

Acknowledgments

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Use of Decellularized Nerve Allograft for Inferior Alveolar Nerve Reconstruction: A Case Report

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Injury to the inferior alveolar nerve (IAN) has been reported to occur in 0.4% to 22% of patients undergoing routine removal of third molars.¹ Within this group, 25% of patients might not have recovered within 1 year of the nerve injury, and up to 0.9% of patients might have permanent injury.² Other than the removal of impacted teeth, osteotomies and dental implants are the most common procedures associated with IAN injury. Sacrifice of the IAN can also complicate tumor resections, resulting in anatomic continuity defects of the IAN. Injury to the IAN can cause significant patient morbidity such as bite wounds and burn injuries of the lower lip. Therefore, any treatment that provides functional recovery after IAN injury is of potential value to the patient. In rare and specific situations, procedures such as IAN lateralization or transposition can be performed to avoid nerve injuries.

In the presence of a segmental defect of the IAN, autologous nerve grafts such as the sural and greater auricular nerves have long been considered the reference standard for IAN reconstruction. The use of autologous nerve grafts, however, has been hampered by donor site morbidity. For instance, autogenous nerve donor site morbidities have included a second operative site and sensory loss or neuroma formation, with the potential for neuropathic pain. In the hope of circumventing the potential morbidities associated with the harvesting of autologous nerve grafts, the concept of a preformed tissue space created by a nerve guidance conduit (NGC), such as cadaveric grafts or absorbable synthetic and natural conduits, for peripheral nerve reconstruction has been described.^{3,4} Alternatives to autologous nerve grafts must achieve similar neurosensory recovery compared with their autologous nerve graft counterparts to be considered viable alternatives. Currently, the US Food and Drug Administration has approved synthetic NGC for peripheral nerve and cranial nerve repair classified as either absorbable or nonabsorbable. Although the published data investigating synthetic NGCs in trigeminal nerve microsurgical repair have been limited, consisting mainly of case reports and case series, no ideal synthetic NGC has been identified to date with regard to IAN or lingual nerve reconstruction.^{5,6} End-to-end coaptation of the proximal and distal nerve stumps in a tension-free manner is a well-established surgical principle; however, in specific situations (ie, long nerve gaps) in which coaptation precludes

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primary tension-free repair, NGCs have emerged as a surgical option.⁷

In the present report, we used a commercially available decellularized nerve allograft, Avance (AxoGen, Alachua, FL), for the reconstruction of a segmental IAN defect secondary to extraction socket preservation with an allogeneic bone graft. The present study highlights an uncommon mechanism of injury to the IAN and also reports on a novel application for a decellularized nerve allograft for reconstructing a large IAN defect. The Avance graft is a processed graft, produced by processing human nerve tissue with a combination of detergent decellularization, chondroitin sulfate proteoglycans degradation, chondroitinase treatment, and γ -irradiation sterilization.⁸

Case Report

The patient was a 62-year-old woman with medical history significant for hypothyroidism and anxiety disorder, both of which were well controlled with Zoloft and Synthroid. She was referred because of numbness of her left lip and chin after extraction of her mandibular left first molar with immediate socket preservation using allogeneic bone grafting material 7 months earlier. The patient reported numbness of her left lip, chin, and anterior gingiva that had not improved since the initial surgery. The neurosensory examination was significant for severe hypoesthesia of the left IAN distribution. The oral examination findings were unremarkable, with normal healing of the surgical site. A panoramic radiograph (Fig 1) depicted radiodense grafting material within the tooth socket extending beyond the IAN canal shadow. A decision was made to obtain a computed tomography scan to better delineate the position of the graft material relative to the nerve canal. The computed tomography images demonstrated bone grafting material proximal to the canal in some cuts and obliterating the canal space in others (Fig 2). From the radiographic, clinical, and

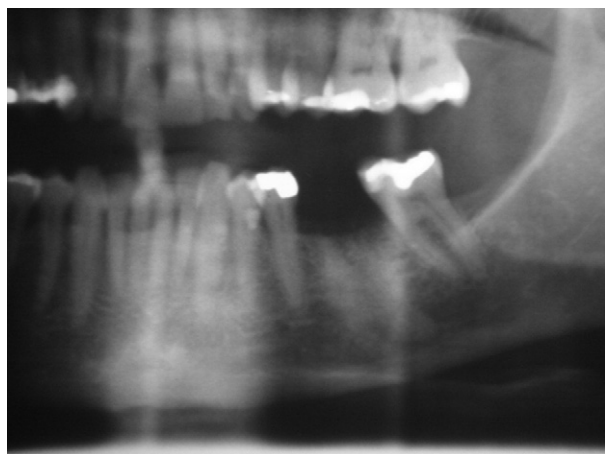


FIGURE 1. Panoramic film depicting allogeneic bone graft material in socket of the left mandibular first molar extending beyond apices of dental socket.

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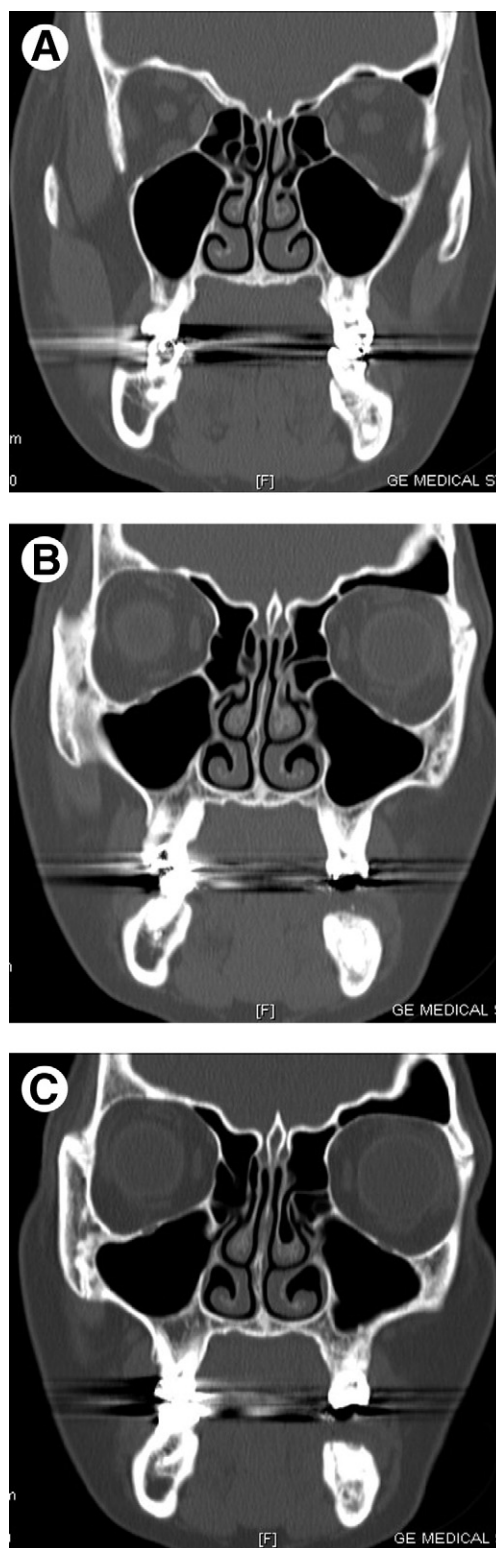


FIGURE 2. A, Coronal computed tomography scan showing mandibular canal proximal to allogeneic bone graft material. B, Coronal computed tomography scan demonstrating lack of mandibular canal due to obliteration of canal by bone graft material. C, Coronal computed tomography scan with evidence of presence of mandibular canal distal to bone graft material.

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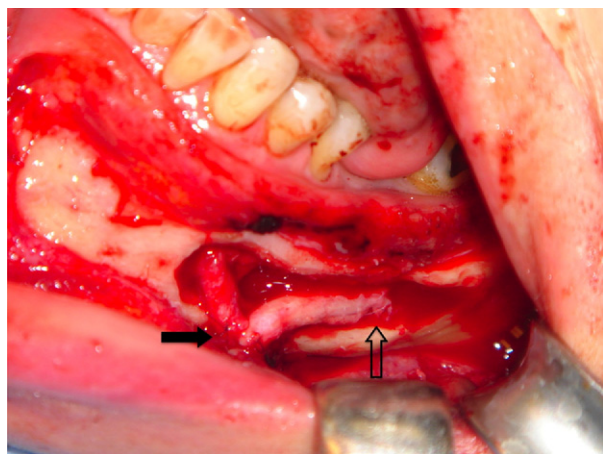


FIGURE 3. Intraoperative clinical photograph of 3- to 4-mm diameter Avance nerve allograft sutured in place to mental nerve distally (solid arrow) and proximal IAN stump (open arrow) in tension-free manner.

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neurosensory findings, the patient was offered exploratory trigeminal nerve microsurgery to remove the graft material, with the potential for a nerve allogeneic nerve graft if indicated, because she had declined autogenous grafting.

The patient was taken to the operating room approximately 8 months after initial injury. The nerve was approached by way of an intraoral vestibular incision, allowing skeletonization of the mental nerve and lateral decortication of the IAN using a series of rotary and hand instruments under copious irrigation. The area proximal to the graft site was initially decorticated, with no evidence of the IAN present. The decortication was extended anteriorly to the mental foramen, which was decorticated circumferentially, allowing exposure of the incisive branch and distal stump. Posteriorly, the canal was decorticated until viable proximal IAN was exposed. The bone graft material was excised to delineate the IAN canal space. The incisive branch was sacrificed to allow distalization and primary repair of the nerve; however, this was not possible owing to the length of the nerve gap and the resulting significant tension that would have developed without an interpositional graft. A 3- to 4-mm diameter Avance nerve graft was passively adapted in place and sutured using 7-0 nylon sutures at the level of the epineurium (Fig 3). Gelatin foam sponge was placed over the nerve graft, and primary closure of the soft tissues was performed.

The postoperative course of wound healing was uneventful. Postoperative sensation, measured using 2-point discrimination, von Frey hairs, pinprick, thermal sensation, and vibration sense, did not show any significant changes at 3 weeks postoperatively. However, by 5 months after surgery, the patient reported tingling and itchiness of the affected side of her chin and was satisfied with the sensory improvement thus far. On sensory examination using von Frey hairs, the patient responded to 4.56 g at 5 months compared with 6.45 g postoperatively. The static 2-point discrimination test on the side of interest had improved and had recovered to within an acceptable range (S3+ level of the British Medical Research Council Nerve Injury Committee Classification Scheme).⁹ Optimally, the patient might have benefited from earlier surgery regarding the outcome; however, as often occurs with nerve injuries, the referral times can vary, depending on the practice of the referring

clinician. In the present case, the patient was observed for a prolonged period before an appropriate referral was made. In general, most microsurgeons would advocate an earlier referral if no spontaneous sensory improvement had been observed. In the present case, the prolonged time to referral might have resulted in additional degeneration, accounting for the degree of nerve gap observed.

Discussion

Despite advances in the biomaterials currently available to surgeons, nerve autografts remain the reference standard for peripheral nerve reconstruction. To avoid the donor site morbidity associated with autologous nerve grafts, cadaveric nerve tissue allografts have been described for peripheral nerve reconstruction. Allografts have been shown to be as effective as autologous nerve grafts; however, their use has been complicated by the requirement for systemic immunosuppression for approximately 18 months.^{10,11} This alternative modality leaves patients vulnerable to opportunistic infections and tumor formation. Therefore, allograft decellularization was developed to allow the graft to retain the extracellular matrix components and structural organization of the autograft, while avoiding the aforementioned sequelae of the earlier allografts. Alternative contemporary materials used for peripheral nerve reconstruction have included nonabsorbable and absorbable NGCs, which are fabricated from synthetic or natural polymers, respectively. One of the more popular absorbable NGCs is NeuraGen (Integra Neurosciences, Plainsboro, NJ), a bovine type I collagen conduit. Farole and Jamal⁵ recently reported on this material for IAN and lingual nerve injury repair. NeuraGen has only been shown to support nerve regeneration for up to a 5-mm nerve gap in nonhuman primates.¹⁰ A recent study by Whitlock et al¹⁰ compared processed rat allografts comparable to Axogen's Avance human decellularized allograft with NeuraGen collagen conduits in a rat sciatic nerve model. In their study, they used both a short graft model (14 mm) and a long graft model (28 mm). They found profound histologic and functional differences between the 2 materials. Their results indicated that NeuraGen demonstrated a less robust reinnervation of distal targets in gaps greater than a critical length of 10 mm in their model. The study by Whitlock et al¹⁰ does not negate the utility of the type I collagen-derived NGC; however, for cases with large nerve gaps, decellularized nerve allografts might be considered as an alternative material. The decellularized graft, in theory, should allow the Schwann cells to rapidly repopulate the nerve allograft by providing a more biologically relevant microenvironment.¹² Finally, a feature of the decellularized nerve allografts is the removal of neurite inhibitory chondroitin sulfate proteoglycans from the basal lamina. This has been con-

sidered a crucial step in the processing of these grafts, and studies have shown significant increases in axonal ingrowth using chondroitinase-treated grafts compared with untreated nerve grafts.^{12,13}

In summary, a wide variety of NGCs with versatile designs are available to the maxillofacial reconstructive surgeon for trigeminal nerve reconstruction. However, although a myriad of designs have been put forth, no ideal "off-the-shelf" graft material has been identified in the published data. We believe that decellularized nerve allografts should be considered a valid alternative for peripheral trigeminal nerve reconstruction in the presence of large nerve gaps to avoid untoward tension and ischemia, resulting in poor nerve regeneration and fibrosis.

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Infantile Sinonasal Myxoma: A Unique Variant of Maxillofacial Myxoma

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Myxomas are benign, slow-growing, locally invasive neoplasms derived from mesenchymal elements. Maxillofacial myxomas are rare and most frequently involve the jawbones. The origin of most maxillo-

facial myxomas is believed to be odontogenic, although in rare cases, tumors have occurred in the sinonasal area, outside the area of the odontogenic apparatus, and, thus, could not have originated in the odontogenic mesenchyme. In traditional radiographs, maxillofacial myxomas have been described as radiolucent, usually multilocular, with features resembling honeycomb, soap bubbles, or a tennis racket. The borders of the radiographic lesions might be well defined with or without sclerosing margins; however, in 56% of cases the margins have been poorly defined.¹ Imaging techniques such as computed tomography (CT) and magnetic resonance imaging (MRI) can be useful to define the anatomic extent of the tumor and to plan the surgical intervention; however, the final diagnosis requires microscopic analysis.

Maxillofacial myxomas usually affect young to middle-age adults; pediatric cases have been relatively rare and usually occur in children older than 10 years

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