Interdisciplinary Neurosurgery 18 (2019) 100476

Contents lists available at ScienceDirect

Interdisciplinary Neurosurgery

journal homepage: www.elsevier.com/locate/inat

Technical Notes & Surgical Techniques

Localized controlled fibrin glue application with gelatin sponge for hemostasis and dural defect repair: Technical note

Yasunori Nagahama (M.D.)[a,*], Luyuan Li (M.D.)[a], Masaaki Takeda (M.D.)[b], Takafumi Mitsuhara (M.D.)[b], Kaoru Kurisu (M.D.)[b], Matthew A. Howard III (M.D.)[a], Patrick W. Hitchon (M.D.)[a], Satoshi Yamaguchi (M.D.)[a]

[a] Department of Neurosurgery, University of Iowa Hospitals and Clinics, Iowa City, IA, USA
[b] Department of Neurosurgery, Hiroshima University Graduate School of Biomedical and Health Sciences, Hiroshima, Japan

ARTICLE INFO

Keywords:
Cerebral dural venous sinus
CSF leak
Dural closure
Fibrin sealant
Gelfoam
Tisseel

ABSTRACT

Objectives: Hemostasis and dural defect repair are fundamental aspects of neurosurgical procedures. Some significant bleeding may be caused by dural tears (e.g. bleeding from cerebral dural venous sinuses). Various methods have been previously reported for these purposes, utilizing commercially available surgical materials such as gelatin sponge and fibrin glue. We describe a simple, yet versatile and flexible technique with a critical modification to the previously known combined use of gelatin sponge and fibrin glue. We then present a few illustrative cases and discuss the utility and advantages of the described technique.

Patients and methods: The described technique involves separate and sequential application of fibrinogen solution followed by thrombin solution of fibrin glue over gelatin sponge, which enables hemostasis or dural defect repair in a localized, controlled manner.

Results: We have utilized this technique effectively for hemostasis and dural defect repair in a variety of neurosurgical procedures for over 10 years. We have found the technique to be highly useful and effective, although the effectiveness of this technique may be difficult to quantify objectively and independently of the other standard surgical maneuvers, given that hemostasis and prevention of cerebrospinal fluid leak is multifactorial. We have not encountered any complications specifically attributable to the use of fibrin glue and/or gelatin sponge for this technique.

Conclusion: This technique will add to the neurosurgeons' arsenal for hemostasis and dural defect repair, in addition to the more standard and basic surgical maneuvers.

1. Introduction

Hemostasis is a critical aspect of any surgical procedure, including neurosurgical procedures. Various hemostatic techniques have been described using different hemostatic agents, such as gelatin sponge or fibrin glue or a combination of those agents [4,6,10,13,16]. Use of fibrin glue to control venous bleeding has been previously reported [6,13,16]. Some of these same agents have also been effectively utilized to repair dural defects or reinforce dural closure and thus treat or prevent leakage of cerebrospinal fluid (CSF) and resultant complications [1,3,7,10,12,14].

In this report, we describe a simple, yet versatile and flexible method that can be deployed to achieve and enhance hemostasis and dural closure in a focal, controlled fashion using widely available absorbable gelatin sponge (i.e. Gelfoam) and fibrin glue (i.e. Tisseel). The technique involves separate application of the fibrinogen solution followed by the thrombin solution and use of strategically positioned gelatin sponge, which enables localized and delayed formation of fibrin clot in a controlled manner without unintended widespread and/or premature fibrin clot formation. We subsequently present illustrative cases and discuss our experience of utilizing this technique for hemostasis and dural defect repair in a variety of neurosurgical procedures, highlighting the utility and advantages of this technique.

2. Material and methods

Tisseel (Baxter Healthcare Corporation) and Gelfoam (Pfizer) are routinely used as fibrin glue and absorbable gelatin sponge, respectively, for this technique. The fibrin glue product consists of two separate, attached vials primarily containing fibrinogen and thrombin

* Corresponding author at: Department of Neurosurgery, University of Iowa Hospitals and Clinics, 200 Hawkins Drive, Iowa City, IA 52242, USA.
E-mail address: yasunori-nagahama@uiowa.edu (Y. Nagahama).

https://doi.org/10.1016/j.inat.2019.100476
Received 29 April 2019; Accepted 18 May 2019

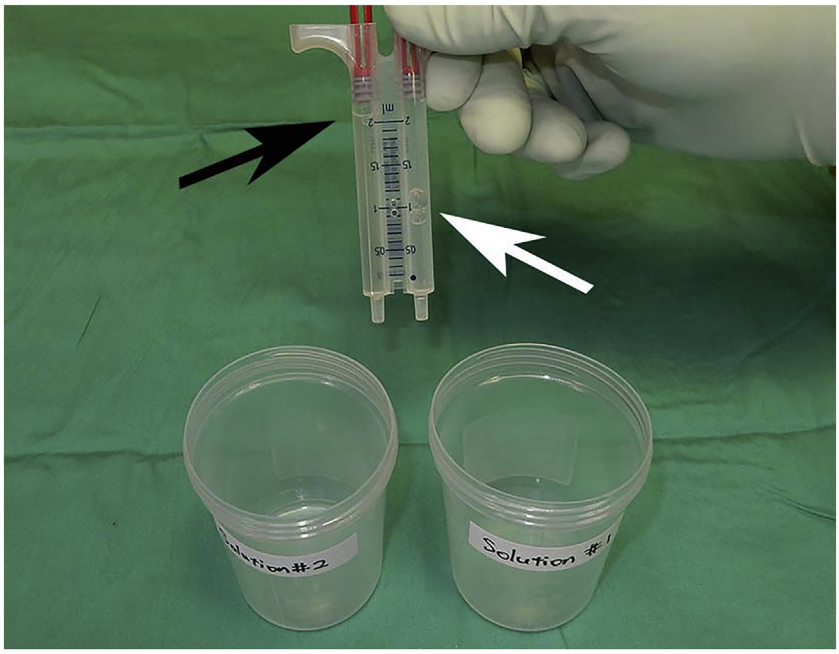

Fig. 1. Intraoperative photograph showing separation of a fibrin glue product (Tisseel) into the fibrinogen and thrombin solutions.
The fibrinogen solution of Tisseel on the right (white arrow) and the thrombin solution of Tisseel on the left (black arrow) were poured separately into two small plastic cup containers labeled as "solution #1" on the right and "solution #2" on the left, respectively, without use of the dual-syringe spray tip. Note that air bubbles were moving up more slowly in the thicker fibrinogen solution on the right side (white arrow) than the other thrombin on the left side (black arrow).

derived from human plasma. The two solutions typically are mixed to immediately form fibrin clot as they are sprayed out of a dual-syringe system. For the technique described here, however, once the solutions are appropriately thawed, the two types of solution are poured separately into two small plastic cup containers without use of the dual-syringe spray tip (Fig. 1) and then drawn separately into two small syringes (e.g. 3-cc syringes). The two solutions in the two separate vials can be distinguished by the thickness/viscosity of the solutions: the thicker solution containing fibrinogen and the thinner solution containing thrombin. An easy way to identify the two solution types is to flip the vials once or twice and observe the movement of small air bubbles in the separate vials. The fibrinogen solution is thicker, and air bubbles move up more slowly in the fibrinogen solution than in the thrombin solution. To facilitate communication among the surgical staffs (e.g. surgeons and scrub nurses/technicians), we typically name and call the fibrinogen solution either "solution #1" or "solution A" and the thrombin solution either "solution #2" or "solution B," and label the plastic cup containers and syringes containing them accordingly.

Gelfoam is cut into different sized pieces as necessary and appropriate. Pieces of Gelfoam are first soaked well with the fibrinogen solution. One or more pieces of Gelfoam are then placed at an area of interest (e.g. a bleeding point over a dural sinus tear, a site of CSF leak repair). Once the fibrinogen-soaked Gelfoam is appropriately positioned, the thrombin solution is applied over the Gelfoam to form fibrin clot. When applying the thrombin solution, use of a needle with the syringe helps to effectively apply only the minimal necessary amount of solution over the Gelfoam without wasting the solution. The needle also enables easier application of the thrombin solution focally over the Gelfoam, even over angled, sloped surgical fields. Gentle pressure can be applied over the Gelfoam directly (e.g. fingers, microsurgical instruments) or indirectly (e.g. using cottonoid patties) for a short period of time (e.g. ~1 min) as needed to allow formation of fibrin clot and its adhesion to the underlying/neighboring structure(s), especially for hemostasis. Even prior to application of the thrombin solution, formation of fibrin clot may begin as the fibrinogen contained in Gelfoam comes into contact with natural thrombin present in the patient's blood. The same mechanism may also facilitate formation of fibrin clot and adhesion even after application of the thrombin solution.

The described technique may be useful for various purposes during neurosurgical procedures. One of the utilities of this technique is hemostasis in a wide range of situations. This technique will be neither sufficient nor appropriate for controlling arterial bleeding, but may be quite versatile in controlling venous bleeding. It can be effectively used alone or in combination with other techniques to control bleeding from the cerebral dural venous sinuses, cortical or bridging veins, and cranial or spinal epidural space. Hemostasis of resection cavities (e.g. after tumor resection) may be enhanced with this technique.

In addition, this technique may be used for reinforcement of dural closure or repair of dural defects. In managing dural defects and resultant CSF leak, the most basic and important step is primary dural closure with non-absorbable suture. However, if primary dural closure is not possible or not adequate (e.g. limited exposure, lack of adequate dural edges), this technique may become useful along with other more standard measures (e.g. fat/muscle grafts, lumbar drainage). Pieces of fibrinogen-soaked Gelfoam may be positioned in the intradural or extradural space in one or multiple layers prior to application of the thrombin solution. We have found it quite effective to place a piece of fibrinogen-soaked Gelform which is larger than the size of the dural defect into the intradural space to plug the defect from the inside and apply the thrombin solution. Because fibrinogen-soaked Gelfoam remains soft and pliable, it can be easily inserted through a smaller dural defect and positioned and widened intradurally. As the thrombin solution is applied, the combination of the Gelfoam and fibrin glue forms a stable and effective water-tight sealant from inside the intradural space.

3. Results

The authors have utilized this technique effectively over the last 10 years without any significant complications specifically attributable to use of gelatin sponge or fibrin glue (e.g. allergic responses). Two illustrative cases are presented below.

CASE 1. Hemostasis of cerebral dural venous sinus (Fig. 2).

A 51-year-old female presented with vertigo and right-sided hearing impairment and was noted to have a right-sided cerebellopontine angle tumor concerning for vestibular schwannoma on magnetic resonance imaging (MRI) study. She underwent right retrosigmoid craniotomy for resection of the tumor. During exposure, brisk venous bleeding was encountered from a tear at the transverse/sigmoid sinus junction. The

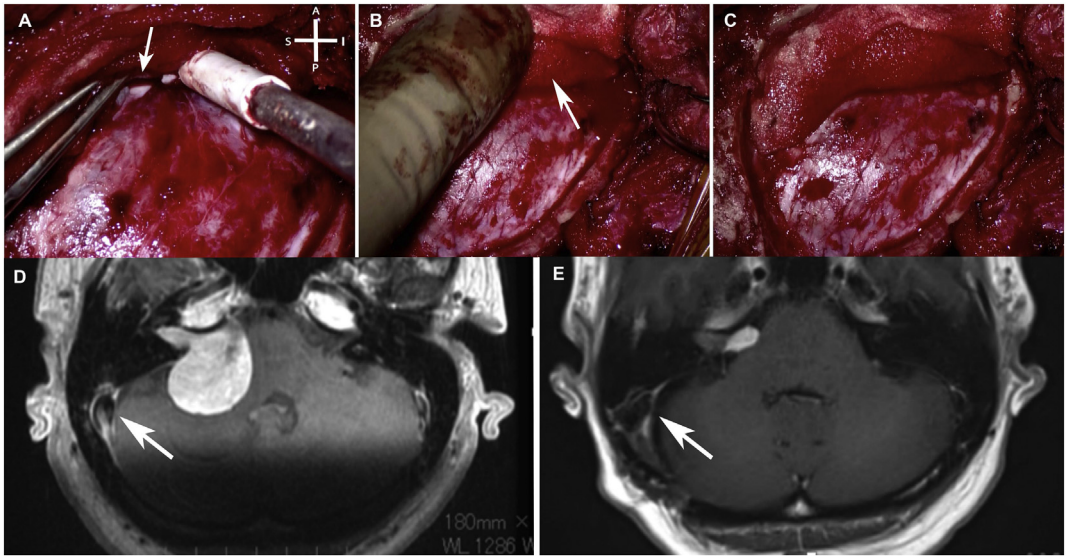

Fig. 2. Intraoperative photographs and pre- and post-operative MRIs for a 51-year-old female patient who underwent right-sided retrosigmoid craniotomy for resection of vestibular schwannoma.
(A) A surgeon's view intraoperative photograph captured with the surgical microscope shows a bleeding point at the transverse-sigmoid sinus junction (white arrow). A piece of fibrinogen-soaked Gelfoam was just placed over the bleeding site with micro-forceps as the bleeding was controlled with micro-suction. Note that the orientation of the surgical field is indicated with a cross sign with the accompanied letters (A = anterior, P = posterior, S = superior, I = inferior) (B) The fibrin/Gelfoam mixture covering the bleeding site (white arrow) after application of the thrombin solution was held in place with gentle direct manual pressure for a short period of time to achieve adequate hemostasis. (C) Adequate hemostasis was finally achieved with the controlled fibrin/Gelfoam technique. (D) Preoperative MRI showed a homogenously enhancing tumor in the right cerebellopontine angle concerning for vestibular schwannoma along with the contrast enhanced patent right transverse-sigmoid sinus junction (white arrow). (E) Postoperative MRI showed persistent patency of the venous sinus junction, as well as appropriate resection of the tumor.

bleeding was immediately and effectively controlled with the controlled fibrin/Gelfoam technique. The remainder of the procedure was uncomplicated. The postoperative MRI revealed patency of the venous sinus as well as appropriate tumor resection without any complications.

CASE 2. Repair of a dural tear (Fig. 3).

A 56-year-old male presented with severe left upper extremity radicular pain in the C6 dermatome and was noted to have cervical spondylosis with left-sided foraminal stenosis at C5–6 on an MRI study. He underwent C5–6 anterior cervical diskectomy and fusion. During the procedure, CSF leak from a small dural tear was encountered. Due to limited exposure through the narrow disc space, primary dural closure with non-absorbable suture was not feasible. We therefore repaired the dural defect with the controlled fibrin/Gelfoam technique. Specifically,

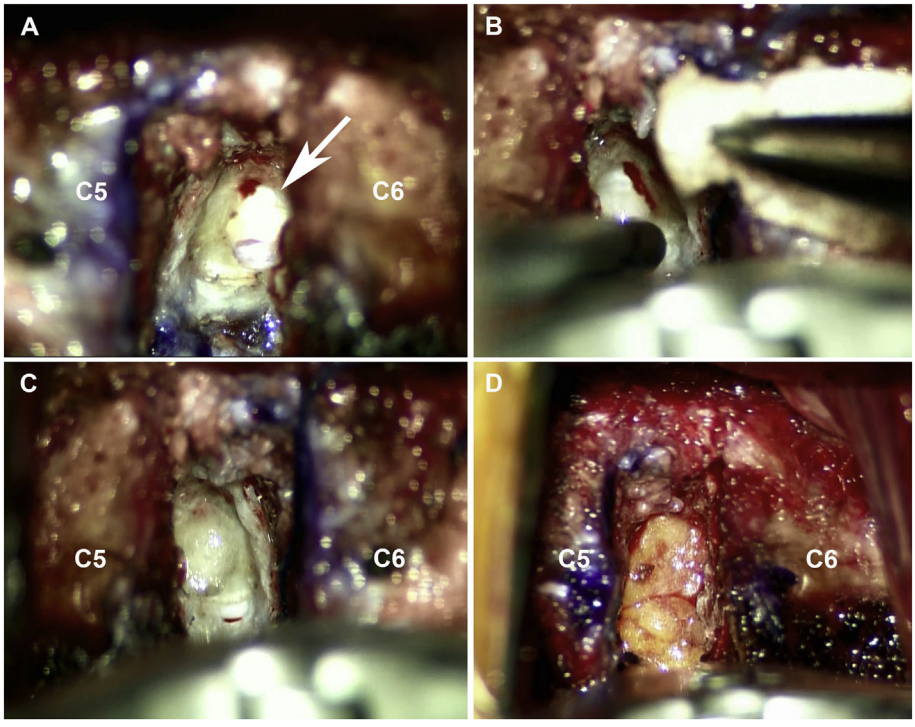

Fig. 3. Intraoperative photographs for a 56-year-old male who underwent C5-6 anterior cervical diskectomy and fusion.
(A) A small dural defect with the underlying spinal cord (white arrow) was encountered, which was visible through the narrow disc space between the C5 and C6 cervical vertebral bodies. (B) A piece of soft and pliable fibrinogen-soaked Gelfoam, larger than the size of the dural defect, was passed through the narrow disc space to be placed in the intradural space. (C) The thrombin solution was applied to create an effective fibrin/Gelfoam sealant to plug the dural defect from inside the intradural space, once the Gelfoam was inserted through the smaller dural defect and positioned within the intradural space. (D) A small piece of fibrinogen-soaked adipose tissue was placed over the dural defect, followed by application of thrombin solution, to reinforce the dural defect repair.

we inserted a piece of fibrinogen-soaked Gelfoam slightly wider than the size of the dural defect into the intradural space through the dural defect, followed by application of the thrombin solution. In addition, a piece of fibrinogen-soaked adipose tissue was placed over the dural defect, followed by application of the thrombin solution. Because we did not observe any further CSF leak with Valsalva maneuver, we decided not to place a lumbar drain. The patient was kept at bedrest with the head of the bed elevated only for the first night. He did not develop a CSF leak postoperatively. The key to the dural defect repair in this case was the use of a piece of Gelfoam larger than the size of the dural defect, which enabled formation of an effective water-tight fibrin/Gelfoam sealant plugging the dural defect from inside of the intradural space.

4. Discussion

Hemostasis is one of the most fundamental aspects of any surgical procedure, including neurosurgical procedures. Achieving appropriate dural closure or repair of dural defects is another critical aspect of many neurosurgical procedures, especially in skull base and posterior fossa procedures and spinal procedures. Various techniques using different commercially available products such as fibrin glue, individually or in combination, have been described to obtain hemostasis or repair dural defects [1,3,4,6,10,12–14,16] when more basic and standard methods are inadequate or insufficient. In this report, we described a simple, yet versatile and flexible method to enhance venous hemostasis and dural closure in a localized, controlled manner taking advantage of widely commercially available absorbable gelatin sponge and fibrin glue, in particular Gelfoam and Tisseel.

Use of fibrin glue alone for venous hemostasis has been previously described as an effective technique [6,13,16]. However, one limitation of this technique is the limited control that surgeons may have over where and when fibrin clot will form. Simultaneous application of fibrinogen and thrombin solutions with a standard dual-syringe system with rapid formation of fibrin clot, potentially in a widespread and infiltrating (e.g. into narrow spaces) fashion, may be desirable in some situations but undesirable in other situations. In fact, Sekhar et al. has reported two cases of complications (transient brainstem edema with dysarthria in one patient and posterior temporal venous infarct requiring bone flap removal in the other patient) associated with use of fibrin glue into the superior petrosal sinus that were attributed to suspected uncontrolled reflux of fibrin glue into the cerebral/brainstem veins as an embolic agent [13]. Tavanaiepour et al. described a case in which injection of fibrin glue into the posterior cavernous sinus resulted in permanent sensory trigeminal nerve deficit likely secondary to compression of the trigeminal ganglion, and therefore recommended controlling the volume and pressure of fibrin glue during application [15]. Toyooka et al. reported relative safety of fibrin glue injection into the cavernous sinus during transcavernous surgeries, but noted changes in venous drainage pattern in 25% of their cases and thus discussed the importance of limiting injection volume to avoid significant venous congestion [16].

The controlled fibrin/Gelfoam technique described here enables surgeons to have better control over the localization and timing of fibrin clot formation. Gelfoam provides a matrix that, by keeping the viscous fibrinogen solution in a localized area within itself, facilitates localized fibrin clot formation once the thrombin solution is applied. In addition, separate application of the fibrinogen solution followed by the thrombin solution allows surgeons to control the timing of fibrin clot formation, and thus provides them with more time to manipulate fibrinogen-soaked Gelfoam and optimally position the Gelfoam. Initial application of the fibrinogen solution is preferred over the thrombin for two reasons. First, the fibrinogen solution stays more easily with Gelfoam due to its more viscous consistency without running down and spreading wide. Second, based on our experience, the fibrinogen solution by itself, as opposed to the thrombin solution, appears to be more effective and important in achieving hemostasis, presumably because the fibrinogen may become exposed to natural thrombin present within the patient's blood and start forming fibrin clot.

A variety of methods for fibrin glue application have been described, sometimes along with other materials and often in the context of dural closure and prevention of CSF leak. Sawamura et al. described their technique using an aerosol spray device to spray fibrinogen/thrombin solution, and reported its superiority to sequential or simultaneous application without the device in prevention of CSF leak [11]. Nakajima et al. described a rubbing method in which fibrinogen solution was applied and manually rubbed over sutured dural closure sites, followed by spraying of the fibrinogen/thrombin solutions, which decreased the risk of CSF leak compared to the spray method [9]. Nagata et al. reported that a mesh-and-glue technique in which they first placed fibrinogen-soaked absorbable polyglycoic acid mesh over a dural closure/suture line and applied thrombin solution significantly decreased the risk of pseudomeningocele formation [8]. Separate application of autologous fibrinogen and thrombin on oxidized regenerated cellulose (Surgicel) has been previously reported for hemostasis and prevention of CSF leak, as well as transposition of a vessel for microvascular decompression [10].

The combined use of fibrin glue and gelatin sponge has been previously reported for prevention of CSF leak after transsphenoidal surgeries, where fibrinogen solution followed by diluted thrombin solution were applied to a gelatin sponge prior to placement of the fibrin-soaked sponge [1]. In this method, dilution of thrombin presumably lengthened the time needed for fibrin clot formation, thus providing surgeons more time to manipulate the gelatin sponge. The combined use of Gelfoam and fibrin glue has been previously described for various purposes other than hemostasis or dural closure, including reinforcement of mucosal closure during frontal sinus cranialization [7], protection of the olfactory nerve during clipping of anterior communicating artery aneurysms [2], and closure of cortical and ependymal defects after intraventricular/paraventricular tumor resection [5].

The controlled fibrin/Gelfoam technique can be highly useful and effective in dural defect repair, especially when primary dural closure is not possible and the exposure of the dural defect is limited, as highlighted by the second illustrative case. Because fibrinogen-soaked Gelfoam remains soft and pliable, it can be easily inserted through a smaller dural defect. Controlled delayed fibrin clot formation provides surgeons with sufficient time to optimally position the Gelfoam. The fibrin/Gelfoam, wider than the dural defect and placed within the intradural space, creates an effective water-tight sealant.

The controlled fibrin/Gelfoam technique further extends the utility of fibrin glue in a wide range of situations in neurosurgery because of improved manipulability. The effectiveness of this technique may be difficult to quantify objectively and independently of the other standard surgical maneuvers given that hemostasis and prevention of CSF leak is multifactorial and could be influenced by other related factors (e.g. coagulopathy, venous pressure, positioning of patients, patients' weight, intracranial/intrathecal pressure, completeness of primary dural closure). However, we have routinely used this technique over the last 10 years, and we have found it highly useful without any serious complications directly attributable to the products used for this technique.

In this report, we detailed our technique of using widely commercially available and commonly used fibrin glue and absorbable gelatin sponge as a simple, yet versatile and flexible method to obtain venous hemostasis and enhance dural closure/repair in a localized, controlled manner. This method is certainly not to obviate the other more basic and standard surgical maneuvers, but to complement them. As highlighted by the illustrative cases, the technique can be effectively applied in a variety of neurosurgical situations, and will be a useful addition to the neurosurgeons' arsenal for hemostasis and dural defect repair.

Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Acknowledgements

The authors would like to thank Faith L. Vaughn for her assistance with final editing of the manuscript.

References

[1] F. Campos, S. Fujio, S. Sugata, H. Tokimura, R. Hanaya, M. Bohara, et al., Effect of thrombin concentration on the adhesion strength and clinical application of fibrin glue-soaked sponge, Neurol. Med. Chir. (Tokyo) 53 (2013) 17–20.
[2] H. Cho, K.I. Jo, J.Y. Yeon, S.C. Hong, J.S. Kim, Feasibility and efficacy of olfactory protection using Gelfoam and fibrin glue during anterior communicating artery aneurysm surgery, J. Korean Neurosurg. Soc. 58 (2015) 107–111.
[3] R. Gazzeri, M. Galarza, A. Alfieri, M. Neroni, R. Roperto, Simple intraoperative technique for minor dural gap repair using fibrin glue and oxidized cellulose, World Neurosurg. 76 (2011) 173–175.
[4] Gazzeri R, Galarza M, Fiore C, Callovini G, Alfieri A: Use of tissue-glue-coated collagen sponge (TachoSil) to repair minor cerebral dural venous sinus lacerations: technical note. Neurosurgery 11 Suppl 2:32–36; (discussion 36, 2015).
[5] T.Y. Jung, S. Jung, S.G. Jin, Y.H. Jin, I.Y. Kim, S.S. Kang, et al., Prevention of postoperative subdural fluid collections following transcortical transventricular approach, Surg. Neurol. 68 (2007) 172–176 discussion 176.
[6] N. Krayenbuhl, A. Hafez, J.A. Hernesniemi, A.F. Krisht, Taming the cavernous sinus: technique of hemostasis using fibrin glue, Neurosurgery 61 (E52) (2007) discussion E52.
[7] Y. Murai, T. Mizunari, S. Kobayashi, A. Teramoto, Surgical technique for the prevention of cerebrospinal fluid leakage after bifrontal craniotomy, World Neurosurg. 81 (2014) 344–347.
[8] K. Nagata, S. Kawamoto, J. Sashida, T. Abe, A. Mukasa, Y. Imaizumi, Mesh-and-glue technique to prevent leakage of cerebrospinal fluid after implantation of expanded polytetrafluoroethylene dura substitute–technical note, Neurol. Med. Chir. (Tokyo) 39 (1999) 316–318 discussion 318-319.
[9] S. Nakajima, T. Fukuda, M. Hasue, Y. Sengoku, J. Haraoka, T. Uchida, New technique for application of fibrin sealant: rubbing method devised to prevent cerebrospinal fluid leakage from dura mater sites repaired with expanded polytetrafluoroethylene surgical membranes, Neurosurgery 49 (2001) 117–123.
[10] N. Nakayama, H. Yano, Y. Egashira, Y. Enomoto, N. Ohe, N. Kanemura, et al., Efficacy, reliability, and safety of completely autologous fibrin glue in neurosurgical procedures: single-center retrospective large-number case study, World Neurosurg. 109 (2018) e819–e828.
[11] Y. Sawamura, K. Asaoka, S. Terasaka, M. Tada, T. Uchida, Evaluation of application techniques of fibrin sealant to prevent cerebrospinal fluid leakage: a new device for the application of aerosolized fibrin glue, Neurosurgery 44 (1999) 332–337.
[12] R.W. Seiler, L. Mariani, Sellar reconstruction with resorbable vicryl patches, gelatin foam, and fibrin glue in transsphenoidal surgery: a 10-year experience with 376 patients, J. Neurosurg. 93 (2000) 762–765.
[13] L.N. Sekhar, S.K. Natarajan, T. Manning, D. Bhagawati, The use of fibrin glue to stop venous bleeding in the epidural space, vertebral venous plexus, and anterior cavernous sinus: technical note, Neurosurgery 61 (E51) (2007) discussion E51.
[14] C.I. Shaffrey, W.D. Spotnitz, M.E. Shaffrey, J.A. Jane, Neurosurgical applications of fibrin glue: augmentation of dural closure in 134 patients, Neurosurgery 26 (1990) 207–210.
[15] D. Tavanaiepour, S. Jernigan, M. Abolfotoh, O. Al-Mefty, Fibrin glue injection for cavernous sinus hemostasis associated with cranial nerve deficit: a case report, J. Neurol. Surg. Rep. 76 (2015) e72-74.
[16] T. Toyooka, N. Otani, K. Wada, A. Tomiyama, H. Ueno, K. Fujii, et al., Effect of fibrin glue injection into the cavernous sinus for hemostasis during transcavernous surgery on the cerebral venous draining system, Oper Neurosurg. 13 (2017) 224–231.