may lead to complications such as delay in wound site healing, an absence of healing, or meningitis due to the CSF fistula.

In cases where it is not possible to repair the dura with a waterproof technique or after surgeries where the possibility of CSF fistula development is high, dural sealants intended for CSF fistula development prevention are utilised. Synthetic dural materials, fibrin adhesives, and cyanoacrylate-containing adhesives are used to prevent CSF fistula in cases with a dural defect.

In this study, 128 cases who exhibited a high possibility of CSF fistula development and who were treated with cyanoacrylate (CA) to repair the dural defect were evaluated by comparing their results with the literature data.

Materials and Methods

CA was used to repair the dural defect in all cases. Artificial dura material was not used in any case, and in cases with dural defects, the fascia or muscle graft was thinned, and patches were made for duraplasty. Dural leaves were sutured with the continuous method with 3-0 vicryl applied in 3 mm intervals. In 5 cases with skull base fracture, the dura was not stitched with primary suture, and CA was applied directly on the dural leaves and fracture. The demographic distribution of the cases is shown in Table 1.

The mean age of the cases was 43,7 and 9 cases had otorrhea and/or rhinorrhoea symptoms detected with a trauma-related epidural haematoma. 84 cases were operated due to supratentorial intra-axial pathologies, 13 cases due to Arnold Chiari malformation, 11 cases due to posterior fossa pathologies, and 11 cases due to a glial tumour or haematoma extending to the lateral ventricle. The gap between the dural leaves was large in 18 cases who received posterior fossa surgery; therefore muscle was thinned, and patches were made. Galea was also used for duraplasty in cases where supratentorial surgery was administered. Artificial dura material was not used in any case

Surgical Technique

There was otorrhea in 5 cases with epidural haemorrhage together with mastoid bone fracture, and rhinorrhoea in 4 cases with frontal sinus fracture and cerebral contusion. Since primary repair of the dura was not possible in cases with mastoid fractures, CA (Glubran 2) was administered onto the dural leakage and the fracture after the epidural haematoma had been evacuated. Decompressive craniectomy was performed in cases with frontal sinus fracture, and CA was administered after the frontal sinus was obliterated by fascia.

In all cases, the edges of the dura were sutured using 3-0 vicryl with continuous suture with approximately 3 mm intervals. In cases with dural defects, the fascia or muscle flap was thinned and used for patching purposes. CA drawn into a syringe was applied by dropping from a height of several centimetres along the incision lines (Figure 1), and it was ensured that the sealant was dispersed into a thin layer. Care was taken so that the sealant would not adhere to the surrounding tissues during this process. Since it dries very quickly, contact with the aspirator was

CONTACT Ziya ASAN ziyaasan@gmail.com Ahi Evran Universitesi Egitim ve Arastirma Hastanesi Beyin ve Sinir Cerrahisi Klinigi, Kırşehir 40000, Turkey

Table 1. Demographic characteristics of the patients and surgery types.

Surgery Type	Number of cases	Duraplasty with galea/muscle + C.A.	Direct Application of C.A.	CSF Fistula (early/late period)[b]	Mean Follow-up (month)	Mean Age (years)
Supratentorial approaches (not related ventricle or cistern)[a]	84	67	17	3/1	8 months	42,3
Posterior Fossa Haematoma	6	3	3	0/0	15 months	49,8
Posterior Fossa Tumour	5	2	3	0/0	13 months	59,5
Arnold Chiari Malformation	13	13	0	0/2	12 months	38,6
Cranial Base Fracture (with CSF Fistula)	5	0	5	0	14 months	34,3
Frontal Sinus Fractures (with CSF Fistula)	4	0	4	0	17 months	46,5
Supratentorial (ventricle / cistern related)	11	3	8	1/0	11 months	53,1
Total	128	88	40	4/3	9,7 months	43,7

C.A: cyanoacrylate, CSF: cerebrospinal fluid
[a]"Supratentorial approaches (not related ventricle or cistern) section" consists of patients had intradural lesion approaches of hemorrhage or tumor and had dural tearings or defects and dural repair was performed with C.A. at the end of the surgery.
[b]Early period: before discharge, late period: after discharge (mean follow-up time of patients died after surgery weren't calculated in the section.)

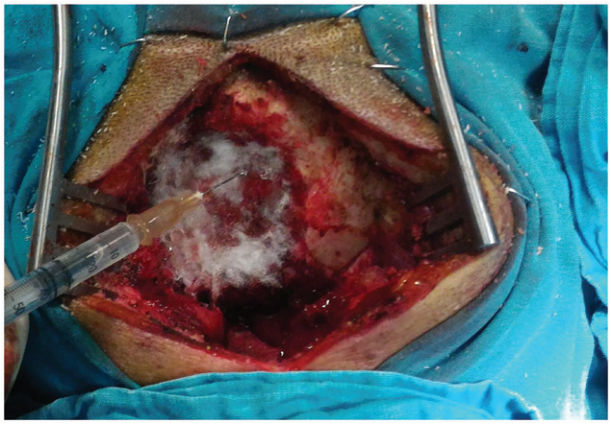

Figure 1. Dripping C.A on dural leaves after primary dural repair. Fibrillar surgicell left on defect to prevent adhesion of C.A from other tissues.

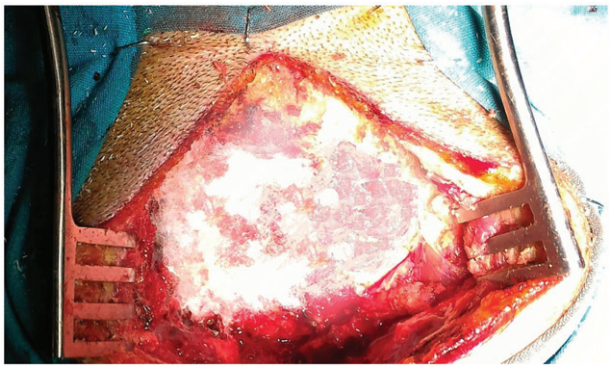

Figure 2. A few minutes later following dural closure of posterior fossa. Dried cyanoacrylate and confirmation of there's no CSF fistula after peep procedure.

avoided. If the sealant could not completely cover the defect on the incision, spreading of the sealant was ensured by remote, light force aspiration. After the application, an absence of a CSF leakage was confirmed by applying positive-end-expiratory-pressure (PEEP) for 5–10 s (Figure 2). In cases where CSF leakage had been detected, additional instillation was applied exclusively to the defect area where the leakage had emerged. The instillation method was also applied to cases who received posterior fossa surgery, and it was attempted to ensure that CA did not escape into the subarachnoid space (Ethics committee approval was obtained from Ahi Evran Univesity Clinical Research Local Ethics Committee on 26.09.2017 no:2017-14/156).

Results

CSF leakage was observed in 4 cases in the early postoperative period. Meningitis was not encountered in the follow-up period in any case. There were no symptoms of hypersensitivity reaction or chemical meningitis that could be associated with the administered cyanoacrylates.

Subcutaneous CSF collection developed in the occipital region in 2 cases who were operated due to Arnold Chiari malformation. It was determined that, in cases who demonstrated no CSF leakage out of the skin, subcutaneous CSF collection mostly appeared in the evenings and was noticed in the morning. A 3-day lumbar drainage procedure was administered to the patients who reported experiencing occasional CSF collection during the follow-up period of approximately 3–4 months, and it was observed that CSF collection no longer appeared in subsequent controls. Other cases with subcutaneous CSF collection were treated using conservative methods. None of the cases were re-operated due to CSF fistula.

The mean follow-up period in all cases was 9,7 months. One patient to whom temporal lobectomy had been administered and who had been determined to have lung carcinoma metastasis according to pathological examination was found to have died in the third postoperative month. CSF fistula was not observed during the follow-up period.

Discussion

CSF fistula is one of the most frequently encountered surgical complications following neurosurgical interventions. While no wound healing is seen in skin tissue in contact with CSF, CSF fistula may develop on the skin if the appropriate intervention is not carried out and this may cause complications such as meningitis which can have a morbid and mortal progression.[1]

There are defined risk factors for developing a CSF fistula after cranial surgeries. Craniotomy and the presence of a large craniectomy defect, the presence of opened pneumatized spaces, the presence of defects larger than 1 cm after dura was sutured, and old age are factors that increase the likeliness of CSF fistula development in supratentorial region surgeries.(2) Closure of the dura with interrupted suture method is another risk factor. Skull base pathology, cerebellopontine angle and posterior fossa surgeries are cases where CSF fistula is more frequently seen.[2]

Other risk factors that include incidental dural defects that occur near the bone margins during craniotomy or the opening of burrholes, the dura mater not being cut properly during dural opening and the resulting irregularities in the dural leaves, reduction of size due to drying of dura mater in long-term surgeries, and reduction of dura size due to bipolar coagulation for

stopping epidural haemorrhages can provide an appropriate environment for CSF fistula development. In situations where there is a large defect in the dura mater, synthetic dura materials that cannot integrate with the dura may also cause CSF fistula development in the postoperative period.

In cases where CSF fistula has developed, and primarily conservative treatments have been tried, treatments that reduce intrathecal CSF pressure can be applied. Additionally, lumbar drainage applications may provide closure of the dural defect by reducing the intrathecal CSF pressure.[3,4]

CSF fistula may develop on the skin since wound healing does not occur in cases where subcutaneous CSF collection develops after cranial surgery. Skin and subcutaneous tissues also serve as a barrier obstructing CSF fistula development. For this reason, elastic bandage application is one of the alternative methods occasionally used so that the subcutaneous CSF collection can be evacuated with a syringe and the subcutaneous tissues can attach to the bone.

The presence of a craniectomy defect is also another risk factor for CSF fistula. The use of autogenous grafts or cranioplasty materials in situations where the craniotomy flap cannot completely cover dura are methods that also prevent CSF fistula. In situations where the dural defect is large or unable to be closed with primary repair, autogenous grafts or synthetic drainage materials are used for duraplasty.[5,6]

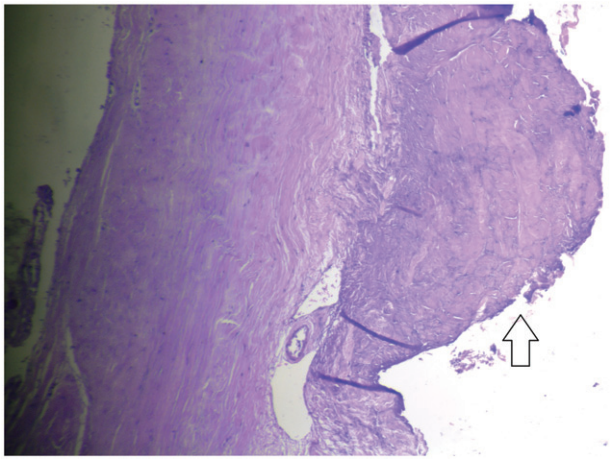

Figure 3. C.A. as a pink colored thin layer on duramater. The material didn't effect on dural tissue after re-operation at 15th month. Cell morphology is normal and collagen fibers have mild irregularity (H&E x50).

In recent years, the frequency of the use of dural sealants for the repair of dural defects has increased. Dural sealants can be utilised to prevent CSF fistula to close dural defects in skull base pathologies where primary repair is difficult, or routinely after primary suturation in posterior fossa surgeries.

Although it has been known for a long time that CA is an agent used for dural repair to prevent CSF fistula, there are not many literature studies showing its results. Cohen-Gadol AA et al. described the results of CA use after transsphenoidal surgery regarding preventing CSF fistula.[7] Areas of CA use outside neurosurgery have been described as endovascular treatment of arteriovenous malformations,[8] treatment of gastric varices,[9] treatment of urinary fistula,[10] and treatment of aortic dissection.[11]

However, it has been identified that it also had toxic effects on neural tissue.[12] After CA undergoes polymerisation in the tissue where it is applied, it can cause heat increase and can transform into acrylacetate and formaldehyde.[13,14] For this reason, its direct contact with neural tissues is not recommended. However, no studies indicating the neurotoxic effect of CA in its clinical use have been found in the literature. In our study, no side effects associated with the administered CA were encountered in the early or the late period. It was observed in cases of skull base fracture that, while dural repair could not be performed, no side effects were caused by CA administered to the mastoid bone and the frontal sinus.

The histopathological effects of CA on the dura mater after being used in the first surgery of a follicular thyroid carcinoma metastases case who showed dural infiltration and was subsequently operated again after 1,5 years due to recurrence are shown in Figure 3.

Today, numerous preparations being used as dural sealants exist. While CA is known to be one of the oldest dural sealants, there are not enough studies in the literature on its surgical outcomes. While reported to be neurotoxic in in-vitro studies, no side effects were encountered following its use in the epidural space. Many studies exist in the literature today that explain its use in endovascular treatment, namely in preventing CSF fistula following pituitary surgery, and still, no symptoms associated with its neurotoxic effect have been recounted.

The comparison of the results we obtained on CA to similar dural sealants has been presented in Table 2.

Table 2. Comparison of previously reported results of dural sealants were used to prevent CSF fistula.

	Dural Sealant	Supratentorial (CSF.f/Total)	Infratentorial (CSF.f/Total)	Cranial base and Pituitary (CSF.f/Total)	Frontal Sinus	Complications	Overall CSF Rates
Graziano et al.[15] $n=77$	Vivostat	4/60	0/17	0/0	0/0	0	5,2% 4/77
Kumar et al.[16] $n=216$	Bioglue	0/114	2/53	0/41	0/0	SSI: 2 (1%)	1% 2/216
Than et al.[17] $n=100$	DuraSeal	0/0	2/100	0/0	0/0	0	2% 2/100
Osbun et al.[18] $n=120$	Duraseal	1/84	1/36	0/0	0/0	0	0,8% 1/120
Cosgrove et al.[19] $n=111$	Duraseal	1/58	4/53	0/0	0/0	M: 2 (1,8%) SSI: 8 (7,2%)	4,5% 5/111
Weinstein et al.[20] $n=116$	DuraSeal	?/72	?/44	0/0	0/0	M: 3 (2,6%) SSI: 4 (3,4%)	6,9% 8/116
Yang et al.[21] $n=4$	? (Fibrin glue)	0/0	0/0	0/0	0/4 (P.I)	0	0% 0/4
Asan et al. (Present study) $n=128$	Glubran-2	5/95	2/24	0/5	0/4	0	5,5% 7/128

It must be taken into consideration that CA must be applied with a different method compared to the usage of other dural sealants to obtain good results. The remarkable fast-drying property of the material and its highly strong adhesive effect allow its effectiveness to be experienced in the early intraoperative period. It was also seen in revision surgeries that, CA, did not detach from the area it had been applied to and did not undergo meltdown. On the other hand, with other dural sealants, symptoms of meltdown or tearing off can be encountered in revision surgeries. The application of CA in the form of a very thin layer can produce the required level of success. The fact that it can be administered in minimal volumes allows prevention of compressive effects on surrounding tissues. Due to its quick-drying property, adherence to surrounding tissues can be prevented. As little as 1 ml of CA was found to be sufficient in all of the total 128 cases, it was utilised in. It has been concluded that, along with other dural sealants, CA is one of the successful preparations that can prevent CSF fistula.

Conclusions

CA is a preparation which dries rapidly, adheres to dura mater strongly and can prevent CSF fistula. The use of CA with the appropriate technique increases the possibility of success. CA is one of the suitable preparations which can be used in intracranial surgeries where the possibility of CSF fistula development is high and in sinus fracture cases where skull base fracture and CSF fistulas have developed.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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