A Novel Use of Umbilical Perinatal Graft in Subungual Exostosis Resection

Juan Carlos Goez, DPM*
Roger Lee Kilfoil, Jr, DPM*
Chen-An Wang, DPM*
Zachary Sax, DPM*
Farzana Arif, MD†

Nail pathologies have a broad range of origin and may sometimes be complicated in presentation or clinical course, specifically when the pathology remains recalcitrant after treatment. In this case report we discuss a pathologic disorder that was initially misdiagnosed as a pyogenic granuloma surrounding an ingrown nail but was later found to be a benign neoplastic bone growth, Dupuytren exostosis, also known as a subungual exostosis. Operative treatment was deemed appropriate for the patient, and the exostosis was resected, leaving a soft-tissue void at the distal toe. The remaining void was filled with a perinatal graft, the use of which has been deemed effective anecdotally in both chronic and acute lower-extremity wounds but has not been widely discussed in the lower-extremity literature. This graft was placed to aid in wound healing over a potentially difficult wound bed. As amniotic, chorionic, and umbilical grafts become more prevalent in lower-extremity surgery, its antitumor effects should be further explored and published. This is the first case report, to our knowledge, of the successful use of a perinatal graft in the setting of a bone tumor, and it demonstrates that certain benign neoplasms can be treated with resection and placement of a perinatal graft while helping to prevent chronic wounds at surgical sites. (J Am Podiatr Med Assoc 110(4): 1-5, 2020)

Subungual tumors are well documented in the modern literature and represent a variety of malignant and benign processes that can affect the subungual region of the feet and hands. In the case of ossifying lesions, radiographs are of paramount importance in initial diagnosis of the tumor. Accurate diagnosis of the subungual tumor must then be confirmed by histopathologic examination via biopsy or after the tumor has been excised.[1] In cases of skin lesions with underlying osseous pathology, there may be an increased incidence of surgical site complications and subsequent chronic ulceration. Graft application in these particular cases can avert further intervention.

Subungual exostoses are benign osteochondral neoplasms that occur on the distal phalanx and typically result in painful deformities that may be compounded by an underlying infection of the digit. Patients typically present with a painful soft-tissue mass on the distal digits that may alter the appearance of the nail.[1] This nonspecific presentation can lead to a misdiagnosis of onychocryptosis, onychomycosis, and paronychia. These tumors currently have an unknown etiology, but trauma and chronic infection are possible origins.[2] They may also be treated via complete resection, with a recurrence rate as low as 6%, although in doing so the nail matrix may become damaged, leading to dystrophic nail growth.[1] A systematic review by DaCambra et al[3] concluded that there is currently weak evidence to guide both surgical and conservative management of subungual exostoses. In addition, the study highlighted onychodystrophy as the most common postoperative sequela after exostectomy.[3]

Use of a perinatal graft is not well documented in the setting of musculoskeletal tumors in general, and neither has it been characterized in the treatment of subungual exostoses. In addition, the

*Department of Surgery, South Nassau Communities Hospital, Oceanside, NY.
†Department of Pathology, South Nassau Communities Hospital, Oceanside, NY.
Corresponding author: Roger Lee Kilfoil, Jr, DPM, Department of Surgery, South Nassau Communities Hospital, 830A Atlantic Ave, Baldwin, NY, 11755. (E-mail: Rogerkilfoiljr@gmail.com)

use of these products has historically been contraindicated in patients with previous diagnoses of cancers due to the regenerative nature of such grafts rich in growth factors that may cause unwanted growth of any of the latent neoplastic cells. Recent evidence suggests that human amniotic membrane grafts have anticancer effects. The study by Nikenejad et al[4] in 2014 showed that amniotic membrane grafts inhibited angiogenesis, induced apoptosis, and arrested the cell cycle of tumors. Based on the current evidence, it is believed that amniotic membrane grafts have the ability to mediate anticancer effects through HSP90, a protein that prevents cancer cells' progression from cell arrest through apoptosis while encouraging angiogenesis.[4,5] The exact mechanism that amniotic membrane grafts have on cancer cells is still unknown and further research is needed, but it is hypothesized that this anticancer trait arises from the targeting of tumor cells and suppressing further growth by expressing cytotoxic cytokines specific to the tumor.[6,7] Cryopreserved umbilical graft use in the lower extremity has been reported in the treatment of tendinitis of the Achilles, anterior tibial, peroneal, and posterior tibial tendons, as well as on chronic wounds.[8,9]

The primary source of these anti-inflammatory cytokines and the aforementioned tensile strength is derived from the amnion layer of these grafts. This layer consists of an accumulation of cuboidal epithelium stratified with type I and III collagen networks containing a mix of fibroblasts and mesenchymal stem cells. All of these components contribute a myriad of various growth factors, including, but not limited to, vascular endothelial growth factor, hepatocyte growth factor, keratinocyte growth factor, transforming growth factor β basic fibroblast growth factor, and platelet-derived growth factor.[4,10-12] Of paramount importance to this study are mesenchymal stem cells' ability to improve bone regeneration in in vitro and in vivo studies, aiding in the regeneration of osteoid scaffolding.[13] The benefits derived from these factors are maintained with the advent of cryopreservation, which the graft used in this study had undergone, further contributing to the ability to fill the soft-tissue and osseous void created from the exostosis resection.

This increased tensile strength afforded to sites treated with these membrane grafts, as well as the presence of scar-limiting matrix proteins, makes perinatal grafts good candidates for the surgical treatment of subungual exostoses. They can be uniquely placed in areas with increased shearing force and heightened demand for stability, most specifically on areas that participate in active propulsion. For these reasons, the use of a perinatal graft was deemed an exemplary modality to treat the surgical void created by excision of a subungual exostosis found in a patient seen by our service.

Case Report

A 39-year-old woman with an unremarkable medical history presented with a 2-month history of an unsuccessfully treated nail pathology. The patient had dropped a large glass bottle onto her left first toe 2 months earlier that was misdiagnosed and treated as a paronychia with no improvement. Physical examination revealed a swollen, tender, erythematous hallux consistent with paronychia (Fig. 1). However, on radiographic examination an ossified projection off of the medial aspect of the distal phalanx on the affected toe was revealed. The radiograph was consistent with subungual exostosis, and the patient was subsequently scheduled for surgical removal of the exostosis in an operative setting. Anticipating a large soft-tissue defect that would remain at the site overlying the excised bony prominence, an umbilical-derived perinatal graft (Clarix; Amniox Medical Inc, Miami, Florida) was prepared for use.

The left hallux wound was examined while the patient was under general anesthesia in an operative environment. On active expression of the operative site, 0.5 mL of purulence was demonstrated, which was then subsequently cultured. The soft-tissue defect was then excised and removed from the field for pathologic examination. The exostosis was then made visible and freed from surrounding soft-tissue structures. The fin-shaped osteophyte was removed with a double-action bone cutter and passed from the field for pathologic examination (Fig. 2). A clear margin was then excised from the distal phalanx, at which point the remaining bone was rasped to produce a smooth surface of medullary bone. The wound was then copiously irrigated, revealing an open wound measuring $2 \times 2 \times 1$ cm with exposed bone at the base. The umbilical graft was cut into two pieces, leaving one layer as an onlay over the exposed bone and the second layer sutured to the surrounding skin and nail (Fig. 3).

The patient was then bandaged with nonadherent gauze and a dry sterile dressing. On discharge the patient was instructed to return to the office in 1 week. The wound was evaluated weekly, and the sutures were removed at the second week's



Figure 1. Painful hallux at presentation with associated radiographic image.

postoperative visit. The patient was followed regularly, and the toe healed uneventfully. At 12-month follow-up the wound had healed with very little scarring and no radiographic or clinical recurrence of the tumor (Fig. 4).

Pathologic Specimen

Sections of lesional tissue show the skin with trabecular bone and fibrocartilaginous overgrowth. There are areas where lamellar bone are flush with dermal tissue without fibrocap. Findings were consistent with subungual exostosis (Figs. 5 and 6).

Although early lesions have been known to show calcification of hyaline cartilage, mature lesions have lamellated trabecular bone with a thin distal fibrocap that may be imperceptible and without a distinct perichondrial layer.[6]



Figure 2. Intraoperative photographs of resection of exostosis.

Discussion

The use of cryopreserved umbilical cord has emerged as a promising treatment option for complex foot wounds. Human placental membranes are rich in extracellular matrix proteins, growth factors, and cytokines that are known to induce osseous scaffolding, angiogenesis, and dermal fibroblast proliferation for ideal wound repair and regeneration.[11] The myriad of positive attributes found in these grafts are particularly helpful in



Figure 3. Placement of the amniotic umbilical graft.



Figure 4. Affected hallux 12 months after resection and graft placement.

patients with a propensity for chronic wounds or in those with more complicated wound beds.

Previous studies using defects in the parietal bone of rats compared with scaffold alone showed early bone regeneration, including an increase in

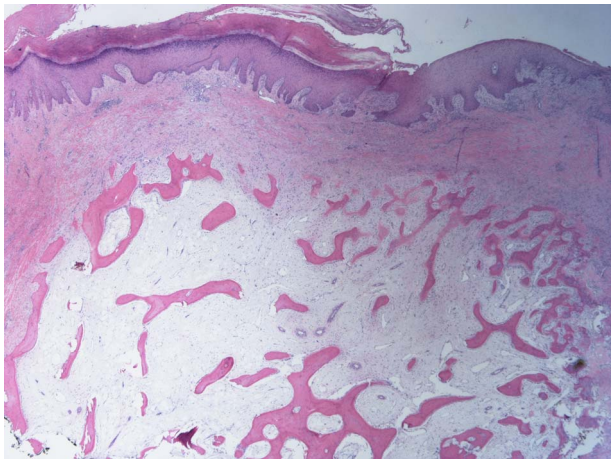


Figure 5. Low-power view showing dermal tissue with normal trabecular bone and fibrocartilaginous overgrowth consistent with subungual exostosis.

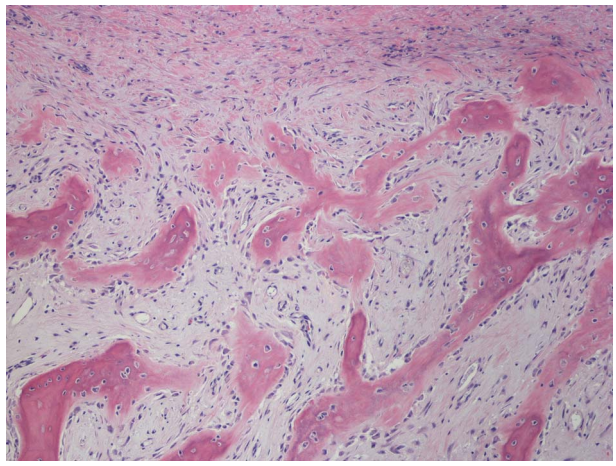


Figure 6. High-power view showing lamellar bone without fibrocartilaginous cap flush with dermal tissue without fibrocap.

osteogenic gene expression in human dental pulp stem cells in co-culture.[15] This characteristic increase in localized bone regeneration at the graft site was apropos in our case of exostectomy due to the large osseous void after the procedure. We believe that ample bone regrowth at the surgical site on follow-up imaging studies was a direct result of the propensity for these grafts to create short- and long-term osseous scaffolding. In addition, the dermal and epidermal remodeling exhibited considerable coalescence with surrounding tissues, reaffirming the site's ability to withstand normal loads during active propulsion. This may have been derived from a combination of the graft's inherent growth factors and its robust tensile strength.

In cases of lower-extremity wounds, either iatrogenic or secondary to patient comorbidities, these grafts allow for a breadth of use while maintaining the integrity of the surrounding and underlying tissue. Using these grafts may also aid in osseous and soft-tissue remodeling while preventing acute inflammation and breakdown at the very sites they are placed. Their use in areas of weightbearing as well as in sites that regularly tolerate shearing and tensile forces has promising potential and deserves further study.

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