Case Report

The migration of the bovine-derived xenograft particles: A case series

Hessam Nowzari, Chang Teoh,[1] Angel Emmanuel Rodriguez

Private Practice, Beverly Hills, CA, USA, [1]Private Practice, Central, Hong Kong, China

The work belongs to the *Private Practice, Beverly Hills, CA, USA*

Abstract:

The long-term safety of xenografts and their potential association with disease are valid concerns. Bovine bone substitutes which are by far the most commonly used xenografts in dentistry are not biodegradable. The aim of the present report was to raise awareness on the long-term risks of the bovine-derived xenografts. Patients who experienced clinical complications after xenografting are reported. Patients' demographic, significant medical, and dental findings are reported. Complications included migration/encapsulation/displacement of the graft material, chronic inflammation, and soft-tissue disturbances/fenestrations. Albeit some xenograft complications are not significant enough to compromise the initial outcomes achieved, the xenografted particles seemed to be left intact favoring conditions for migration. The authors observed the inability of the human host to biodegrade the xenograft particles. The intact/migrated bovine bone particles present a risk to patients and may contribute to long-term clinical complications in implant dentistry.

Key words:

Anorganic bovine bone substitutes, bone transplantation, bovine-derived graft, complications, dental implant, maxillary sinus, xenograft

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Address for correspondence:
Dr. Angel Emmanuel Rodriguez, Private Practice, 120 South Spalding Drive, Suite 201, Beverly Hills, CA 90212, USA.
E-mail: angelrdzp@gmail.com

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INTRODUCTION

The frequency of surgeries involving bovine-derived xenografts has increased significantly in implant dentistry. The long-term safety of xenografts and their potential association with disease are valid concerns. Bovine bone substitutes which are by far the most commonly used xenografts in dentistry are not biodegradable. Based on our observations, it seems that the host is unable to degrade and replace the xenograft particles, contrary to the currently accepted "safety" concept of the "slow turnover" of bovine-derived xenografts. However, research reporting about clinical complications remained scarce.[1,2]

Biodegradation is the naturally occurring breakdown of materials by the host biological activity, and phagocytosis is a major mechanism used to remove mineral particles. Mechanical properties of the graft interface and its surrounding tissues are critical for the host response. The microstructural and mechanical properties of the xenograft bovine bone substitutes appear to be quite resistant to humans' capability to degrade it. In cases of clinical complications associated with the intact/migrated xenograft particles, the resolution of the complications is often achieved by the removal of the graft materials. The surgical removal of the migrated xenograft particles requires thorough clinical evaluation, diagnosis, and advanced surgical skills.[1,3,4]

The authors' clinical impression/observations are supported by other studies that have revealed the migration potential of the bovine-derived bone particles after bone augmentation procedures. Seok *et al.* analyzed the mechanisms of migration by histologic section and energy dispersive X-ray microanalysis using *in vivo* animal experiments and evidenced the distant migration of the xenograft (Bio-Oss).[5] The inability of the human host to eliminate the xenograft particles may contribute to the eventual migration/complications associated with the intact xenografted particles.

The aim of the present report was to raise awareness on the long-term risks of the bovine-derived xenograft migration and/or displacement from the surgical site associated with foreign body reactions, encapsulation, chronic inflammation, and soft-tissue fenestrations.

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CASE REPORTS

All patients were provided with the written informed consent documents. Identities of the patients and health-care providers have been excluded from the study. Primary ethical approval was obtained by the competent local authority. Patients' demographic, significant medical, and dental findings are reported. The following descriptions are the overviews of the affected patients.

Case 1

Three years ago, a 34-year-old healthy female was referred for the extraction of maxillary right central incisor and socket augmentation which was performed using xenograft particles (Bio-Oss) sealed with free gingival punch graft. The patient proceeded with her orthodontic treatment which took over 1 year to complete. At the completion of the orthodontic treatment, a Straumann bone level implant was placed in optimal three-dimensional (3D) position together with contour augmentation using xenograft particles (Bio-Oss) covered by a collagen membrane (Bio-Gide). The final position of the implant was confirmed with radiographs. The buccal contour was restored with the grafting procedure uneventfully. Two months after implant placement, implant exposure and insertion of provisional restoration was performed to finalize the soft-tissue contour. Definitive screw-retained single crown was delivered after tissue maturation. At the time of final restoration insertion, xenograft particles were detected at the peri-implant sulcus. Radiographically, migrated xenograft particles were clearly detected "embedded" in the peri-sulcus area [Figure 1].

Case 2

A 70-year-old healthy female patient was referred for a consultation due to a fractured maxillary right lateral incisor. Examination revealed her tissue biotype to be "thin" and the tooth fractured beneath the gingival level with little coronal tooth structure left for a predictable definitive post crown restoration. After careful discussion with the patient, the tooth was removed and a full-thickness flap was raised. The buccal bone was missing. A Straumann NC implant was placed in proper 3D position together with autogenous bone chips covering the exposed implant surface and contour augmentation using xenograft (Bio-Oss Collagen) and covered by a collagen membrane (Bio-Gide). The final position of the implant was confirmed radiographically. The treatment proceeded well uneventfully. At 2 months after implant placement, implant was exposed and a healing abutment was inserted. At the removal of healing abutment, xenograft particles were detected on the buccal side of the future peri-implant sulcus. A provisional screw-retained restoration was inserted. Although the buccal contour was improved with the grafting procedure, a minor depression on buccal aspect was evident. As the patient had a low lip line, a final screw-retained single crown was delivered after soft-tissue maturation. Three years after xenografting, more xenograft particles were noticed surfacing in the peri-implant sulcus at this time [Figure 2].

Case 3

A 45-year-old healthy female was referred to the office with a fractured maxillary right central incisor. Examination revealed her tissue biotype to be "thin" and the tooth fractured below the gingival level with little coronal tooth tissue left for a predictable definitive post crown restoration. The patient had a high lip line and would like to proceed quickly as the existing crown was loose. The treatment plan consisted in extraction with an immediate implant placement and loading. The maxillary right central incisor was removed with atraumatic measures, and a minimal flap was elevated. Although the integrity of the buccal bone was maintained during extraction, the buccal cortical was ≤1 mm. A Straumann regular connection (RC) implant was placed in correct 3D position for a screw-retained implant-supported restoration. The gap between the implant surface and the buccal bone was filled with xenograft (Bio-Oss) particles. Connective soft-tissue graft harvested from the palate was secured on the buccal side subperiosteally by sutures. An immediate screw-retained implant-supported temporary crown was fabricated and connected to the implant. It was relieved from any occlusal contact. The treatment proceeded uneventfully, and the impression was taken 3 months after implant placement. Upon detachment of the temporary restoration on implant, multiple xenograft particles were clearly embedded in the peri-implant sulcus, although the patient had no discomfort associated. The final position of the implant was confirmed with radiograph. The treatment proceeded well uneventfully. After two months of healing post implant placement, the dental implant was exposed and healing abutment was inserted. At the removal of healing abutment, a few xenograft particles were found on the buccal side of the future peri-implant sulcus. A provisional screw-retained restoration was inserted for peri-implant sulcus development. Although the buccal contour was improved with the grafting procedure, a minor depression on buccal aspect was evident. As the patient had a low lip line, a final screw-retained single crown was delivered after soft-tissue maturation. Xenograft particles were noticed surfacing in the peri-implant sulcus 6 years after grafting procedures [Figure 3].

Case 4

A 55-year-old healthy female was referred for an ailing maxillary right central incisor carrying a post crown restoration. The tooth affected by periapical periodontitis had been giving her swelling and discomfort. The long-term prognosis was doubtful, and after careful discussion, she decided to replace the tooth with an implant restoration. Examination revealed that her tissue biotype was "thin." Following extraction, in order to allow the area to heal before implant placement, a temporary cantilever fixed restoration was provided using maxillary premolar as abutment. At 6 months post extraction, the buccal soft-tissue contour showed collapse. A Straumann bone level implant was placed in correct 3D position with autogenous bone chips on implant surface. Contour augmentation was carried out with composite mixture of autogenous bone chips and xenograft (Bio-Oss) particles. The graft was covered by a collagen membrane (Bio-Gide). The buccal contour was fully restored with the grafting procedure, and the treatment proceeded well uneventfully. The implant was exposed 6 weeks after implant placement, and a provisional restoration was inserted to further develop the soft-tissue contour. At the time of final restoration insertion, xenograft particles were detected at the peri-implant sulcus. The implant restoration successfully restored esthetic and function together with new restoration on premolar. In the radiograph of final restoration, 3 years post xenografting, migrated xenograft particles were clearly detected "floating" in the peri-sulcus area [Figure 4].

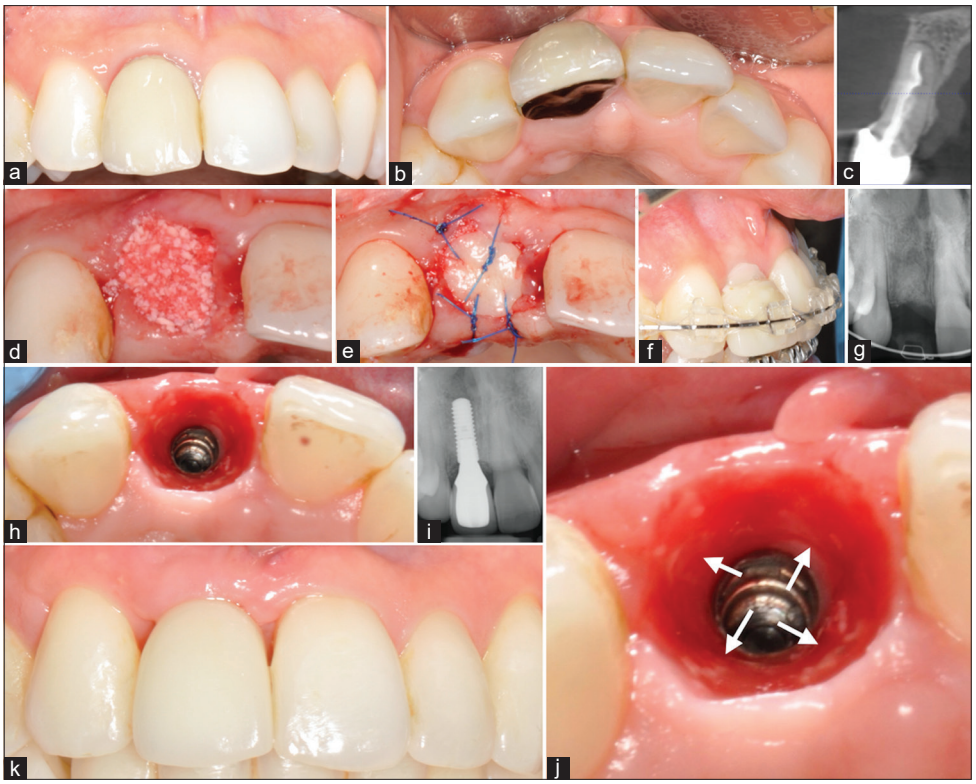

Figure 1: Clinical photography and radiograph from baseline (a-c); Bovine-derived xenograft (d); Gingival graft (e); Profile clinical photograph, notice alveolar ridge collapse, regardless of augmentation materials (f); Radiograph of the xenografted site (g); Occlusal view (h); Implant radiograph at 3-year follow-up (i); Clinical photographs from final result and the intact/migrated xenograft particles (j and k)

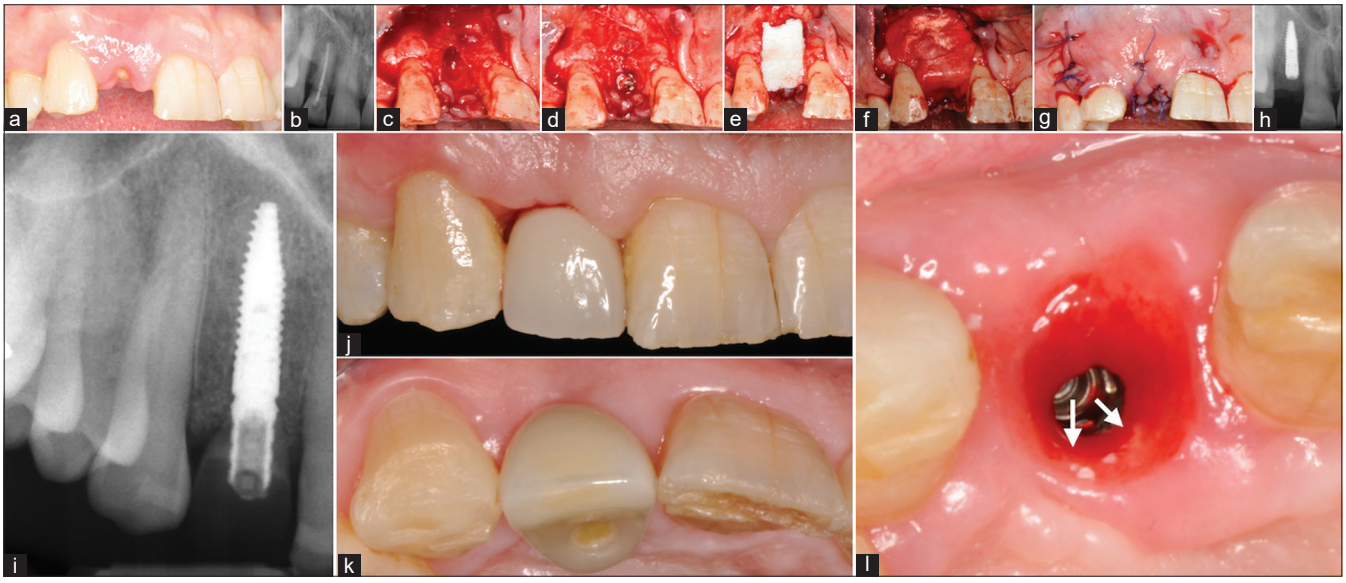

Figure 2: Clinical photography and radiograph from baseline (a and b); Post extraction (c and d); Bovine-derived xenograft (e and f); Flap sutured (g); Final implant position (h); Implant radiograph at 3-year follow-up (i); Clinical photographs from final result and the intact/migrated xenograft particles (j, k, and m)

Case 5

A 62-year-old healthy female patient was referred in April 2018 after removal of the left mandibular lateral incisor. The tooth was removed after an unsuccessful root canal treatment. Examination revealed that her tissue biotype was "thin" type. There was a small depression on the buccal contour, and radiograph indicated minor bone loss in the left mandibular lateral incisor area. After careful discussion with the patient, the treatment plan was to replace the missing left mandibular lateral incisor with dental implant. A full-thickness flap was elevated to expose the alveolar bone in the left mandibular lateral incisor area, and a collapse of the buccal contour was evident. A Straumann SC implant was placed in correct 3D position with no direct implant surface exposure, although

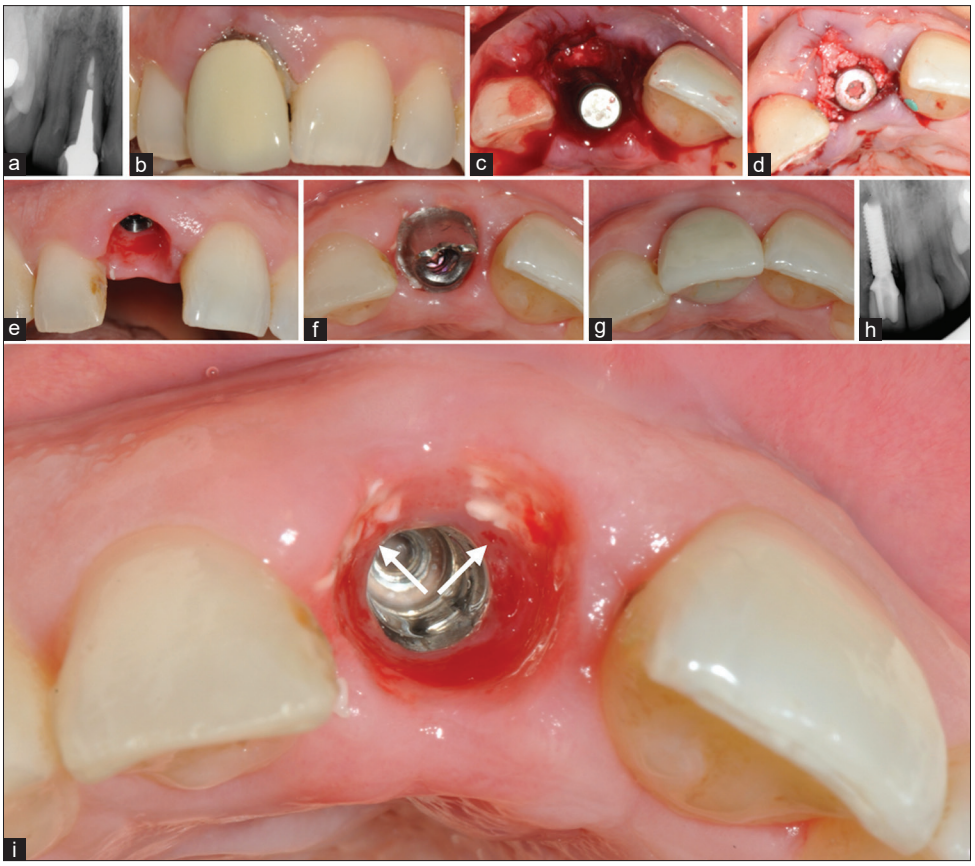

Figure 3: Radiograph and clinical photography at baseline (a and b); Implant placement and xenograft procedure (c and d); Final screw-retained single crown and radiograph (e-h); Notice the intact/migrated xenograft particles at 6-year follow-up (i)

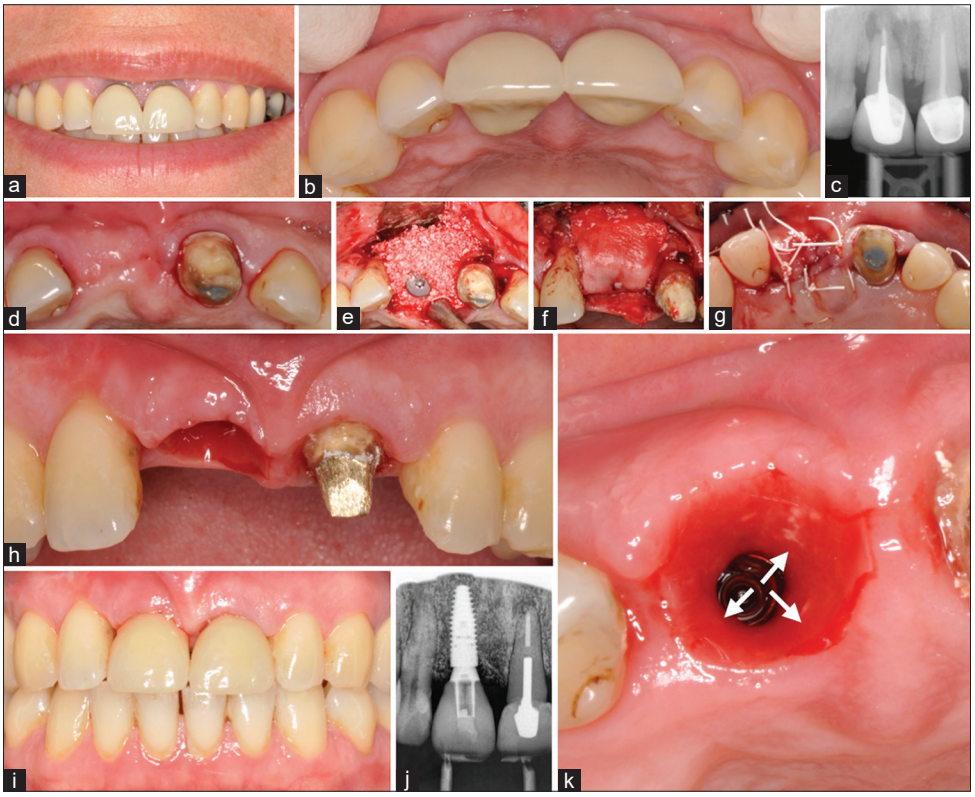

Figure 4: Clinical photography and radiograph from baseline (a-c); Implant placement with simultaneous xenograft surgical procedure (d-g); Clinical photograph and periapical radiograph from final result (h-j); Observe the intact/migrated xenograft particles (k)

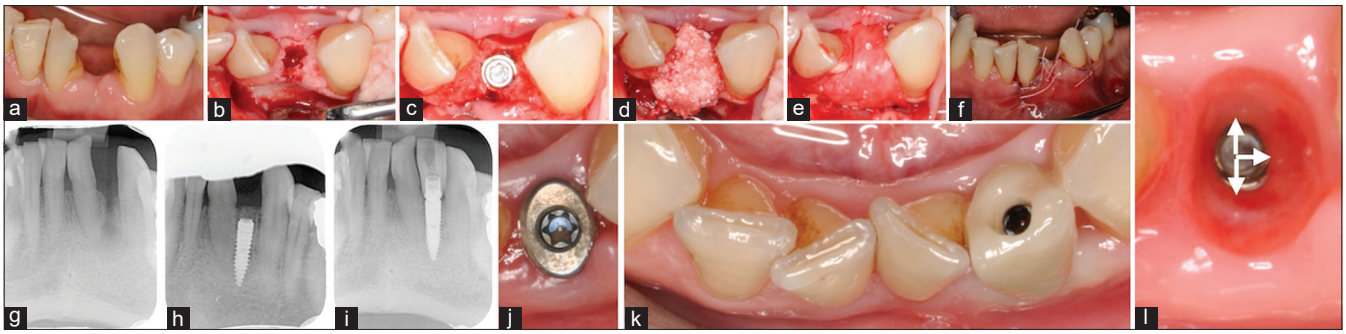

Figure 5: Clinical photography from baseline (a); Implant placement with simultaneous xenografting (b-f); Radiographs from baseline to 2 years after xenografting (g-i); Healing abutment (j); Clinical photograph from final result (k); Notice the intact/migrated xenograft particles (l)

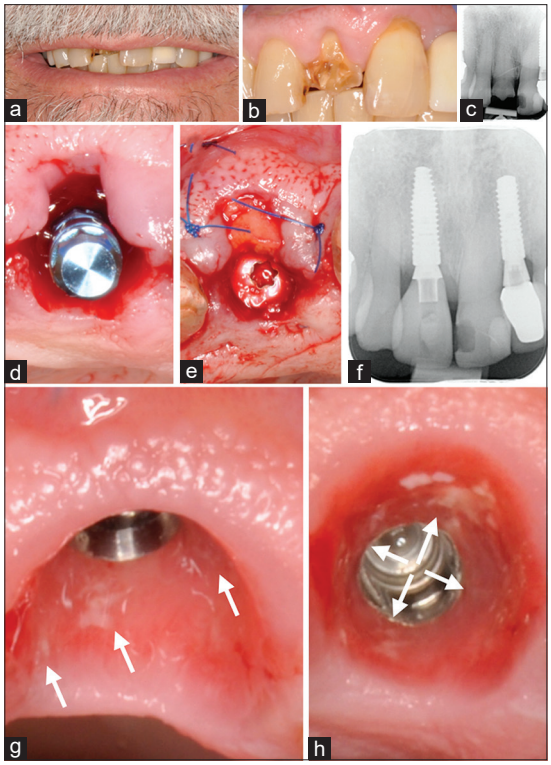

Figure 6: Clinical photography and radiograph from baseline (a-c); Simultaneous tooth extraction, implant placement, xenografting, and soft-tissue graft (d and e); Final screw-retained restoration and periapical radiograph (f); Radiograph of the final restoration, notice the presence of the xenograft particles in the peri-implant sulcular area. Clinical photographs of the intact/migrated xenograft particles 3 years post xenografting (g and h)

the buccal bone was very thin. Contour augmentation was performed using xenograft (Bio-Oss Collagen) over the implant, which was covered by a collagen membrane (Bio-Gide). A primary tension-free closure was achieved with multiple sutures. The final position of the implant was confirmed with radiograph. The treatment proceeded well uneventfully. Two months after implant placement, implant was exposed and a healing abutment was inserted. A definitive screw-retained implant-supported restoration delivered shortly after the tissue maturation had completed. Two years after xenografting, bone particles were clearly detectable in the peri-implant sulcus [Figure 5].

Case 6

A 71-year-old healthy male patient presented with a fractured right maxillary central incisor. Examination revealed his tissue biotype to be "thick" and the tooth fractured below the gingival level with little coronal tooth tissue left. The patient had a low lip line and would like to replace the fractured right maxillary central incisor with a dental implant. The case was approached by the extraction of the right maxillary central incisor with an immediate implant placement along with immediate loading with a temporary screw-retained crown. The right maxillary central incisor was removed with atraumatic measures and the flap was elevated. The buccal bone was intact, and a Straumann RC implant was placed in correct 3D position for a screw-retained implant-supported restoration. The gap between the implant surface and the buccal bone was filled with xenograft (Bio-Oss) particles. Connective soft-tissue graft harvested from the palate was secured on the buccal side subperiosteally by sutures. An immediate screw-retained implant-supported temporary crown with the correct emergence profile was fabricated and connected to the implant. It was relieved from any occlusal contact. The treatment proceeded uneventfully, and the impression was taken 2 months after implant placement. The buccal contour was fully restored with the soft-tissue graft. Upon detachment of the temporary restoration on implant, multiple xenograft particles were clearly embedded in the peri-implant sulcus, although the patient had no discomfort associated. An implant screw-retained restoration was delivered as the final prosthesis. Three years after xenografting, at the delivery stage, xenograft particles were still present in the peri-implant sulcus. A radiograph of the final restoration had shown the presence of xenograft particles in the peri-implant sulcular area [Figure 6].

Case 7

An 80-year-old healthy male patient presented with a fractured maxillary anterior fixed partial denture supported by a natural tooth and a dental implant. Examination revealed that his tissue biotype was "thick" and the abutment tooth was fractured below the gingival level with little coronal tooth tissue left [Figures 1 and 2]. Whereas, the implant had a fractured abutment screw left inside the implant [Figures 3-5]. There was no information on the type or brand of implant; hence, it was not possible to order prosthetic components for that particular implant. After careful discussion with the patient, the treatment plan was to remove the tooth and immediately replace it with

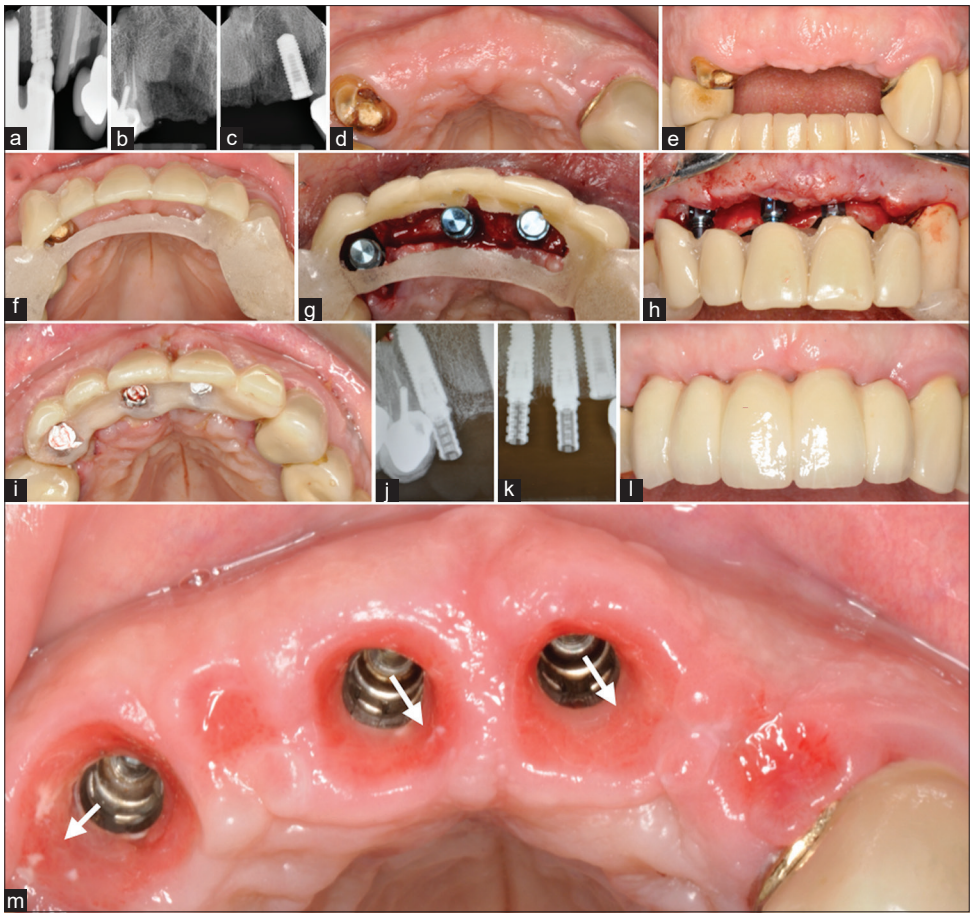

Figure 7: Radiographs and clinical photography at baseline (a-e); Implant placement, bovine-derived xenograft procedures, and immediate screw-retained temporary maxillary prosthesis (f-i); Radiographs of the implants placed (j and k); Final screw-retained maxillary prosthesis (l); Clinical photograph at 4 years of the intact/migrated xenograft particles (m)

dental implant. At the same time, two more implants would be placed in maxillary anterior section. The implant with the fractured screw was left buried as sleeping implant. The tooth was removed. The buccal bone was intact. A Straumann RC implant was placed in correct 3D position, together with other implants for a screw-retained implant-supported restoration. The gap between the implant surface and the buccal bone was filled with xenograft (Bio-Oss) particles as shown in the postoperative radiograph. Followed by the delivery of the screw-retained implant-supported restoration. Acceptable emergence profile was achieved. The treatment proceeded uneventfully, and the impression was taken 2 months after implant placement. The buccal contour was fully restored with the soft-tissue graft. An implant screw-retained restoration was delivered as the final prosthesis. At the delivery stage, 4 years after grafting procedures, xenograft particles were still present in the peri-implant sulcus, although the patient had no discomfort associated with the xenograft particles [Figure 7].

DISCUSSION

During the past three decades, the replacement of missing teeth with implant-supported restorations has become increasingly common. While implant-supported restorations do not share the risk of dental caries that natural teeth are subject to, they are susceptible to peri-implant mucositis and peri-implantitis, just as the natural dentition is subject to gingivitis and periodontitis. The inability of humans to biodegrade the bovine bone xenografts presents a long-term risk in implant dentistry that could contribute to clinical complications and may favor the eventual migration of the intact particles.

Many authors have suggested the "slow-turnover" or "slow-resorbing" concept for the resorption and replacement of bovine bone xenografts.[6] However, no scientific article or clinician has ever demonstrated the complete biodegradation and replacement of the bovine bone substitutes in humans.[7-9] On the contrary, the presence of bovine bone particles without significant size change has been found in humans even after 20 years.[10] Evidence suggests that the human host is unable to biodegrade the xenograft particles. The bovine bone xenograft is not biodegradable.[1]

In accordance with other studies, the present consecutive clinical cases observed the host inability to biodegrade the particles favoring the migration of the xenograft material. Seok *et al*. demonstrated the migration potential of the xenograft particles (Bio-Oss) in an *in vivo* animal experiment. The same authors reported a clinical case where lymphatic vessels of the submandibular gland contained foreign materials that were morphologically similar to those of the maxillary sinus in a human.[5] The xenograft particle microscopic structural and mechanical properties may play a role

in their resistance to the human biodegradation. Migration and/or displacement of the xenograft materials have been associated with clinical complications. Rodriguez and Nowzari reported resolution of the xenograft clinical complications by the surgical removal of the bone graft material.[1]

Peri-implant mucositis is defined as reversible inflammatory changes of the peri-implant soft tissues in the absence of bone loss. Peri-implantitis is defined as an inflammatory process affecting the tissues around an osseointegrated implant in function, resulting in loss of supporting bone. While there is a sulcus and junctional epithelium associated with dental implants, the connective tissue fibers are oriented parallel to the long axis of the implant and the attachment is an adhesion. Whether the difference in the nature of connective tissue fiber arrangement attachment results in greater risk of attachment loss for implants is not known. The prevalence of peri-implantitis has been reported to be as low as approximately 1% to as high as 47%; the prevalence of peri-implant mucositis is generally greater, ranging from 19% to 65%.[11] For most of cases, the usual onset of peri-implantitis occurs within 3 years of function.[12] Periodontal and peri-implant bone turnover is a balanced dynamic process that involves resorption and formation, controlled and influenced by the local production of cytokines, with a wide range of inflammatory, hemopoietic, metabolic, and immunomodulatory properties. Peri-implant xenograft particles may elicit a pathological immune response regulated by key cytokines (tumor necrosis factor-alpha, interleukin [IL]-1ß, transforming growth factor-β, and IL-10) that control the progression and/or suppression of the inflammatory response.[13] However, there is no known cytokine level threshold to differentiate between a stable site and the initiation of a pathologic process in peri-implant tissues. Xenograft bone particles have been associated with lymphocytes and macrophages. Chronic overproduction of pro-inflammatory cytokines released by monocytes/macrophages and lymphocytes in response to the host inability to resorb the xenograft particles could lead to the breakdown of the peri-implant tissues compromising the outcome long term.

In addition, due to the microscopic structural properties of the xenograft bone particles, the particle may also serve as bacterial reservoirs, further contributing to possible long-term dental-implant-related complications. The dental implant-related surgical devices/products can and do get colonize by periodontal pathogens (bacteria/viruses) during intraoral manipulation.[14] Microbial colonization occurs within minutes while performing surgical procedures, regardless of infectious control protocols. These studies have reported lower outcome success rates once periodontal pathogens have colonized the biomedical products, suggesting that proper control of periodontal pathogens in the oral cavity might increase prognosis/outcome of dental-related surgeries.[14,15] However, bacterial colonization over the xenograft particles may be an inevitable event during intraoral surgical procedures given the particle microstructural topography and clinician manipulation. The continuous balance that exists between the host immune response, potential subgingival pathogens (bacteria/viruses), and graft materials determines the clinical condition not only around teeth but also around osseointegrated dental implants.[16]

The plausibility of bovine-derived bone substitutes in producing immune reactions, disease transmission, and clinical complications is present.[1] Albeit some xenograft complications are not significant enough to compromised the initial achieved outcomes, as the regular turnover of host tissues continues through lifetime, xenografts particles seemed to be left intact favoring conditions for long-term complications.

CONCLUSION

The bovine bone xenograft is not biodegradable. Albeit some xenograft complications are not significant enough to compromise the initial outcomes achieved, the authors' clinical impression/observations revealed the inability of the human host to biodegrade the xenograft particles. The intact/migrated bovine bone particles may pose a risk to patients and contribute to long-term clinical complications in implant dentistry.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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