Diatoms: A novel cause of granulomatous inflammation of the head and neck

Thabet AlHousami, BDS, MS,[a,b] Ivan J. Stojanov, DMD,[c,d] Padraig Deighan, PhD,[e] Daniel D. Rhoads, MD,[f] Devaki Sundararajan, BDS,[g] Jeremy Lassetter, DDS, MS,[h] Yuri Shamritsky, DMD, DDS,[i] Sadru Kabani, DMD, MS,[j] and Vikki Noonan, DMD, DMSc[g]

Objective. We report the first 4 cases of intraoral nonnecrotizing granulomatous foreign body reactions to diatoms, plausibly as a result of exogenous material introduced following iatrogenic or traumatic injury.

Study Design. Clinical and histopathologic findings of 4 intraoral cases of nonnecrotizing granulomatous foreign body reaction to diatoms, single-celled algae belonging to the taxonomic phylum Bacillariophyta, are reported.

Results. The lesions presented either in the jaws or in the soft tissue overlying the alveolar bone, in some instances mimicking an inflammatory lesion of odontogenic etiology. Microscopically, the lesions presented as nonnecrotizing granulomatous inflammation associated with either spherical and radially symmetric or rectangular and bilaterally symmetric diatomaceous foreign material.

Conclusion. The diagnosis of a diatom-associated foreign body reaction necessitates familiarization with the histopathologic features of these organisms to accurately characterize the nature of such lesions. (Oral Surg Oral Med Oral Pathol Oral Radiol 2021;131:565−571)

Diatoms are microscopic, single-celled algae (or microalgae) that belong to the taxonomic phylum Bacillariophyta. Bacillariophyta are composed of photosynthetic species that are found richly in aquatic ecosystems.[1]

The name diatom is derived from the Greek word *diatoms* ("cut in half") and refers to their characteristic 2-part cell walls made of silica.[2] Diatoms inhabit every environment where water is present, in both freshwater and marine ecosystems, and in moist soil, as long as there is sufficient light and nutrients. They are considered to be the most diverse and widely spread group of unicellular microalgae, with reports of 100,000 species in 200 to 1200 genera[3-6]; the variation among reports is due to the limited knowledge about their diversity. Diatoms are divided into 2 morphologically distinct orders: the Centrales (or Biddulphiales) and the Pennales. The Centrales have valve striae that are arranged in relation to a point (an annulus or a central areola) and tend to appear radially symmetric. The Pennales have valve striae arranged in relation to a line and appear bilaterally symmetric.[7] Their cell size can reach 500 μm in diameter but typically ranges from <5 to 200 μm.[4,8,9]

The diatom frustule (i.e., cell wall) contains large amounts of silica, and this silica persists after diatoms die. Over time, large accumulations of dead diatoms can settle to the ocean floor. This material, which can be mined from the ocean, is often described as diatomite or diatomaceous earth, which has many industrial uses including as pest control, as polishing agents, and in water filtration.

Given the ubiquitous nature of these organisms, opportunities for exposure and scenarios whereby diatoms could be introduced are numerous. For example, pulmonary inflammatory foreign body reactions of noninfectious origin caused by the aspiration of diatoms have been well documented in the literature,[10,11] and diatoms are frequently utilized as indicators of death by drowning[12,13]; however, to the best of our knowledge, a granulomatous foreign body reaction to diatoms involving the hard and soft tissues of the oral cavity has not previously been described and invariably requires a different etiology.

Granulomatous inflammation in the oral cavity may be foreign body associated, related to systemic disorders, or

Statement of Clinical Significance

We have identified a novel cause of granulomatous inflammation occurring in the oral cavity that has not been previously recognized. Knowledge of this unreported entity will facilitate identification of such lesions via histopathologic analysis and help establish optimal patient management.

[a]Department of Endodontics, Boston University Henry M. Goldman School of Dental Medicine, Boston, MA, USA.
[b]Department of Basic and Clinical Oral Sciences, Faculty of Dentistry, Umm Al-Qura University, Makkah, Saudi Arabia.
[c]Department of Oral and Maxillofacial Medicine and Diagnostic Sciences, Case Western Reserve University School of Dental Medicine, Cleveland, OH, USA.
[d]Department of Pathology, University Hospitals Cleveland Medical Center, Cleveland, OH, USA.
[e]Department of Biology, Emmanuel College, Boston, MA, USA.
[f]Cleveland Clinic Lerner College of Medicine (CCLCM), Case Western Reserve University, Cleveland, OH, USA.
[g]Division of Oral and Maxillofacial Pathology, Boston University Henry M. Goldman School of Dental Medicine, Boston, MA, USA.
[h]Adirondack Oral & Maxillofacial Surgery, Glens Falls, NY, USA.
[i]North Shore Endodontic Associates, Peabody, MA, USA.
[j]Strata Pathology Services, Lexington, MA, USA.
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infectious in etiology and most commonly occurs in the setting of traumatic/iatrogenic implantation of exogenous material.[14] We describe 4 cases of diatom-associated foreign body granulomatous inflammation involving the jaw and adjacent soft tissue and present the associated clinical, radiographic, and histopathologic features. To date, diatom-associated granulomatous inflammation of the oral cavity has not been reported and diatoms have not been previously recognized as a potential cause of granulomatous inflammation in the oral cavity.

CASE 1

A 53-year-old male patient was seen in consultation by oral and maxillofacial surgery for evaluation and management of a slowly enlarging right mandibular radiolucency over many years, with soft tissue extension. The patient reported an abscess in the area 6 months previously. Computed tomography of the facial bones and a panoramic radiograph demonstrated an expansile lytic lesion of the right mandibular body measuring 1.2 × 2.2 × 1.7 cm and involving the roots of teeth 27 to 31, with buccal and lingual cortical destruction (Figure 1A and 1B). Additionally, a soft tissue lesion eroding the buccal cortical bone measured 0.7 × 2.1 × 2.2 cm. A panoramic radiograph taken 12 years previously showed a 2.0 × 1.0 cm radiolucency centered around the roots of tooth 30 (Figure 1C). Prior dental work was done on teeth 29 and 30.

An incisional biopsy was performed and the histopathologic findings included nonnecrotizing granulomatous inflammation with abundant foreign material measuring between 8 and 12 μm in greatest dimension (Figure 2). The foreign material was either spherical and radially symmetric or rectangular and bilaterally symmetric, with prominent cell walls consistent with diatoms. The foreign material was nonrefractile by polarized light and the cell walls were not highlighted by Gomori methenamine silver (GMS) or acid-fast bacilli (AFB) histochemical stains.

CASE 2

A 38-year-old female farmer presenting with vague discomfort in the edentulous region of tooth 30 was seen in consultation by an oral and maxillofacial surgeon. Her social and medical histories were unremarkable. The patient reported a history of extraction of tooth 30 following failed root canal therapy. No evidence of sinus tract or cortical expansion was appreciated on clinical examination. Given the presence of a well-demarcated radiolucency at the site just below the crest of the alveolar bone on imaging studies, the differential included a residual inflammatory odontogenic lesion, a developmental odontogenic cyst, a central giant cell lesion, or an incipient odontogenic tumor, among others. The lesion was curetted and removed from a lateral approach to the extent feasible in an effort to preserve the alveolar crest and submitted for histopathologic evaluation. The histopathologic features showed multiple fragments of fibrous connective tissue exhibiting epithelioid histiocytes and aggregates of multinucleated giant cells throughout,

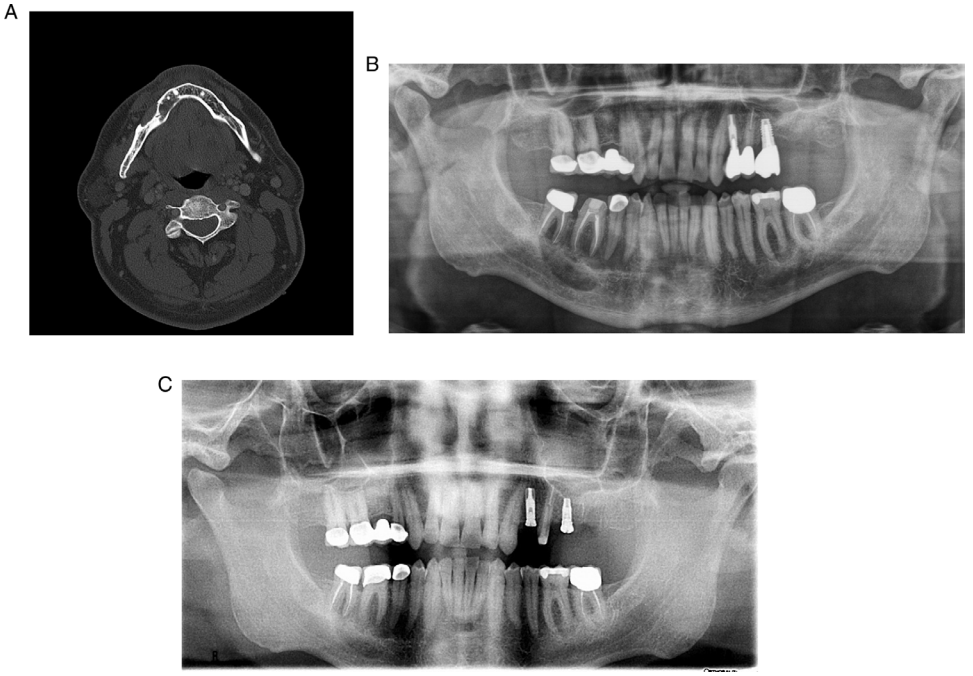

Fig. 1. **(A)** Computed tomography showing an expansile lytic lesion of the right mandibular body with buccal and lingual cortical destruction. **(B)** Panoramic radiograph at the consultation visit showing a radiolucency involving the roots of teeth 27 to 31. **(C)** A panoramic radiograph taken 12 years previously showing a radiolucency centered around the roots of tooth 30.

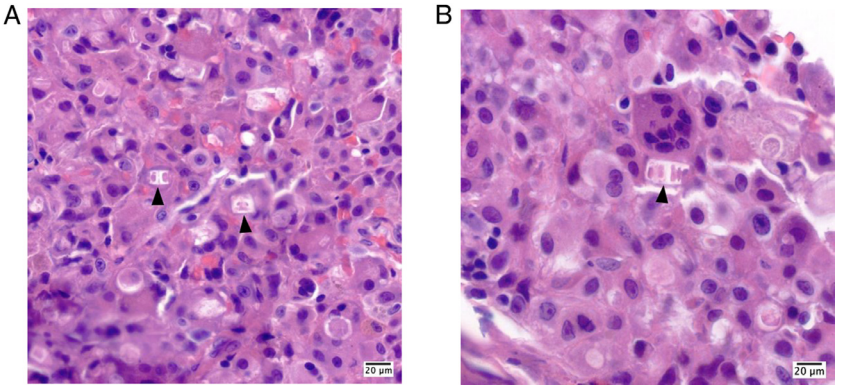

Fig. 2. **(A), (B)** Histopathologic findings indicating nonnecrotizing granulomatous inflammation with abundant foreign material exhibiting spherical and rectangular bodies (oil immersion photomicrograph, magnification × 1000). Examples of foreign bodies consistent with diatoms are indicated (black arrowheads).

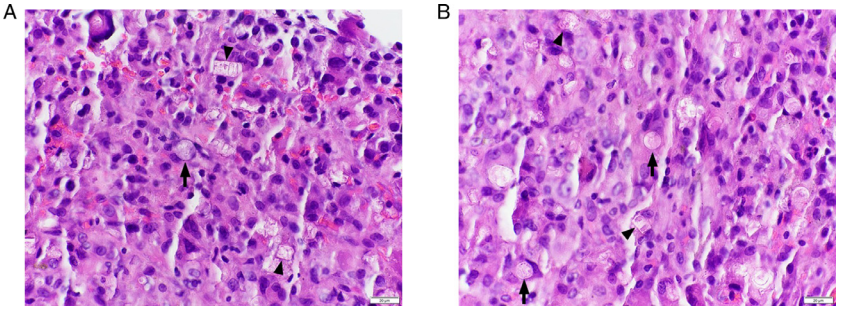

Fig. 3. **(A), (B)** Hematoxylin and eosin stain revealing geometrically shaped spherical bodies with a distinctive spoke-wheel arrangement (black arrows) and rectangular-shaped and bilaterally symmetric nonrefractile exogenous bodies (black arrowheads) within the connective tissue (magnification × 60).

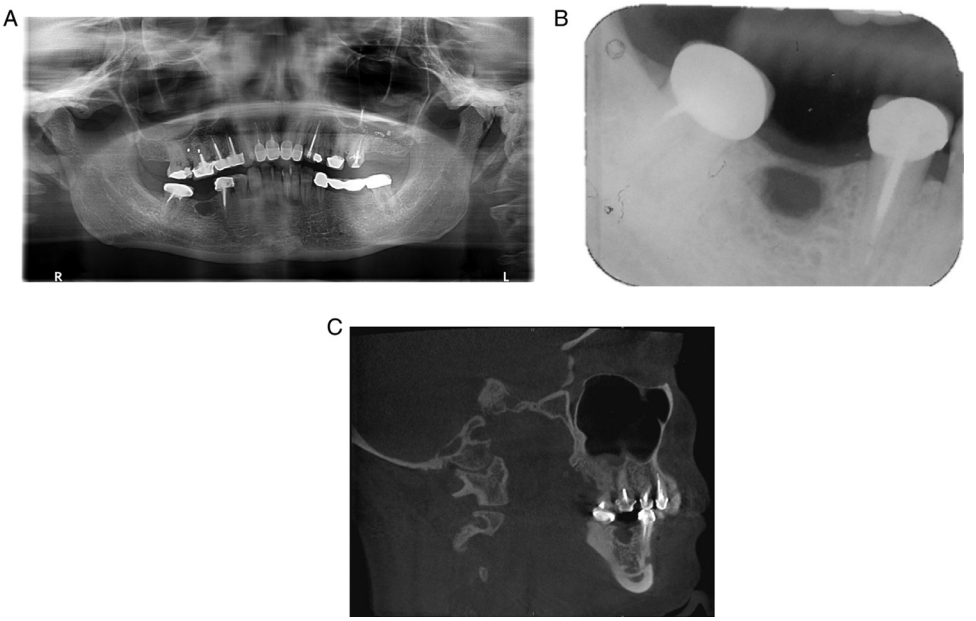

Fig. 4. **(A), (B)** Panoramic and periapical radiography showing a well-circumscribed radiolucent lesion just below the crest of the alveolar bone of tooth 30. **(C)** Sagittal cone beam computed tomography section showing a well-defined corticated hypodensity in the posterior body of the mandible, right side.

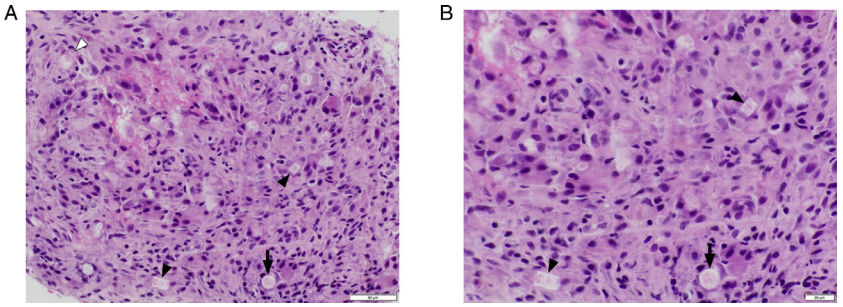

Fig. 5. Fragments of fibro-granulation tissue exhibiting numerous circular (black arrows) and rectangular geometrically shaped particles (black arrowheads) associated with aggregates of epithelioid histiocytes. Note a diatom particle within a multinucleated giant cell (white arrowhead). Hematoxylin and eosin stain **(A)** magnification × 40 and **(B)** magnification × 60.

many of which were associated with geometrically shaped circular and rectangular nonrefractile exogenous bodies measuring between 5 and 22 μm in greatest dimension. The findings were consistent with a nonnecrotizing granulomatous inflammatory foreign body reaction to diatoms (Figure 3). AFB and GMS stains were performed and were negative, and examination under polarized light did not reveal the presence of refractile exogenous material.

One year later, the patient returned to the dental clinic with a chief complaint of persisting pain in the edentulous area of tooth 30. Upon radiographic examination, a well-circumscribed radiolucent lesion measuring approximately 1.5 × 1.3 cm was appreciated in the region of tooth 30 at the site of previous biopsy (Figure 4). Under local anesthesia, the overlying crestal alveolar bone and tooth 31 were removed to ensure that the lesion could be completely curetted. The lesional tissue was submitted for histopathologic examination and the histopathologic features were consistent with the findings noted in the original biopsy (Figure 5). This lesion is favored to represent progression of residual disease rather than recurrence as a result of initial conservative efforts to preserve the adjacent dentition.

CASE 3

A 42-year-old male patient reported to the endodontist for evaluation and management of an asymptomatic radiolucency measuring approximately 0.9 × 1.7 × 1.8 cm associated with the roots of endodontically treated tooth 3 discovered incidentally by his dentist on routine radiographic examination (Figure 6). Periapical radiographs revealed an oval, well-defined radiolucency located apical to tooth 3. Previous root canal treatment had been performed on tooth 3 approximately 7 years before the visit. The patient did not report any symptoms, and his medical history was not significant. Given the periapical localization, the differential diagnoses considered included a periapical cyst, periapical granuloma, periapical scar, developmental odontogenic cyst, central giant cell lesion, and an incipient odontogenic tumor, among others.

Under local anesthesia, an apicoectomy was performed, the lesion was curetted, and the lesional tissue was submitted for histopathologic examination. The histopathologic findings showed multiple pieces of fibro-granulation tissue exhibiting numerous round and rectangular geometrically shaped exogenous bodies throughout measuring between 4 and 16 μm in greatest dimension, many of which were associated with multinucleated giant cells and aggregates of epithelioid histiocytes. Some of the round structures exhibited a distinctive peripheral spoke-wheel arrangement. Birefringence was not appreciated on examination with polarized light. A diagnosis of diatom-associated nonnecrotizing granulomatous foreign body reaction was made (Figure 7). Double refractile structures were not visible on polarization microscopy and AFB and GMS stains were negative.

CASE 4

A 66-year-old female patient in good systemic health presented to the oral surgeon in consultation for evaluation of a painless submucosal mass measuring approximately 1.0 × 0.8 cm in greatest dimension in the region of the left mandibular vestibule. Per patient report, the lesion developed in the 3-month interval following the uncomplicated extraction of tooth 19 performed under the care of her general dentist. On clinical examination the mass was palpably firm and subtly mobile beneath the vestibular mucosa. Imaging studies revealed the presence of a linear and subtly radiopaque change in the right posterior mandibular buccal soft tissue approximating the extraction site of tooth 19 (Figure 8). At the time of biopsy, the surgeon grossly identified the presence of exogenous material notable for a pale yellow color and rubbery consistency suggestive of dental impression material; however, upon further inquiry, the patient could not recall an impression procedure. The surgeon excised the surrounding soft tissue mass and submitted this tissue for histopathologic evaluation. The histopathologic findings showed multiple pieces of fibro-granulation tissue exhibiting nonnecrotizing granulomatous

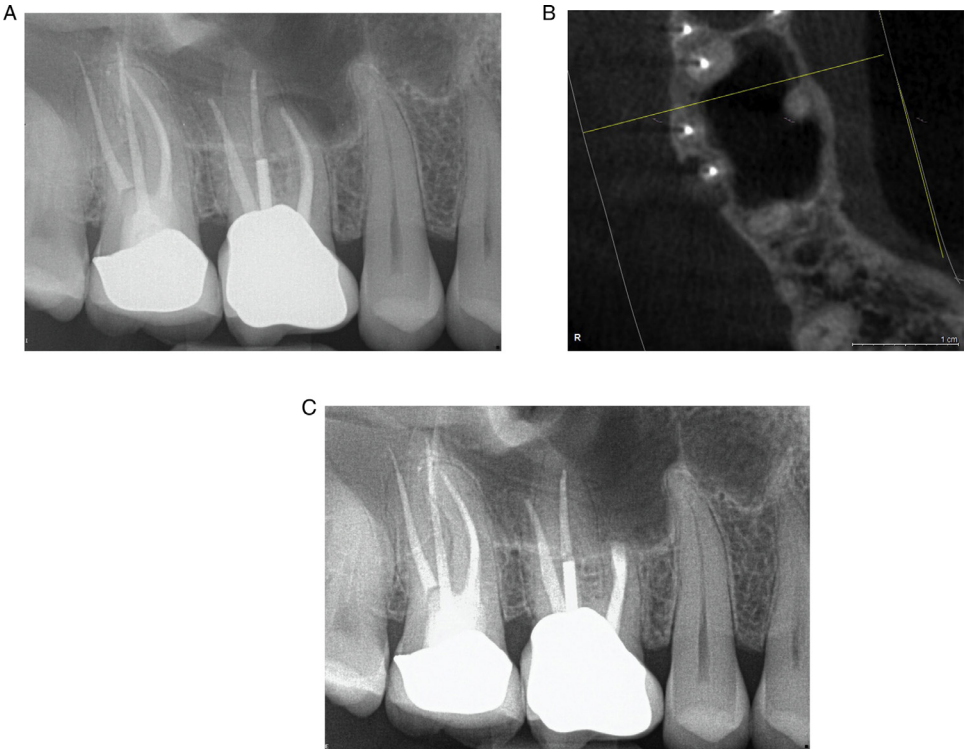

Fig. 6. **(A)** Periapical radiograph showing a unilocular radiolucent lesion at the root apex of tooth 3. The tooth had been endodontically treated approximately 7 years previously. **(B)** Axial cone beam computed tomography section showing a unilocular radiolucent lesion. The mesiobuccal root apex exhibited a discontinuous buccal cortical plate with a hypodense region at the apical root end. Both the periodontal ligament and lamina dura were indistinct. **(C)** Periapical radiograph at 1-year follow-up examination.

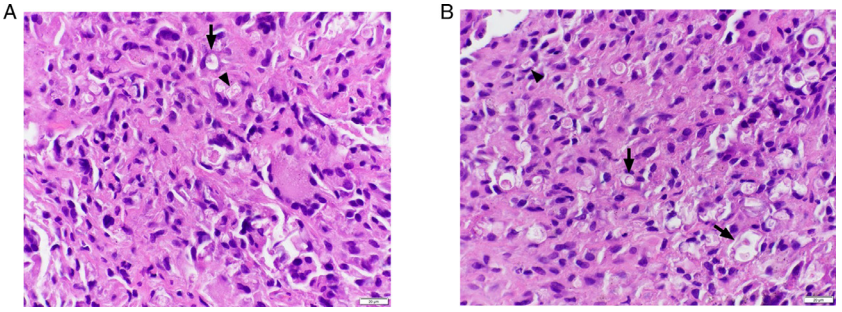

Fig. 7. Hematoxylin and eosin stain illustrating diatom-associated nonnecrotizing granulomatous foreign body reaction. **(A)** Particles of diatoms surrounded by histiocytes and foreign body giant cells (magnification × 60). **(B)** Diatoms within the granulation tissue (magnification × 60). Round spherical (black arrows) and rectangular-shaped exogenous bodies are noted (black arrowheads).

inflammation characterized by sheets of epithelioid histiocytes, siderophages, and scattered multinucleated giant cells with exogenous bodies throughout. The nonrefractile foreign bodies were either spherical or rectangular in shape, with some of the round structures exhibiting a circumferential spoke-wheel arrangement, and measured between 8 and 12 μm in greatest dimension (Figure 9). AFB and GMS stains were performed and were negative. A diagnosis of diatom-associated nonnecrotizing granulomatous foreign body reaction was made.

DISCUSSION

To the best of our knowledge, granulomatous foreign body reactions against diatoms have not been previously reported in the head and neck and have only been reported in the lungs following death by drowning. Diatoms, a microalgae, are found in every habitat where water exists and constitute diatomaceous earth, a natural siliceous fine powder consisting of 5- to 200-μm particles of fossilized diatom remains.[8,9] Diatoms do not occur naturally in humans but are instead acquired through exposure. Plausible mechanisms whereby a

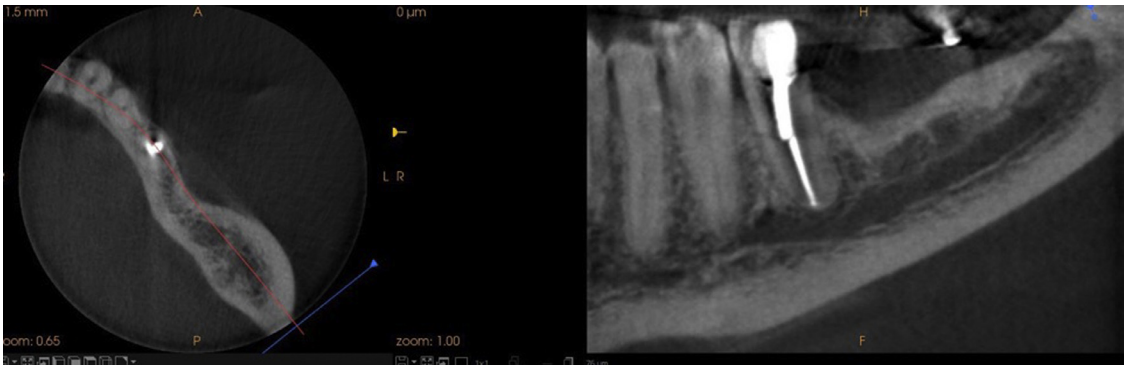

Fig. 8. Computed tomography demonstrating a subtle radiopaque change in the region of the left mandibular buccal vestibular soft tissue approximating the extraction site of tooth 19.

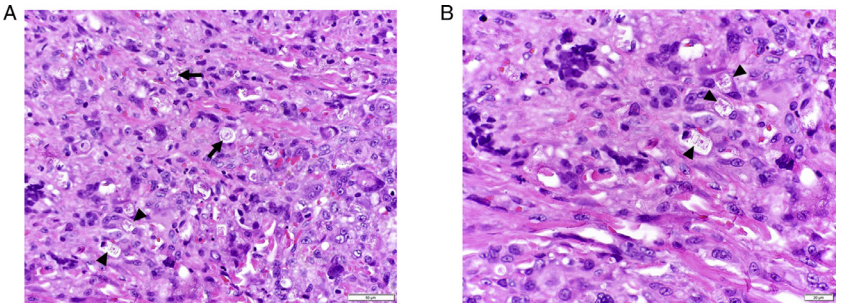

Fig. 9. Hematoxylin and eosin stain illustrating diatom-associated nonnecrotizing granulomatous foreign body giant cells. Round spherical (black arrows) and rectangular-shaped (black arrowheads) particles of diatoms surrounded by histiocytes and multinucleated giant cells: **(A)** magnification × 40 and **(B)** magnification × 60.

living individual could be inoculated with diatoms include iatrogenic introduction of materials that have a high composition of diatoms, ingestion of diatom-containing material, aspiration of water containing diatoms with subsequent circulation throughout the body, or inhalation of airborne diatoms that are dispersed in the atmosphere.[15] It is worth noting that the patient in case 2 lives on a farm. Because diatomaceous earth is used as an alternative to conventional pesticides for the treatment of parasites in organic animal production and for grain treatment,[16,17] the organisms may be found on food and runoff water from farms using diatoms for agricultural purposes, which may be a source of introduction of these organisms into the water supply. Such food and water contaminated with diatoms are plausible sources of exposure, with either subsequent traumatic impregnation of the diatoms into the oral soft tissues or contamination of sites of recent dental treatment.

Iatrogenic mechanisms of exposure may potentially underlie diatom-associated granulomatous foreign body reactions in the oral cavity, because dental alginate, used as impression material, is approximately 60% diatomaceous earth by weight.[18] It is conceivable that iatrogenic impregnation of the oral tissues with diatomaceous earth−containing alginate during dental impression making, particularly following a dental procedure resulting in either manipulation of the gingival soft tissues or after recent extraction, may be a cause of diatom-associated granulomatous inflammation. Though iatrogenic implantation is a favored source of inoculation, impregnation of the oral soft tissues with diatoms or introduction of the organisms into a healing extraction socket following dietary ingestion is another plausible etiology because diatomaceous earth may be used in organic farming in lieu of pesticides and added to the diet of animals to reduce the effects of parasites, as an alternative to prophylactic medications.[17]

Although the etiology of the granulomatous response to diatoms is enigmatic, one potential factor contributing to the foreign body granulomatous host response on exposure to diatoms may be related to the size of the organism. The severity of the host tissue response to silica particles has been shown to be inversely proportional to the size of the silica particles.[19] Large fragments of silica (2.5 gm) have been shown to stimulate a minor host response, whereas smaller fragments, 1 to 12 μm, induce a rapid foreign body−type reaction.[19] It is therefore hypothesized that diatomaceous earth−containing material introduced into the oral cavity induces a foreign body granulomatous response secondary to a cellular sensitization reaction to silicon dioxide.[20]

CONCLUSION

To the best of our knowledge, we report the first 4 cases of diatom-associated nonnecrotizing granulomatous foreign body reactions occurring in the jaws. Diatomaceous earth is a major component (up to 60%) of alginate impression materials and other dental materials and is ubiquitous in the natural world and in industry, including food production. This provides a rational basis for understanding the occurrence of this previously unreported condition and why it may have a predilection for the oral cavity and jaw. Light microscopic examination of hematoxylin and eosin−stained sections is deemed sufficient to identify the characteristic features of diatom bodies for diagnosis and appropriate recognition of this granulomatous inflammation as foreign body related and not infectious is necessary for optimal patient management.

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Reprint requests:

Thabet AlHousami
Boston University Henry M. Goldman School of Dental Medicine
Department of Endodontics
635 Albany Street
201, Boston
MA 02118.
thabet@bu.edu