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Fibrin glue-coated collagen matrix is superior to fibrin glue-coated polyglycolic acid for preventing cerebral spinal fluid leakage after spinal durotomy

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After surgery for intradural lesions, dural reconstruction is essential for preventing cerebrospinal fluid (CSF) leakage, which can cause serious complications. However, there is currently no established intraoperative procedure. While hydrophobic polyglycolic acid (PGA) sheets and fibrin glue are effective for dural reconstruction, the usefulness of hydrophilic artificial dura mater made of a porous collagen matrix has also been reported. This study aimed to compare the ability of a fibrin-coated porous collagen matrix and a fibrin-coated PGA sheet to prevent CSF leakage during spinal surgery. This study included 319 patients who underwent surgery for intradural lesions requiring dural reconstruction. Patients in the PGA sheet group (group P) and the porous collagen matrix group (group C) were compared. The median age was 60 years. A total of 319 patients were included, with 219 in Group P and 100 in Group C. CSF leakage occurred in 11 patients (5.0%) in Group P and 0 patients in Group C ($P < 0.05$). This is the first report showing the superiority of a porous collagen matrix sheet over a PGA sheet in preventing CSF leakage during spinal surgery. The porous collagen matrix is hydrophilic and may be more effective against CSF leakage than hydrophobic PGA sheets.

After surgery for intradural lesions, dural reconstruction is essential for preventing cerebrospinal fluid (CSF) leakage. However, even with dural reconstruction, open CSF leakage can cause serious complications, such as wound infection leading to meningitis, hypomyelination, cerebral hemorrhage, and nerve root compression syndrome[1]. Various dural repair techniques have been described, such as watertight closure of the spinal dura with fibrin glue[2]; the use of expanded polytetrafluoroethylene sheets[3]; and the use of autologous fat, fascia, and muscle grafts[4]. Polyglycolic acid (PGA) sheets and fibrin glue are used in surgery to withstand high pressure, such as air and bile leaks[5,6], and are widely used for dural reconstruction[7–10]. The PGA sheet is absorbed within 8 weeks[11], and the fibrin glue is replaced by collagenous connective tissue within 4 weeks after the operation[12]. Recently, an absorbable artificial dura mater made of a porous collagen matrix was developed that is considered helpful for dural reconstruction in patients requiring dural repair even without fibrin glue[13]. After the porous collagen matrix has adhered to the dura mater, platelets infiltrate to form a fibrin clot. The resulting membrane coats the dural closure and prevents early CSF leakage[14]. In animal experiments on pigs, the dural formation time of the collagen matrix with the periosteum was approximately 3.0 min[15].

However, postoperative spinal fluid leakage still occurs in 1.3-10% of patients[16,17].

Both the PGA sheet and the porous collagen matrix are placed over the dural closure and repair the dura mater, so close contact with the dura mater is essential.

PGA sheets are hydrophobic and harden when exposed to moisture, so they must be used in combination with fibrin glue[7] to facilitate contact with the dura mater. In contrast, the collagen matrix easily absorbs water[18] and readily contacts the dura mater. However, fibrin glue application is still recommended even when the collagen matrix is used if a 1 cm margin from the dural suture is not available[19]. We hypothesized that a hydrophilic collagen matrix would be more advantageous than a hydrophobic PGA sheet for preventing CSF leakage in the wet surgical field after dural suturing and that a collagen matrix with fibrin glue would reduce the rate of

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Age	Sex	Level	Disease
54	F	Cervical	Intradural extramedullary tumor Schwannoma
63	F	Cervical	Intramedullary tumor Subependymoma
62	M	Lumbar	Intradural extramedullary tumor Schwannoma
70	F	Thoracolumbar	Intradural extramedullary tumor Schwannoma
66	F	Cervical	Dumbbell tumor Schwannoma
49	M	Thoracic	Intradural extramedullary tumor Schwannoma
55	F	Lumbar	Intradural extramedullary tumor Schwannoma
35	F	Sacral	Arachnoid cyst
37	M	Cervical	Dumbbell tumor Schwannoma
20	F	Sacral	Tethered cord syndrome Alagille syndrome
30	M	Cervical	Dumbbell tumor Schwannoma

Table 1. Characteristics of CSF leakage patients.

Factor	Total, *n* (%) (*N* = 319)	CSF leakage (+), *n* (%) (*N* = 11)	CSF leakage (−), *n* (%) (*N* = 308)	*P* value
Age (years)	60.0 (49.0–71.0)	54.0 (35.0–63.0)	60.0 (49.0–72.0)	0.06
Female	166 (52)	7 (63.6)	159 (51.6)	0.55
Cervical	72 (22.6)	5 (45.5)	67 (21.8)	0.13
Thoracic	131 (41.2)	2 (18.2)	129 (42)	0.13
Tumor	274 (85.9)	9 (81.8)	265 (86)	0.66
Dumbbell tumor	35 (11)	3 (27.3)	32 (10.4)	0.11
Cervicothoracic intramedullary tumor	17 (5.3)	1 (9.1)	16 (5.2)	0.46
Schwannoma	170 (53.3)	8 (72.7)	162 (52.6)	0.23
Meningioma	61 (19.1)	0 (0)	61 (19.8)	0.13
Operation time (min)	222 (171–290)	258 (140–457)	216 (170–280)	0.33
Blood loss (g)	120 (50–258)	125 (60–325)	120 (50–257)	0.80
Bed rest (days)	3 (3–4)	5 (4–13)	3 (3–3.8)	< 0.001
JOAs improvement rate (%)	70.0 (43.7–85.7)	64.7 (47.1–85.7)	72.2 (45.5–85.7)	0.89

Table 2. Comparison of patients with and without CSF leakage. Median (25% quartile–75% quartile). JOA improvement rate (%) = ([post JOA] − [pre JOA]/[total JOA] − [pre JOA]) × 100. *JOAs* Japanese Orthopedic Association score.

postoperative CSF leakage in cases involving narrow surgical fields, such as the spinal surgical field, where a margin of at least 1 cm between the dural suture and the collagen matrix is difficult to achieve. However, there have been no reports on the use of a porous collagen matrix with fibrin glue or on the use of PGA sheets and a porous collagen matrix for preventing CSF leakage in the presence of fibrin. This study aimed to compare the ability of a fibrin-coated porous collagen matrix and a fibrin-coated PGA sheet to prevent CSF leakage during spinal surgery.

Results

To answer this clinical question, we included 319 patients with intradural lesions. We excluded patients whose dural lesions were caused incidentally by spinal decompression or other means. The median age was 60 (49–71) years, and 166 patients were female. Among the 319 patients in this study, 275 had spinal cord tumors, five had spinal cord herniation, seven had syringomyelia, and 26 had membranous lesions. CSF leakage occurred in 11 patients (3.4%) (Table 1).

The CSF leakage group had a significantly longer period of bed rest (5 days, $P < 0.001$) (Table 2). All patients in the CSF leakage group experienced headaches. Patients in the CSF leakage group underwent repeat dural repair with the same material and spinal drainage. The clinical recovery rate did not differ between the two groups (Table 2). The present study revealed no statistically significant difference between the CSF leakage group and the no CSF leakage group, but there was a significantly longer history of persistent preexisting headaches and bed rest among those who experienced CSF leakage. A comparison of group P (219 patients) and group C (100 patients) revealed that there were more cervicothoracic intramedullary tumors in group C and more schwannomas in group P. There were significantly fewer cases of postoperative CSF leakage in group C (11 patients in group P, 0 patients in group C) ($P < 0.05$) (Table 3). Surgeon B had a shorter operation time and less blood loss, whereas Surgeon C performed more difficult operations, such as those on dumbbell tumors and intramedullary tumors. There were no significant differences in postoperative CSF leakage (Table 4)

Factor	Group C (collagen matrix), *n* (%) *N* = 100	Group *P* (polyglycolic acid), *n* (%) *N* = 219	*P* value
Age (years)	60.5 (49.0–72.8)	60.0 (49.0–70.0)	0.62
Female	52 (52)	114 (52.1)	0.99
Cervical	24 (24)	48 (22)	0.77
Thoracic	36 (36)	95 (43.6)	0.22
Tumor	83 (83)	191 (87.2)	0.39
Dumbbell tumor	12 (12)	23 (10.5)	0.70
Cervicothoracic intramedullary tumor	11 (11)	6 (2.7)	0.005
Schwannoma	44 (44)	126 (57.5)	0.03
Meningioma	18 (18)	43 (19.6)	0.76
Operation time (min)	232 (179.5–285.5)	213 (164.5–274.5)	0.25
Blood loss (g)	153.5 (60–259.0)	110.0 (50.0–255.0)	0.41
Bed rest (days)	3 (3–4)	3 (3–4)	0.77
JOAs improvement rate (%)	71.8 (51.4–85.7)	71.1 (45.1–87.1)	0.90
Cerebrospinal fluid leakage	0 (0)	11 (5)	0.02

Table 3. Comparison between the collagen matrix and polyglycolic acid groups. JOA improvement rate (%) = ([post JOA] − [pre JOA]/[total JOA] - [pre JOA]) × 100. *JOA* Japanese Orthopedic Association.

Operator	A	B	C	
Cases	100, *n* (%)	87, *n* (%)	132, *n* (%)	*P* value
Age (years)	60.0 (51.3–70.0)	62.0 (48.0–72.0)	59.0 (47.0–72.0)	0.93
Female	54 (54)	45 (51.7)	67 (50.8)	0.89
Dumbbell tumor	5 (5)	10 (11.5)	20 (15.2)	< 0.05
Cervicothoracic intramedullary tumor	4 (4)	1 (1.2)	12 (9.1)	< 0.05
Operation time (min)	220.5 (175.8–290.3)	185.0 (142.0–228.0)	243.0 (186.0-299.5)	< 0.0001
Blood loss (g)	180.0 (90.0–403.8)	65.0 (30.0–110.0)	158.5 (66.3-263.8)	< 0.0001
Cerebrospinal fluid leakage	5 (5)	2 (2.3)	4 (3.0)	0.57

Table 4. Comparisons among operators. Median (25% quartile–75% quartile).

Discussion

CSF leakage can cause serious complications. However, in this study, a fibrin-coated porous collagen matrix did not cause postoperative open CSF leakage and was superior to a PGA sheet. To our knowledge, this is the first report showing that a porous collagen matrix sheet is superior to a PGA sheet for preventing CSF leakage in spinal surgery when fibrin glue is used.

CSF leakage after durotomy

The rate of CSF leakage after a planned dural incision is 0 ~ 10%[17]. In this study, group C had more patients with intramedullary tumors, and group P had more patients with schwannomas; however, there was no difference between the two groups in terms of CSF leakage.

As in a previous report[20], no risk factors for CSF leakage were identified.

Watertight suturing of the dura mater is important for dural reconstruction to prevent CSF leakage. Nevertheless, even if primary closure is achieved, CSF can leak from the needle hole in the sutured area. This problem cannot be solved by changing the suture method[21].

Dural repair with PGA sheets

Various dural repair techniques after dural suturing have been documented. Polyglycolic acid (PGA) sheets and fibrin glue are widely used for dural reconstruction. The use of a combination of PGA mesh and fibrin glue for dural repair satisfies these criteria, as evidenced by an average pressure resistance of approximately 160 mm Hg before membrane rupture when the margin is 5 mm[10]. The PGA mesh is typically absorbed within eight weeks[22], whereas the fibrin glue is replaced by collagenous connective tissue within four weeks after surgery[12]. Hence, this approach seems to fulfill the conditions for effective dural repair. However, postoperative spinal fluid leakage still occurs in 1.3-10% of patients[16,17]. The results of this study are comparable to those of previous reports.

The degree of adhesion of the initial PGF sheet to the dura in a wet environment such as the surgical field is questionable.

Dural repair with a collagen matrix

The collagen matrix is an effective and safe cranial and spinal dural substitute[23]. A key benefit of the use of the collagen matrix is its complete replacement by the patient's tissue within a short timeframe, which contrasts with the use of whole tissue[24]. In animal studies, collagen has been recognized as an inert and easily manageable adhesive substance. Collagen fibers act as a framework for the integration of collagen generated by infiltrating fibroblasts[25]. In animal experiments on pigs, the dural formation time of the collagen matrix with the periosteum was approximately 3.0 min[15]. The degree of adhesion of the initial collagen matrix to the dura is suitable.

Additionally, the collagen matrix was found to be useful for dural reconstruction in 110 patients requiring dural repair[13]. Nevertheless, reports of the utility of a porous collagen matrix alone have shown that CSF leakage and pseudomeningocele formation occur in 4.3-5.2% of patients[13,19]. A porous collagen matrix should be placed alone if overlap with autologous dura mater can be achieved; however, if an overlap of more than 1 cm is difficult, the use of fibrin glue is recommended[19]. We believe that applying fibrin glue to the collagen matrix is useful in spinal surgery, as it is difficult to obtain sufficient margins in spinal surgery because of the narrow operating area. In the present study, the use of the collagen matrix coated with fibrin glue did not result in CSF leakage, and the fibrin glue-coated collagen matrix was superior to the fibrin glue-coated PGA with regard to the prevention of CSF leakage after spinal durotomy. On the other hand, fibrin glue-coated collagen and fibrin glue-coated PGA are placed on the dura and may result in textiloma[26–28]. Although this has not yet occurred in the more than one year that has elapsed since the operation, long-term follow-up is necessary.

PGA sheets are hydrophobic and harden when exposed to moisture, so they must be used in combination with fibrin glue. The collagen matrix, on the other hand, easily absorbs water[18]. It is possible that the hydrophilicity of the collagen matrix allows it to be more effective at preventing CSF leakage than hydrophobic PGA sheets.

This study has several limitations. First, it was retrospective. Second, the same surgeon did not perform the surgery in all patients. However, the first author has been involved in most surgeries as a surgeon or assistant, and the procedures for dural suturing, laminectomy, and drainage management were consistent across all patients. There were no significant differences in postoperative CSF leakage among operators. Third, we evaluated all patients with MRI at one year postoperatively, but the timing of the MRI evaluation was inconsistent. Although there is no CSF accumulation in the operative field on imaging at one year postsurgery, CSF may accumulate subcutaneously in the early postoperative period. Finally, this was a single-center study.

Conclusions

This is the first report showing the utility of a fibrin-coated collagen matrix and the superiority of a porous collagen matrix sheet over a PGA sheet in preventing CSF leakage during spinal surgery when fibrin glue is used. In narrow surgical fields where it is difficult to secure the suture and Duragen margins, such as in spinal cord surgery, it may be better to use fibrin glue in addition to the collagen matrix. This technique might be a good addition to surgical options for dural repair and might reduce spinal fluid leakage, which can cause significant events.

Methods

The study included 319 patients who underwent surgery in our department for intradural lesions requiring dural reconstruction from 2006 to 2023. A comparison was made between patients in whom CSF leakage occurred and those in whom leakage did not. We used fibrin glue-coated polyglycolic acid (PGA) for dural reconstruction in our department, but since 2019 (the year the collagen matrix was introduced in our country), we have used a fibrin glue-coated porous collagen matrix (Fig. 1). Patients with and without CSF leakage were compared. In addition, patients in the PGA sheet group (group P) and the porous collagen matrix group (group C) were compared. Both materials were placed at the site of dural suturing and coated with fibrin glue. The operations were performed by three board-certified spinal surgeons approved by the board of the Japanese Society for Spine Surgery and Related Research. We have made no changes with respect to laminectomy, dural suturing, or drain management. We made two comparisons, one between patients with and without CSF leakage and one between patients treated with a PGA sheet or collagen matrix. The two groups were compared in terms of age, sex, disease, and whether reoperation was performed due to postoperative CSF leakage.

The Japanese Orthopedic Association score was used to clinically evaluate the patients and measure the rate of symptom improvement via a previously reported method[29]. The JOA score is measured on a 17-point scale for the cervical spine, 11 for the thoracic spine, and 29 for the lumbar spine. The higher the score is, the better the clinical performance. We defined postoperative CSF leakage as persistent CSF leakage from the surgical wound that lasted and required reoperation.

Statistical analysis

The data were analyzed via the Wilcoxon test, Fisher's exact test and the Kruskal–Wallis test.

P values less than 0.05 were considered to indicate statistical significance. JMP software was used for the statistical analyses (version 16, SAS Institute, Cary, NC, USA).

Ethics

This research protocol was approved by the ethics committee on clinical research of Kagoshima University (approval no. 230027). All methods were carried out in accordance with relevant guidelines and regulations. Informed consent was obtained from all the patients.

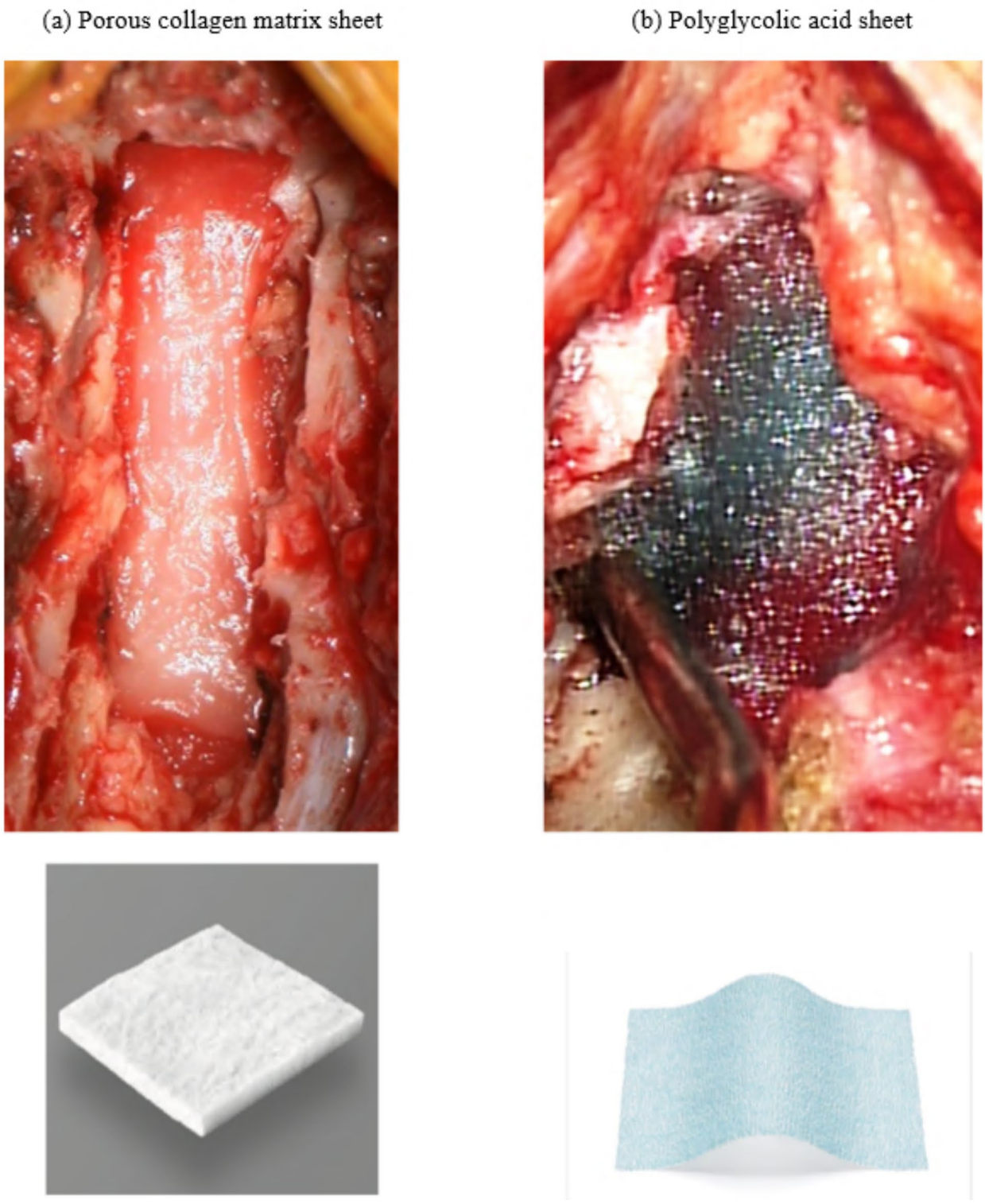

Fig. 1. (**a**) Porous collagen matrix sheet placed on the dura mater. The collagen matrix is hydrophilic and easily contacts the dura mater. (**b**) Polyglycolic acid sheet placed on the dura mater. The polyglycolic acid sheet is hydrophobic and hardens when exposed to moisture, so it must be used with fibrin glue.

Data availability

The datasets produced and/or analyzed in this study are accessible upon reasonable request from the corresponding author.

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Author contributions

H. Tom., IK, H. Tok., H. Taw., TO, and TK participated in the recruitment, data collection, and analysis. H. Tom. wrote the manuscript. H. Tom. and KI performed the surgery as lead operators. NT contributed to the study design and study conception. All authors have read and approved the final manuscript.

Declarations

Competing interests

The authors declare no competing interests.

Additional information

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