Use of Expanded Polytetrafluoroethylene Grafts in the Prevention of Peridural Fibrosis: An Experimental Study

Peridural Fibrozisin Önlenmesinde Ekspanded Polytetrafluoroethylene Greflerin Kullanımı: Deneysel Bir Çalışma

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Abstract: The aim of this study was to investigate whether expanded polytetrafluoroethylene (ePTFE) grafts prevent peridural fibrosis (PF). Seven adult dogs were anesthetized with intramuscular injection of xylazine + ketamine HCl, and were operated on between LS and SI via a posterior approach. Total laminectomies were performed at L5, L6, and L7, and the spinal dura mater and associated tissues from L5 to S1 were exposed. In the control region of the spine (L5-L6), we performed a discectomy and removed the ligamentum flavum and epidural fat. In the next section (L6-L7), we performed a discectomy but left the ligamentum flavum and pediculated fat graft in the laminectomy defect. At L7-S1, we performed the same procedures as were done at the previous level, but inserted an ePTFE graft in place of the ligamentum flavum and fat graft. Three dogs were sacrificed after 3 months, another two dogs after 6 months, and the last two after 9 months. Histopathological evaluation of tissues from the animals sacrificed at 3 months revealed +3 grade PF at the control level, and +2 grade PF at the level with the preserved ligamentum flavum and fat graft in all three dogs. At the ePTFE graft level, two animals showed +2 grade PF and one showed +1 grade PF. Specimens from the four dogs sacrificed at 6 and 9 months showed +3 grade PF at all levels. The results demonstrated that ePTFE grafts do not effectively prevent PF throughout the 9-month period after laminectomy with discectomy.

Key Words: Expanded polytetrafluoroethylene graft, fat graft, laminectomy membrane, peridural fibrosis

Özet: Bu çalışmada ekspanded polytetrafluoroethyelene (ePTFE) greft'in peridural fibrozis'i (PF) önleyici etkisi araştırıldı. Yedi adet yetişkin köpek L5-S1 arasından posterior yaklaşımla xylazine + ketamine HCl anestezidele ameliyat edildi. L5 ve S1 arasındaki tüm spinal seviyeler ortaya konularak L5, L6 ve L7 total laminektomi yapıldı. Kontrol grubu olarak L5-L6, ligamentum flavum ve pediküllü yağ grefti grubu olarak L6-L7, ve ePTFE grubu olarak L7-S1 seviyeleri seçildi. Üç köpek üç ay, 2 köpek 6 ay, ve 2 köpek 9 ay sonra sacrificiyedildi. Üç aylık grubun histopatolojik değerlendirilmesinde kontrol seviyesinde +3 derece PF, ligamentum flavum ve pediküllü yağ grefti seviyesinde +2 derece PF ve ePTFE grefti seviyesinde iki köpekte +1 derece PF gözlemdi. 9 aylık gruba tüm seviyelerinde +3 derece PF bulundu. 9 aylık süre sonunda laminektomi ve disekktomi sonrası gelişen PF'yi önledi ekspanded ePTFE greftin koruyucu etkisinin olmadığını sonucuna varıldı.

Anahtar Kelimeler: ekspanded polytetrafluoroethyelene greft, laminektomi membrani, peridural fibrozis, yağ grefti
INTRODUCTION

Poor results after lumbar disc surgery have been collectively termed "failed back surgery syndrome" (FBSS) (6,9,10-12,17,28,32,45,48). Peridural fibrosis (PF) is an important cause of FBSS, and is part of the normal physiological tissue response to laminectomy (5,10,12,16,32). This response may be extensive due to fibrous organization of hematomas, technical failure, and various other issues related to surgical trauma (10,32). The characteristic structure of PF is the so-called "laminectomy membrane," which is hypertrophic fibrous tissue that envelopes the dura at the surgical site. The most common clinical signs of extensive PF are recurrent back pain and radiculopathy (4,32,44).

Expanded polytetrafluoroethylene (ePTFE) is a synthetic material that produces a mild perigraft reaction. It is commonly used in general and cardiovascular surgery for repairing tissue defects (2,19). In this study, we evaluated whether or not ePTFE grafts effectively prevented PF from affecting the dura and spinal nerve roots in dogs after spinal surgery.

MATERIALS AND METHODS

Seven mixed-breed dogs weighing 20±5 kg were anesthetized with an intramuscular injection of 10-mg/kg xylazine (Rompun, Bayer, Istanbul) and 20-mg/kg ketamine HCl (Ketalar, Eczacibasi, Istanbul). A 20 G cannula was placed for venous access, and 2.5 g ampicillin were administered intravenously (i.v.) as preoperative prophylactic therapy. We made a dorsal midline incision extending from L4-S1, opened the thoracolumbar fascia, and then dissected the paravertebral muscles subperiosteally. Total laminectomies were performed at L5-16, L6-L7, and L7-S1 levels. Next, at the L5-L6 level we performed unilateral ligamentum flavectomy and discectomy on the right side only, and removed all epidural fat tissue. This level was considered the control region. At L6-L7, we performed discectomy alone on the right side, preserving the ligamentum flavum and the epidural fat tissue, and leaving pediculated fat tissue in the laminectomy defect. At L7-S1, we performed unilateral ligamentum flavectomy with discectomy on the right, removed the epidural fat, and then placed 2 mm-thick ePTFE graft material (Gore-Tex®, Gore and Associates Inc., Flagstaff, Arizona, USA). Two pieces of ePTFE were placed, one anterior and one posterior to the dura mater, such that the material enveloped the dura completely. The anterior piece was positioned over the posterior longitudinal ligament superficial to the dura mater and covering the discectomy defect. The posterior piece was positioned such that it covered the laminectomy defect and formed a barrier between the posterior surface of the dura mater and the spinal back muscles. Closure was done in standard fashion.

Postoperatively, all the dogs received a normal diet. Three animals were sacrificed at 3 months with 1 g thiopenthal sodium i.v. (Pentothal Sodium, Abott, Istanbul). Another two were sacrificed at 6 months, and the last two at 9 months. Block specimens of the spinal column from L3 to the sacrum were immediately removed and preserved in 10% formalin for histopathological study. Five millimeter-thick slices were prepared macroscopically, and care was taken to preserve the spinal roots within the dura in each slice. The slices were fixed in 10% formalin for another 3 days, and then decalcified with nitric acid solution and dehydrated in a series of 70% to 100% alcohol baths. Specimens were embedded in paraffin, and two sections from each level were histologically prepared and stained with hematoxylin and eosin for microscopic examination. The extent of PF present at each level was graded according to the system described by He et al. (20) (Table 1).

Table 1: The PF grading system used in the study.

<table>
<thead>
<tr>
<th>Grade Description</th>
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<tr>
<td>Only thin fibrous band(s) between the scar tissue and dura mater.</td>
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<tr>
<td>Continuous adherence, but less than 2/3 of the laminectomy defect affected.</td>
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<tr>
<td>Large amount of scar tissue adherence, and/or scarring extended to the nerve roots.</td>
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RESULTS

In the three dogs that were sacrificed at 3 months, histopathological examination of the control region of the spinal column revealed extensive PF involving the dura. There was significantly more fibroblast accumulation at this level compared to the others. At the level with the intact ligamentum flavum and pediculated fat tissue graft, these tissues were being overtaken by proliferating fibrous tissue. Bone regeneration was evident at both this level and the control level, with bone lamellae and pockets of bone tissue (Figure 1). Tissue sections from both these regions also showed chondrocytes outside the disc.
space. We considered these to be remnants from the discectomy. Adjacent to the laminectomy sites, we also observed muscle atrophy and numerous granulomas associated with the suture material. Regarding PF grading, the animals sacrificed at 3 months showed +3 grade PF in the control region of the column. At the next level, the PF grade was +2 and there was marked atrophy of the grafted fat tissue (Figure 2). In two of the three dogs, the ePTFE graft region showed +2 grade PF, whereas in the other dog the PF grade at this level was +1 grade.

The specimens from the animals killed at 6 and 9 months showed extensive PF and bone regeneration at all levels. Significant fibrous tissue formation was visible on gross examination, and the histopathological findings corresponded with this. The PF grade was +3 at all levels, and the fibrous tissue was engulfing the ePTFE graft.

Regarding scarring and other surgery-related changes, all three dogs that were killed at 3 months exhibited prominent perineural adhesions and extensive fibrous tissue formation in the control region and at the level with the intact ligamentum flavum and fat graft. At this stage, the ePTFE graft was forming a barrier between the dura and the fibrous tissue, and was blocking the extension of scar tissue through the perineural space (Figure 3). Fibrous tissue had formed anterior and posterior to the graft, and had covered the laminectomy area. In contrast, in the dogs that were sacrificed at 6 and 9 months, fibrous tissue had invaded the graft completely and was adhering to the dura (Figure 4 and 5).

The ePTFE grafts themselves did not become adherent to the dura in any of the seven specimens. However, fibrous tissue did develop between the graft and the anterior and posterior dura, and this tissue was partially adherent to the peridural tissue at the nerve roots. As mentioned, in the dogs sacrificed at 6 and 9 months, the ePTFE graft was completely invaded by fibrous tissue.

**DISCUSSION**

Peridural fibrosis describes the process by which fibrous tissue replaces epidural fat tissue after spinal surgery (41,44). PF causes clinical signs in 5% to 25% of all cases (6,13,27). As mentioned, it is part of the normal postoperative healing process, and is radiologically evident to various degrees in up to 79%
Figure 4: At 6 months, the ePTFE graft (stars) was invaded by fibrous tissue that had originated both anterior (right side of picture) and posterior (left side of picture) to the dura mater. New bone formation (double arrow) was noted in the discectomy defect (D) anterior to the graft. The fibrous tissue had invaded the ePTFE graft, was covering the nerve root (white arrow), and was adhering to the dura mater covering the nerve. Note the thin arachnoid membrane between the nerve and the dura mater (HE x125).

Figure 5: Similar to the findings at 6 months, at 9 months the specimens showed ePTFE graft invasion by PF (HE x250).

of cases (8,10,16). To date, it has not been proven that peridural scar formation causes radicular symptoms and low-back pain postoperatively (44); however, anterior and posterior adhesion of the dura and nerve roots to epidural fibrous tissues near spinal surgery sites is known to cause intractable pain (41-43).

La Rocca and Macnab (26) postulated that the laminectomy membrane is formed by fibroblasts that migrate from the erector muscles of the spine and cause fibrosis. Prior to the proposal of this theory, Key and Ford (22) had highlighted the importance of the annulus fibrosus in the development of PF. The combination of discectomy and laminectomy in experimental studies revealed that the puncture site of the annulus on the posterior longitudinal ligament might be the site of origin of the dense fibrous tissue that forms anteriorly (15, 22, 36, 44). Repair of the torn posterior longitudinal ligament during discectomy, and remnants of the nucleus pulposus may also play roles in the development of PF.

Based on these theories and data, some authors have stated that materials used to prevent PF must effectively protect the dura mater anteriorly and posteriorly at the surgery site (12, 14, 23, 43). As has been reported by other investigators, we observed PF both anterior and posterior to the dura mater in our specimens (15, 22, 36, 44). This supports the hypothesis that PF originates from both sides, as opposed to just one.

The histopathological findings in several animal studies have revealed that PF starts 2 weeks after spinal surgery and becomes obvious by 4 weeks (12, 43). In animal models, the initial build-up of fibrous tissue after laminectomy and/or discectomy has been shown to resolve within the first 3 months in most cases (9, 20, 43, 44). In our investigation, at 3 months post-surgery we observed more extensive fibrous tissue formation in the control region of the spine than at other levels; however, by 6 and 9 months all three levels were similar, with +3 grade PF.

The dura and the spinal nerve root sheaths are cushioned within epidural fat tissue, and are able to move freely inside the spinal canal and neural foramen. Considering this, numerous investigators have suggested that the use of autogenous or pediculated fat grafts after laminectomy and/or discectomy should decrease epidural adhesions (5, 12, 24, 25, 34, 37, 44, 45, 48). However, the results of various studies on epidural fat in the prevention of PF have been controversial. Some authors have claimed that even though the fat volume decreases gradually over time, it still partially prevents laminectomy membrane formation (5, 24, 25, 34, 37, 47). Others have observed that epidural fat tissue is completely replaced by fibrous tissue postoperatively (12, 48). It has also been reported that a hematoma covers the fat graft after laminectomy and/or discectomy, and that fibrous tissue formation starts once the hematoma is resorbed (9, 32, 44). In their series of 654 patients, Pappas et al. (38) found that the
degree of PF in patients who received a free fat graft was the same as that in patients who did not receive this type of graft. Moreover, it has been noted that, in some cases treated with fat grafting, the spinal dura comes under severe tension due to compression of the graft posteriorly (7,32,33,39). We did not remove the ligamentum flavum in the region where the pediculated fat graft was used. Three months post-surgery, there was no sign of the ligamentum flavum on microscopic examination; however, we did observe some small pockets of fat tissue remaining within the pervasive fibrous tissue. At the 6- and 9-month stages, there was nothing but dense fibrous tissue, and bone had regenerated to cover the entire laminectomy defect.

Several materials have been used in attempts to prevent the formation of PF. These include gelfilm, gelfoam, silastic sheeting, bone wax, steroids, other hemostatic agents, Dacron, carboxymethylcellulose, elastase, and polylactic acid (1,3,9,14,18,21,23,31,35,37,40,43,44,46). Investigations of various solid and gelatinous materials have shown that these are associated with reduced levels of fibrosis (1,3,9,14,18,21,23,28,29,31,35,37,40,43,44,46). Llado et al. (29) demonstrated that ePTFE grafts were highly effective at preventing PF after 3 months, compared to a control group in which no material was used in the laminectomy defect. They noted that ePTFE formed a physical barrier that blocked the extension of fibrosis from the posterior musculature (29). Our results at 3 months post-surgery also showed this, but the effect was lost by 6 and 9 months.

Our histopathological examination of the 3-month specimens revealed more fibrous tissue formation in the control region than in the other two levels, both of which contained a small amount of fibrous tissue. Evaluation at 6 and 9 months showed that fibrous tissue had invaded the ePTFE and become adherent to the dura. There was +3 grade PF at all levels. Previous reports have cited the non-porous nature of ePTFE grafts as the reason why these grafts block the extension of scar tissue to the dura (12,29,30). We used this same non-porous material to envelope the dura mater and hopefully protect it anteriorly and posteriorly, but the graft did not maintain an effective barrier over time.

In conclusion, PF cannot be effectively prevented in the long term by preserving the ligamentum flavum, using a pediculated fat graft, or placing an ePTFE graft at the surgery site. In our opinion, ePTFE grafts are of no benefit for preventing extensive fibrous tissue formation after laminectomy and/or discectomy. New materials that are introduced for this purpose should undergo trials of more than 3 months post-surgery before any opinion is formed about their efficacy.

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