Maxillary sinus grafting is generally a safe procedure. However, intraoperative complications, as well as early and late postoperative complications, may occur. Included in the latter group are graft infections that can be triggered by peri-implantitis. The aim of the present study was to report three cases of late maxillary sinus graft infections and to histologically evaluate the effects of peri-implantitis in the grafted area. In peri-implantitis cases in grafted sinuses, the sole removal of the implant along with accompanying debridement of the infected area may not be sufficient to resolve the infection, and a more-aggressive treatment may be necessary.

Late Maxillary Sinus Graft Infections Due to Peri-implantitis: Case Reports with Histologic Analysis

Tiziano Testori, MD, DDS1/Hom-Lay Wang, DDS, MSD, PhD2
Stephen S. Wallace, DDS3/Adriano Piattelli, MD, DDS4
Giovanna Iezzi, DDS, PhD5/Lorenzo Tavelli, DDS6
Margherita Tumedei, DDS, PhD6
Raffaele Vinci, MD, DMD, MFS7
Massimo Del Fabbro, MSc, PhD8

Maxillary sinus grafting is generally a safe procedure. However, intraoperative complications, as well as early and late postoperative complications, may occur. Included in the latter group are graft infections that can be triggered by peri-implantitis. The aim of the present study was to report three cases of late maxillary sinus graft infections and to histologically evaluate the effects of peri-implantitis in the grafted area. In peri-implantitis cases in grafted sinuses, the sole removal of the implant along with accompanying debridement of the infected area may not be sufficient to resolve the infection, and a more-aggressive treatment may be necessary. Int J Periodontics Restorative Dent 2021;41:903–910. doi: 10.11607/prd.4558

Maxillary sinus grafting is generally a safe procedure, but complications may occur both intra- and postsurgically.1–10 The most common intraoperative complications are sinus membrane perforation and hemorrhage.10,11 Both can be managed intraoperatorically and generally do not require premature termination of the surgical procedure.12–17

Sinusitis, rhinosinusitis, fistulae, migration of the implant into the maxillary sinus, and graft infection are among the most common postsurgical complications.7–10,18–22 Peri-implantitis can lead to graft-associated infection21 with its usual related symptoms and signs.22 The management of such events is often difficult and can be associated with significant discomfort to the patient. An additional surgery is often required to remove the infected grafts, followed by a new grafting procedure. In a clinical study,21 the authors highlighted this problem by showing clinical cases of sinus augmentation in which late infections occurred and subsequently spread into the body of the graft. As a result, the patients had to undergo removal of both the implants and the grafting material.21

A better understanding of the mechanisms of contamination, the biologic response of different bone substitutes to infection, as well as in the possible therapeutic options
to successfully address such complications would improve management of these complex cases. Thus, the present study aims to report on three cases of maxillary sinus graft infection in which xenograft was used for augmentation and to histologically evaluate the effects of peri-implantitis in the grafted area.

Clinical Cases

Case 1

A nonsmoking 52-year-old patient received bilateral sinus elevation with particulate deproteinized bovine bone (0.25- to 1-mm size, BioOss, Geistlich) and simultaneous placement of three implants (NT Implant, Zimmer Biomet) on each side. Treatment was completed 8 months after implant placement with the placement of a three-unit cemented bridge on both sides. Seven years later, the patient complained of discomfort and pain in the maxillary left quadrant. Clinical examination revealed a probing depth of 10 mm around the implant in the second premolar position (site 25; FDI tooth-numbering system) with bleeding on probing and suppuration. Radiographic examination revealed a peri-implant radiolucency (Fig 1a). After removing the vestibular bony wall, the graft in the region of the extracted implant was found to be loosely embedded in connective tissue and unattached to the bony walls. The area was debrided with a surgical curette and copiously flushed with sterile saline solution. The graft that was attached to the bony wall was partially sliced with a piezoelectric saw until the surgeon could see bleeding in the grafted bone (Fig 1c). Postoperative CBCT imaging was acquired. A blood clot was allowed to form, a collagen membrane was placed on the vestibular bony wall, and the site was closed with resorbable sutures. The original three-unit fixed cemented prosthesis was modified into a screw-retained prosthesis. Healing was uneventful, and the dull pain and swelling disappeared within 3 weeks. A CBCT scan at 12 months postoperative showed a healthy sinus, and the patient was clinically symptom-free (Fig 1d).

The retrieved specimens were immediately stored in 10% buffered formalin and processed to obtain thin ground sections with the Precise 1 Automated System (Assing). Biopsy samples were dehydrated in an ascending series of alcohol rinses and embedded in a glycolmethacrylate resin (Technovit 7200 VLC, Kulzer). After polymerization, specimens were initially sectioned longitudinally along the major axis of the implants to a thickness of about 150 µm using a high-precision diamond disc and then ground down to about 30-µm thickness. The percentage of newly formed bone, marrow spaces, and residual biomaterial were estimated under a light microscope (Laborlux, Leitz) connected to a high-resolution video camera (KY-F55B 3CCD, JVC) and interfaced to a monitor and PC (Pentium III 1200 MMX, Intel). This optical system was associated with a digitizing pad (Matrix Vision) and a histometric software package with image-capturing capabilities (Image-Pro Plus, Media Cybernetics).

Histologic results

The investigated sample was composed of four bone fragments. One consisted only of compact bone
with few marrow spaces (Fig 2a), while the remaining three fragments were made up of trabecular bone with marrow spaces and several remnants of biomaterial partially or completely in contact with bone tissue (Fig 2b). Bone trabeculae were of different degrees of maturation, with numerous areas of remodeling.

Areas of mature bone were less intensely stained due to a relatively low affinity for acid fuchsin, while the newly formed bone was more intensely stained. Different stages of bone maturation were identified based on the intensity of staining.

Residual biomaterial particles were surrounded by native bone in many fields. No gaps at the bone biomaterial interface could be observed. In addition, it was possible to detect different stages of bone maturation with the presence of reversal lines and osteons in close proximity to the particles. Wide osteocyte lacunae were present in the areas of new bone formation. In the marrow spaces, many small- and large-sized vessels and moderate inflammatory infiltrate were seen (Fig 2c). Multinucleated cells were observed in a few fields (Fig 2d) despite the clinical signs of infection that the patient presented. In the fragment consisting only of compact bone, inflammatory cells were not evident.

Case 2
A 72-year-old nonsmoking patient was referred for treatment of peri-
implantitis affecting an implant (Astra Tech Dental Implants, Dentsply Sirona) in the maxillary left second premolar position that was supporting a three-unit fixed bridge. The maxillary left sinus was grafted with deproteinized bovine bone (0.25- to 1-mm size, Bio-Oss) 8 years prior. The patient’s chief complaint was mild discomfort in the area. Upon probing, the site exhibited suppuration and a probing depth of 7 mm. During the intraoral examination, a lack of keratinized peri-implant soft tissue was evident. It can be postulated that this factor may have played a role in the onset of peri-implantitis, even if there is limited evidence that a lack of keratinized mucosa is a risk factor. Radiographic assessment revealed a radiolucency around the implant in the implant’s position (Fig 3a). A hopeless prognosis was determined, and the implant was removed by the implantologist who performed the maxillary sinus elevation (T.T.). At the time of implant removal, the surgeon did not conduct a CBCT examination to check the patency of the sinus ostium. The site was debrided with a curette until the surgeon could clinically detect that no additional loose graft particles were present, and hard, bony walls were detected. The area was flushed with sterile saline, a clot was allowed to form, the site was closed, and the patient was placed on antibiotics (Augmentin; 1 g every 12 hours for 5 days). The adjacent implants did not show any sign of peri-implantitis.

The three-unit bridge was converted into a two-unit prosthesis and cemented with provisional cement (Temp-Bond, Kerr). Four weeks later, a fistula was detected in the area (Fig 3b). Because CBCT imaging was not conducted, it can only be assumed that a lack of ostium patency may have been the cause, highlighting the importance of checking ostium patency radiographically before removing a tooth or an implant close to the sinus. The patient was symptom-free other than a dull pain stimulated by intraoral finger pressure. Due to the dull pain under pressure and the presence of the fistula 4 weeks after implant removal, the patient was referred to one of the authors (T.T.). A CBCT scan was taken and showed thickening of the sinus membrane and a blocked sinus ostium (Fig 3c). The patient was advised to undergo the same type of surgical intervention described in the previous case. However, the patient refused. One year later, the patient returned to the same office complaining of a mild spontaneous pain in the area, a bitter taste at the back of the throat upon waking in the morning, and an occasional malodor. A CBCT
evaluation revealed a radiopacity in the maxillary and ethmoidal sinuses (Fig 3d). The patient was prescribed antibiotics (Augmentin; 1 g every 8 hours for 5 days) and referred to an ear, nose, and throat (ENT) specialist, who scheduled the patient for a functional endoscopic sinus surgery (FESS) along with graft removal using an intraoral approach.

Upon resolution of the symptoms following antibiotic therapy, the patient did not follow through with the suggested surgical therapy. Almost a year later, the patient returned with the same symptoms. At this time, the maxillary and ethmoidal involvements were more accentuated, and the graft showed signs of colliquation with dark spots inside the graft when compared to the previous CBCT. At this point, the patient agreed to undergo surgery in order to prevent more severe complications and was scheduled for an FESS with intraoral graft removal under general anesthesia in a hospital setting. Histologic evaluation could not be performed because all of the graft was colliquated at the time of intervention. Upon recovery, a CBCT taken 4 months after the surgery showed a resolution of the radiopacity in the ethmoidal sinus. In the maxillary sinus, a radiopacity was still present (Fig 3e). Despite this radiographic finding, the patient was symptom-free. At this point, the patient could not be followed-up with, and it was not possible to check for re-pneumatization after sinus graft removal in conjunction with FESS. This case highlights that the longer surgical intervention is delayed, the worse the clinical situation becomes.

Case 3

This patient also had an implant site grafted with deproteinized bovine
bone particles (0.25- to 1-mm size, Bio-Oss), which was performed 7 years prior to the present observation. The patient presented with pain and swelling in the maxillary left posterior sextant. Upon probing, there was suppuration at the three implants in the canine and first and second premolar positions of the maxillary left quadrant. The implant in the lateral position showed healthy peri-implant tissues (Fig 4a). The three implants in the maxilla affected by peri-implantitis were removed. Even after the soft tissue completely healed, the patient still exhibited symptoms, and the CBCT demonstrated extensive maxillary involvement. The patient was sent for an ENT evaluation, and the specialist recommended hospitalization to undergo an FESS with the removal of the infected graft via an intraoral approach. The patient was followed up until resolution of symptoms. A CBCT showed complete resolution of the sinus infection. However, an area of incomplete bone remineralization was noted at the site where the implants were removed (Fig 4b).

An implant was placed in the tuberosity region and connected to the mesial implant in the lateral incisor position in order to support a fixed prosthesis. The patient was then enrolled in a supportive maintenance program and was seen once every 3 months.

**Discussion**

The occurrence of late bone graft infection could likely be a consequence of a microbial contamination of the implant surface that propagates apically and circumferentially around the implants. Its onset and severity might be also related to the type of graft material used for sinus floor augmentation. It has been suggested that a graft composed of 100% autogenous bone, or a bone replacement graft that is completely or substantially replaced with newly formed autogenous bone during the healing period, may lead to the formation of a mature trabecular bone with an extensive vascular supply similar to native bone. In such a situation, the healed graft should be able to provide an efficient immune defense against a possible bacterial contamination of the graft with microorganisms derived from an associated peri-implantitis lesion.

In the case of bone graft materials that are nonresorbable or minimally resorbable, as is the case with some bone substitutes of xenogeneic or alloplastic origin, the immunologic potential of the resulting graft may be quite different from that of native bone, as demonstrated in the present histologic reports. During the healing process, the granules of such minimally resorbable materials are surrounded by newly formed autogenous bone. There is evidence that these granules may persist for as long as 20 years, decreasing in percentage but not completely disappearing. The present study showed that implants placed in augmented sinuses with clinical and radiographic signs and symptoms of peri-implantitis have an inflammatory reaction that may disseminate into the whole graft if the peri-implant infection reaches
the grafted material inside the sinus. Comparative histologic studies showed that while vascular invasion of bovine-derived xenograft does occur, it can be reduced with respect to other materials. Based upon the present three case reports and the above findings, the present authors suggest grafting a layer of autogenous bone at the level of the sinus floor to act as a biologic cushion, distancing the biomaterials from possible contamination and thereby preventing a future peri-implantitis infection from spreading within the body of the graft. The concept of using layered bone grafting materials for sinus grafting was proposed by Misch et al over a decade ago. The idea is to utilize graft properties in different layers of grafting in order to take advantage of the maximum benefits of each material. First, there must be at least 5 mm of autogenous bone close to the crestal ridge (either remaining bone height or a combination of remaining bone and additional autogenous bone that is obtained either from a tuberosity or other jaw donor sites, such as the ramus or the area anterior to the sinus cavity). The osteogenic potential of this autogenous grafted layer will facilitate quick conversion into host bone and will function similarly to natural bone, not only expediting healing (implant stability) but also minimizing any potential risk of early or late infection. The middle layer should use a mixture of cortical and cancellous (4:1 ratio) allograft with an osteoinductive capacity so that, over time, it will slowly convert to the host bone for better bone-to-implant contact and long-term stability. The top layer (directly subjacent to the sinus membrane) should be a layer of xenograft (most likely bovine hydroxyapatite) mixed with the remaining allograft so that the osteoconductive and slow resorption properties help maintain the space. Although there are different xenografts with varying compositions, from a biologic point of view, a xenograft containing hydroxyapatite either does not completely resorb or takes a long time to resorb. As stated above, this type of slowly resorbing bone graft may have granules that persist even after 20 years, which was the situation observed in the current report.

The long-term persistence of minimally resorbable biomaterials preserves the graft volume over time and provides mechanical support to the osseointegrated implants, which is clearly a positive effect. However, it can be hypothesized that once such biomaterial undergoes bacterial contamination, if the vascular network does not achieve a sufficient extension within the graft, grafts composed only of bovine bone or other nonresorbable graft materials are potentially more vulnerable to infection due to the immune defense being less efficient than it would be within autogenous bone. Thus, there is a risk that once these materials become infected, the infection could easily propagate within the graft, leading to extensive or total graft failure. For future studies, the present authors propose that a layer of autogenous bone should be placed at the level of the sinus floor when a minimal quantity of crestal bone is present (1 to 2 mm). The aim of this autogenous graft layer would be to create a buffer zone of native bone in order to limit the spread of infection within the graft in case peri-implantitis develops. Further clinical studies are needed to confirm this hypothesis.

Conclusions

If a patient presents with a peri-implant infection in a sinus previously elevated with bone biomaterials, the sole removal of the implant and debridement of the area may not be sufficient to treat the infection. A partial or total graft removal may be the treatment of choice if the signs and symptoms of infection persist after removal of the implants and debridement of the site under a proper antibiotic regimen.

Acknowledgments

The authors declare no conflicts of interest.

References


