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CASE REPORT
Peripheral Nerve

Necrotic Granulomatous Inflammation after Use of Small Intestine Submucosa Matrix for Recurrent Compression Neuropathy

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Summary: Various techniques exist for treating recurrent carpal and ulnar tunnel syndrome, but AxoGuard nerve wrap has shown promising results for treatment of compression neuropathies when used in conjunction with neurolysis and tenosynovectomy. Prior results demonstrate no safety concerns, and there have not been any reported cases of infection, persistent inflammation, or recurrent perineural fibrosis. A 41-year-old, right-hand-dominant woman experienced repeated bouts of carpal and ulnar tunnel syndromes, which were treated with a small intestine submucosa matrix wrap around the median and ulnar nerves in the wrist. Here, we report a case of necrotic granulomatous inflammation 2.5 months after AxoGuard xenograft nerve wrap was placed around the median and ulnar nerves. As a salvage, NuShield placental allograft was wrapped around the median nerve, which has shown promising results at several months follow-up. Placental allograft nerve wraps represent a useful tool in compression neuropathy resistant to autografts, xenografts, and revision decompression operations. *(Plast Reconstr Surg Glob Open 2022;10:e4378; doi: 10.1097/GOX.0000000000004378; Published online 14 June 2022.)*

Carpal and ulnar tunnel surgeries commonly result in favorable outcomes and high patient satisfaction. Nonetheless, 1%–31% of patients report persistent or recurrent carpal or ulnar tunnel syndrome due to perineural fibrosis.[1] Various treatment options exist for recurrent compression neuropathies, including repeat decompression, neurolysis and tenosynovectomy, hypothenar fat pad flaps, and nerve wraps. Revision procedures continue to be a difficult prospect because access to the nerve is complicated by dense fibrous scar tissue.[2]

Nerve wraps are bioabsorbable materials made of autologous tissue or collagen that supply a noncompressive encasement to a previously injured or compressed nerve.[3] They are placed at the interface between a nerve and adjacent tissue. The nerve wrap's wall contains a central slit that facilitates placement around the injured nerve. Once hydrated, it morphs into a soft, nonfriable, and maneuverable wrap that vascularizes and subsequently remodels into the patient's tissue.[4] This new tissue minimizes the potential for soft tissue attachment and enables nerve gliding.

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CASE REPORT

A 41-year-old, right-hand dominant woman with a prior medical history of asthma and chronic generalized pain had been experiencing numbness and tingling in both hands for over 6 years. Carpal, ulnar, and cubital tunnel syndromes were diagnosed on multiple occasions and confirmed with nerve conduction studies. Although her right-sided symptoms improved after two decompression surgeries, the left-sided symptoms were nonresponsive to steroid injections and repeated bilateral carpal, ulnar, and cubital tunnel releases with external neurolysis and neuroplasty.

In July 2021, she underwent left carpal and ulnar tunnel releases with extensive tenolysis of the hand flexor tendons and placement of AxoGuard nerve wrap around the median and ulnar nerves at the wrist. Despite this, she continued to have pain and began to develop redness and swelling around the left volar wrist. Computerized tomography of the left wrist showed a small fluid collection superficial to the flexor tendons (Fig. 1).

Exploration of the left wrist 2.5 months later expressed a fluid that was negative on culture. Further dissection and delineation of the median and ulnar nerves revealed an extensive inflammatory process surrounding them (Fig. 2). Careful external neurolysis of the nerves was

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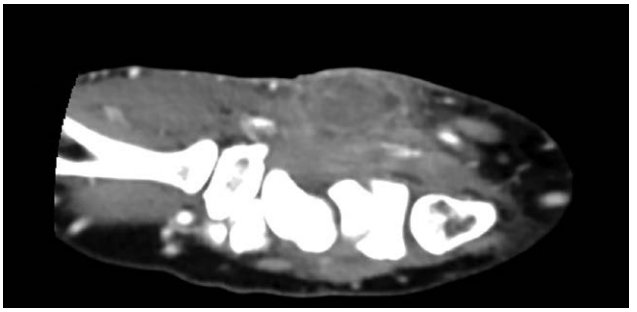

Fig. 1. CT scan with contrast demonstrating a 1.0 × 2.0 × 7.1 cm fluid collection of the subcutaneous tissue superficial to the flexor tendons on the left wrist. There is slight widening of the scapholunate joint space.

performed during removal of this inflamed hypertrophic tissue. The dense inflamed portions of tissue were consistent in size and shape with the previously placed nerve protector wraps (Fig. 3). Histological specimens from median and ulnar nerves demonstrated necrotic granulomatous inflammation with giant cells (Fig. 4).

There was a small area of median nerve fascicle disruption that was repaired. Because the epineurium surrounding the median nerve was involved in the significant area of inflammation and dense tissue, it was necessary to protect the nerve fascicles with additional wrap. Use of autologous vein or a hypothenar fat flap for wrapping the nerve

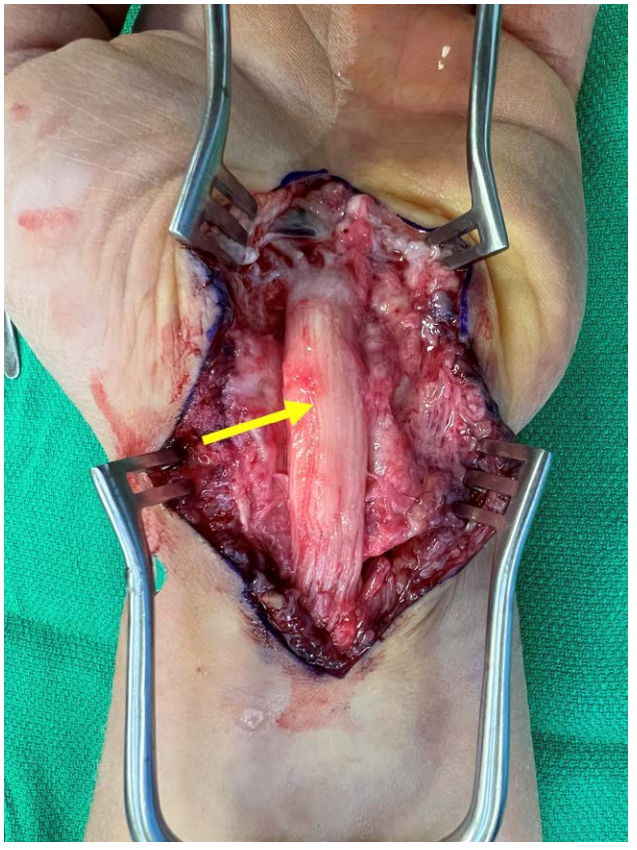

Fig. 2. Nerves in situ. Yellow arrow points toward median nerve with AxoGuard nerve wrap in place.

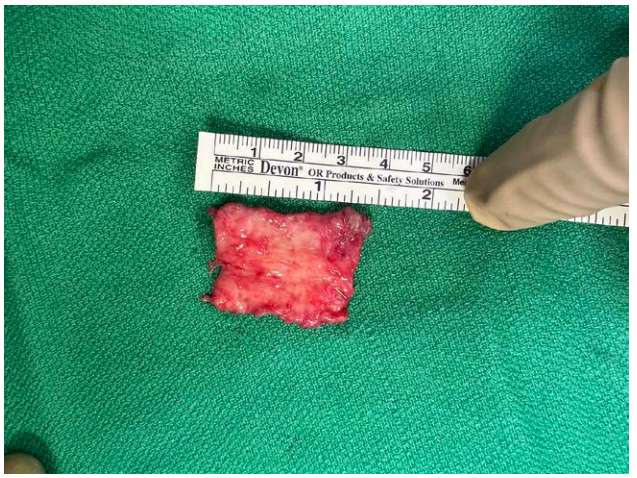

Fig. 3. Explanted specimens. AxoGuard nerve wrap from median nerve. The specimen was 2.5 cm × 3.5 cm.

if needed was discussed, but the patient did not want any additional incisions for flap harvest. Additionally, coverage was needed proximal to the wrist crease, and neither of the flap options would provide that. An allograft was selected to help reduce the risk of postoperative neuroma formation because the patient had a poor response to the AxoGuard nerve protector. NuShield human placental allograft was used on the median nerve at the area of excision of the inflamed connective tissue. Upon further inspection of the ulnar nerve in the hand and wrist, there was no evidence of fascicular or epineural injury; therefore, no wrapping of the ulnar nerve was performed at this level.

Postoperatively, she showed improved range of motion of the left hand and continued paresthesias of the ring finger but otherwise improved at follow-up after 6 months. Longer-term results are pending.

DISCUSSION

Nerve wraps can be harvested from an autologous vein but have also been bioengineered from materials such as

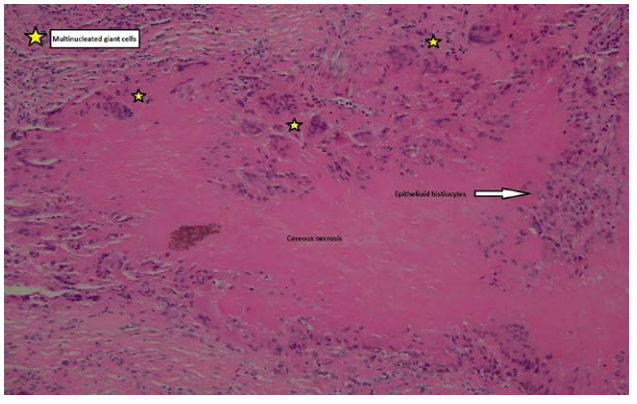

Fig. 4. Histological specimen from median and ulnar nerve AxoGuard wrap. Higher magnification revealed multinucleated giant cells (yellow stars), epithelioid histiocytes (white arrow) with intervening caseous necrosis.

type I collagen, polyvinyl alcohol, and porcine intestinal submucosa, which are now clinically licensed.[5] However, there is a lack of comparative data for functional outcomes and complication profiles between different nerve wrap types. Here, we aimed to describe a case of epineural inflammation following AxoGuard small intestinal submucosa placement around the median and ulnar nerves for recurrent compression neuropathy.

Autograft wraps using the great saphenous vein have been extensively studied for revision compression neuropathy and showed promising results in human and animal studies.[6] The vein's biological compatibility facilitates a smooth gliding surface while simultaneously decreasing fibrotic adhesion formation between the venous intima and epineurium.[1] However, autograft wrap usage is limited by donor site complications and the longer operative time compared with allograft or xenograft wraps. Conversely, a concern with allograft and xenograft nerve wraps is immune tolerance in the host. When rejection does occur, it is on the acute timeline ranging from 3 weeks to 6 months. This process is mediated by macrophages, which innately promote inflammation and recruit adaptive immune cells.

Xenograft wraps are composed of either a mixture of type I and III or purely type I collagen. Wraps made up of mixtures are derived from porcine small intestine submucosa, whereas those made up of solely type I collagen are derived from bovine tendon.[1] Xenograft wraps provide the advantage of no donor site morbidity, but concerns arise from the potential to generate a host immune response or transmit disease. Still, no studies investigating xenograft processing techniques and outcomes for recurrent compression neuropathy found any evidence of rejection or complications.[3,7] The AxoGuard nerve wrap was used in our patient and is the first reported case of rejection that we are aware of.

Human amniotic and placental membranes comprise allografts used as nerve wraps for recurrent compression neuropathy. In addition to lack of donor site involvement, allograft nerve wraps possess inherent anti-inflammatory and anti-fibrotic properties. The membrane represents a novel option for nerve wrapping, and animal studies have demonstrated reduced perineural fibrosis and adhesion formation as compared with those in controls.[1] However, most allograft nerve wraps are non-FDA-indicated, and unfavorable results have been seen when amniotic wraps were placed around flexor tendons, which result in inflammatory responses and local fibrosis.[8] This raised caution for use of allografts as nerve wraps, but the two studies investigating their use reported subjective and objective improvement without the need for subsequent revision procedures.[9,10]

CONCLUSIONS

This case report explored the use of a xenograft nerve wrap in treatment of revision compression neuropathy, which resulted in an unfavorable outcome. As a salvage to reduce postoperative pain, amnion-based wraps were found to mitigate the complication and could provide superior results when compared with those achieved using xenograft-based nerve wraps. The available literature is largely case series or reports, which exemplifies the need for well-designed analytical studies to determine the optimal barrier method for revision compression neuropathy

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