Immune response in hosts with cadaveric dural grafts

Report of two cases

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The use of cadaveric human dura has been critical in the repair of dural defects since the dawn of neurosurgery. Reports in the literature of immune response to this type of graft have been extremely rare. Two patients are presented who received cadaveric dural implants with resulting meningeal signs and cerebrospinal fluid eosinophilia several weeks after surgery. Peripheral eosinophilia was present in one patient. The signs and symptoms resolved temporarily during corticosteroid therapy and permanently upon removal of the offending grafts. These cases illustrate that an immune-type reaction can occur with significant morbidity in patients receiving cadaveric dural grafts. A proposed mechanism for this response is discussed.

KEY WORDS • dura mater • immune response • dural graft

T he search for an ideal substance for dural repair dates back to 1890, when Beach7 suggested gold foil as a way to prevent meningoencephalic adhesions. Since 1895, when Abbe8 first used rubber as a dural substitute, a variety of substances, both organic and inorganic, have been utilized. These include metal foils,9 amnioplastin,10,18,24,25 vycril and/or collagen,10,20,21, 24-26,33,37 fibrin film,1, polyester mesh,16 Silastic membranes,16 and porcine biomembranes.6 To date, however, the substance that has been most widely used is cadaveric human dura mater. This was introduced in 1955 by Sewell, et al.,34 and first reported in humans by Campbell, et al.,28 in 1958. Freeze-dried, or lyophilized, dura is not limited to use in neurosurgery; it has also found application in urology,3,13,18,30 and maxillofacial surgery.14 This substance has come close to fulfilling the criteria for the ideal dural substitute that include prevention of cerebrospinal fluid (CSF) leakage, no increase in infection rate, minimal adhesions or foreign body-allergic reaction, economy, and ease of availability. Several studies in animals12,23 and in humans,2,22,32, 35,56 have shown that lyophilized dura is a safe reliable material and that complications related to its use are rare. The most celebrated, albeit rare, complication is contraction of Creutzfeldt-Jakob disease in patients (four to date) who had received commercially processed lyophilized dura produced by a German company.16 Reports of clinically evident immune reactions to cadaveric dura mater are rare in the literature.1,7,27 We believe that the following two cases represent the first report of such a reaction to Tutoplast.

Case Reports

Case 1

This 30-year-old right-handed Caucasian woman presented with a 1-year history of steadily progressive generalized headaches, neck pain, distal upper-extremity dysesthesias, and bilateral weakness of hand grip. Her medical and surgical histories were noncontributory.

First Admission. The neurological examination on initial presentation was significant only for fine rotatory nystagmus on lateral gaze, and nasal blurring of the disc margins on fundoscopy. Magnetic resonance (MR) imaging revealed a Chiari I malformation with an associated syrinx at C2-3. Laboratory results were normal.

First Operation. The patient underwent a decompressive suboccipital craniectomy with C-1 laminectomy. Caudal displacement of the tonsils was noted, and a Y-shaped durotomy was created for decompression of the posterior fossa and upper cervical region. The dural defect was repaired with a triangular piece of Tutoplast and secured with vicryl sutures in simple running stitches. The procedure was well tolerated. The patient’s initial postoperative course was uneventful and she was discharged in stable condition on the 6th postoperative day.

Second Admission. The patient presented again, 4 1/2 weeks after discharge, with a 1-day history of nausea, vomiting, severe headache, and photophobia. On examination, she appeared ill, with an oral temperature of

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Fig. 1. Photomicrograph showing fibroblastic infiltration of the dural graft, foreign-body giant cells in association with the suture material, and eosinophils. Neovascularization and a mild perivascular lymphocytic infiltrate are also noted. H & E, × 200.

99.2°F, mild meningismus, and a nonfocal neurological examination. Her cervical incision had healed well. Computerized tomography (CT) and subsequently gadolinium-enhanced MR imaging of the head revealed a pseudomeningocele extending from the medullobular region to the C-4 level with minimal enhancement of the dura of the posterior fossa. Resolution of the original cervical syrinx was noted on these studies.

Serological test results were normal. The CSF examination revealed an opening pressure of 250 mm H₂O; CSF cytology demonstrated 595 white blood cells (WBC)/cu mm, with 2% polymorphonuclear leukocytes, 44% lymphocytes, 27% histiocytes, 3% basophils, and 24% eosinophils. The CSF protein level was elevated to 90 mg/dl (normal 15 to 45 mg/dl), and the glucose content was decreased to 26 mg/dl (normal 40 to 70 mg/dl). The patient was treated with intravenous antibiotic medications until the CSF cultures returned to normal, at which time (on the 4th hospital day) antibiotic drugs were withheld. On the same day, oral corticosteroid therapy was begun and her headaches promptly resolved. She improved significantly and was discharged home on the 6th hospital day with a tapered course of methylprednisolone.

Third Admission. Exactly 2 weeks after this discharge, the patient again presented with a 3-day history of recurrent symptoms of nausea, vomiting, and severe headache with a nonfocal neurological examination. A CT scan of the head demonstrated an increase in size of the pseudomeningocele with the absence of hydrocephalus. Laboratory results revealed a peripheral eosinophilia that had not been present on her previous admission. Examination of the CSF revealed an opening pressure of 170 mm H₂O; CSF analysis showed 16,400 red blood cells (RBC) and 256 WBC (233 with correction), with 5% polymorphonuclear leukocytes, 54% lymphocytes, 2% histiocytes, 1% basophils, and 37% eosinophils. The CSF protein level was elevated to 143 mg/dl (120 when corrected for RBC), and the glucose content was decreased to 30 mg/dl.

Second Operation. The patient’s dural graft was replaced with a fascia lata graft from her right thigh. Pathological examination of the dural graft showed evidence of granulation tissue with focal foreign-body granulomatos reaction, eosinophils, and a mild perivascular lymphocytic infiltrate (Fig. 1). Gram staining of the tissue showed polymorphonuclear leukocytes without organisms. Final culture results obtained 3 days later were positive for 1+ Staphylococcus coagulase-negative species. This was thought to represent a contaminant, but she was treated anyway with eight doses of nafcillin postoperatively.

Postoperative Course. The patient made a good recovery with resolution of her headaches and nausea. On the 5th postoperative day she was discharged home in stable condition. At the time of discharge her incision was healing well and she was afebrile.

Case 2

This 34-year-old right-handed Caucasian woman presented with an 8-month history of bilateral arm and shoulder numbness, occipital headache, and numbness in the calves. Her medical and surgical histories were noncontributory.

First Admission. Neurological examination was sig-
significant only for decreased sensation to pinprick bilaterally in the shoulders and arms with preservation of sensation in the hands. An MR image of the head and neck revealed a Chiari I malformation with a syrinx extending from C-4 to T-6. Laboratory results were unremarkable.

First Operation. The patient underwent a suboccipital decompressive craniectomy and C-1 laminectomy. A duraplasty was performed using Tutoplast, which was secured in position with running vicryl sutures. She tolerated the procedure well. Her initial postoperative course was uneventful and she was discharged on the 4th postoperative day.

Second Admission. Four weeks after discharge, the patient returned with a 4-day history of severe headache, fever, neck stiffness, and mild photophobia. On examination she was in mild discomfort with an oral temperature of 99.6°F. She had a stiff neck with a nonfocal neurological examination. A gadolinium-enhanced MR image of the head and cervicotoracic spine demonstrated collapse of the syrinx and expected postoperative changes. A lumbar puncture revealed 112 WBC/μl mm, with 18% polymorphonuclear leukocytes, 77% lymphocytes, and 5% eosinophils. The CSF protein and glucose levels were 62 and 51 mg/dl, respectively, and CSF cultures were negative. A short course of oral corticosteroids was begun and the patient improved dramatically. She was discharged on the 3rd hospital day with a tapering dose of corticosteroids.

Third Admission. The patient again presented 3 1/2 weeks later with progressive headache, neck stiffness, and photophobia. Her examination was unchanged. Lumbar CSF studies were significant for an opening pressure of 210 mm H₂O, 347 WBC/μl mm with 29% polymorphonuclear leukocytes, 50% lymphocytes, 20% histiocytes, and 1% eosinophils. The protein level was 66 mg/dl, and glucose content was 38 mg/dl. Cultures of CSF were negative.

Second Operation. The cadaveric dural graft was replaced with a fascia lata graft and pathological examination of the dural graft, similar to that of Case 1, was significant for a lymphohistiocytic reaction although without the presence of eosinophils. The patient improved symptomatically after the procedure. Studies of CSF on the 8th postoperative day were notable for the absence of eosinophils and a decreased cell count. She was discharged 9 days after surgery in stable condition.

Discussion

The CSF eosinophilia and peripheral eosinophilia in Case 1 and the resolution of both patients' symptoms with corticosteroid therapy and removal of the offending dural graft all suggest an immune response to the Tutoplast dural graft. These factors make it very unlikely that the pseudomeningoecele was the cause of the symptoms in Case 1. The delayed systemic response with lymphocytic infiltration of the graft is highly reminiscent of the well-recognized syndromes of cell- and antibody-mediated graft rejection. A merely local chronic inflammatory response cannot be ruled out, but is less likely.

Reports of immune-type reactions to cadaveric dural grafts are rare in the literature. In 1981, Johnson and Thompson¹⁶ reported a patient who developed fever and meningeal signs 6 months after suboccipital decompression of her Arnold-Chiari malformation was performed using lyophilized dura. This is a much more delayed presentation in comparison to the cases we report here. Their patient manifested CSF pleocytosis with increased reactive lymphocytes and elevated protein levels, although eosinophilia was not reported. Electrophoresis revealed evidence of additional synthesis of immunoglobulins in the CSF. Histological examination of the graft after surgical removal (8 months after placement) showed foreign-body giant cells with mild perivascular lymphocytic infiltration. Park, et al.,²⁷ observed CSF eosinophilia in patients with aseptic meningitis whose posterior fossa was repaired with lyophilized dura. As in our two cases, these patients responded to corticosteroid therapy. Venes²⁸ mentioned an intense inflammatory reaction with the use of lyophilized dura; however, it is not clear if a systemic reaction occurred. She also described (in an editorial comment) two instances of CSF eosinophilia and fever that resolved after removal of the lyophilized dura.²⁹

The lack of an immune reaction to lyophilized dura has been documented in several studies of homologous grafts in both dogs and humans, in some cases with extensive follow-up periods.²²,²³,²⁴,²⁵ Even the use of cadaveric dura in areas of the body without a barrier to immunocompetent cells has not been associated with graft rejection.³⁰ These studies have also documented the neovascularization and infiltration of the graft with fibroblasts and the eventual replacement of the graft with host tissue. It would seem reasonable to assume that the replacement of the graft by host tissue (up to 75% after 6 months)³⁵ is crucial in minimizing allergic reactions in the host. The lack of antigenicity of lyophilized dura has been attributed to the alteration or elimination of histocompatibility antigens.³⁶ It has been theorized that the reduction of moisture in the tissue obtained by freeze-drying causes denaturation of the protein substances associated with antigenic structure. The cadaveric dura (Tutoplast) used in the cases reported here was not processed by freeze-drying, but was dehydrated by immersion at 37°C in acetone, hydrogen peroxide, and sodium hydroxide. The tissue is thoroughly rinsed with sterile water to remove all residue of the chemical agents. Terminal irradiation by γ-irradiation eliminates the use of ethylene oxide which may leave a residue (JM DeMesa, personal communication, 1993). This 18-day process is thought to result in less tissue damage than the process of freeze-drying.

At least three main factors may play a role in the dural graft rejection and systemic response in these patients: replacement of the graft by host tissue may have been delayed or impaired in some way; alteration in histocompatibility antigens, which is presumed to re-
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sult from dehydration, may have been incomplete or may not have occurred; and there may exist a variety of host factors that predisposed to an exaggerated response to the Tutoplast. Our cases illustrate that an immune-type reaction can occur with significant morbidity in patients receiving cadaveric dural grafts.

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References


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