

# Insights into the pathogenesis and clinicopathological spectrum of oral vegetable granuloma. Case series with literature review

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## Abstract

Oral vegetable granuloma represents an inflammatory lesion of foreign body origin resulting from the implantation of vegetable matter. Controversy regarding its pathogenesis is reflected by the various terminologies used to describe the lesion. Its diverse clinical presentations are due to variations in the antigenic potential of the vegetable material and the host response. As the diagnosis is solely histopathological, it is critical to differentiate vegetable granuloma from other oral granulomatous lesions like tuberculosis, sarcoidosis and Wegner's granulomatosis. Here, we report six cases with the varied clinicopathological presentation of hyaline ring granulomas in association with different pathological lesions.

## Introduction

Vegetable granuloma has been described in the literature by variable terminologies including pulse granuloma, chronic periostitis, and giant cell hyaline angiopathy.<sup>1</sup> The vegetable particle elicits a foreign body reaction presenting in most cases as a

granulomatous lesion. The clinical presentation seems to vary in severity from being an asymptomatic nodule to an indurated lesion resembling malignancy depending on the antigenic potential of the vegetable matter and the immune response of the host.<sup>2,3</sup> Cases of vegetable granuloma have been reported both centrally and peripherally.<sup>4</sup> Histopathology forms the basis for the diagnosis of vegetable granuloma. Although vegetable granuloma presents as granulomatous lesions, there are few cases lacking any reaction from the host tissue. In these cases, vegetable granuloma will not exhibit any clinical symptoms and are not identified for a long time. Several cases of inert vegetable granuloma have been identified as accidental findings, especially when they are associated with other oral pathologies.<sup>4,5</sup> The present case series consists of 6 cases of vegetable granuloma presenting with unique clinicopathological features. Some of these cases have vegetable granuloma as the primary pathology, and in some cases, they are just accidental findings (inert in nature) coexisting with other lesions of the oral cavity. The various theories of pathogenesis for oral vegetable granuloma are discussed with a review of the literature.

## Case Reports

### Case 1

A 29-year-old female reported with a complaint of pain and swelling in relation to her left mandibular region since two months. The patient gave a history of extra oral abscess three months back, which was drained. Intraoral examination revealed a partially impacted grossly decayed 38 with pericoronitis. The tooth was submitted for histopathological analysis. The decalcified H and E section showed features of dental caries like Miller's foci of liquefactive degeneration, horizontal clefts and abundant microbial colonization. The pulp chamber had degenerated pulpal tissue with the embedded vegetable material in the form of multiple hyaline rings with varying degree of eosinophilic amorphous material in its lumen (Figure 1A). The vegetable matter was surrounded by a proliferation of dense collagen fibers with minimal inflammation. Spherical gram positive particles were noted within the hyaline rings (Figure 1B). Both the hyaline rings and the amorphous material were positive for periodic acid-Schiff reaction (PAS) (Figure 1C). The extracted site healed without any complications.

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### Case 2

A 29-year-old male complained of growth on the lower anterior tooth region since 6 months. On Intraoral examination, the diffuse swelling was evident extending from 33 to 42 involving the lingual and labial gingiva. Excisional biopsy was done. Histopathology revealed an intact surface epithelium overlying a fibrous connective tissue stroma with multiple foci of calcification suggestive of peripheral ossifying fibroma. The patient returned 1 month later with swelling at the same site. The histopathological features remained the same as that of peripheral ossifying fibroma in addition to multiple eosinophilic hyaline rings (Figure 2A). The rings and the starch were periodic acid-Schiff (PAS) stain positive (Figure 2B). Van Gieson stains revealed collagen condensation in the periphery of the vegetable particle. Follow up did not reveal any further recurrences.

### Case 3

A 44-year-old male patient presented with a chief complaint of sharp pain in the lower left back tooth region since 3 months. Patient provided the history of exfoliation of 38, 1 month back. On intraoral examination, there was an empty socket in relation to 38 with yellowish sequestrum. Excisional biopsy of the sequestrum was done and submitted for histopathological analysis. The decalcified section revealed devitalized mature bone fragments with an irregular border, empty lacunae surrounded by

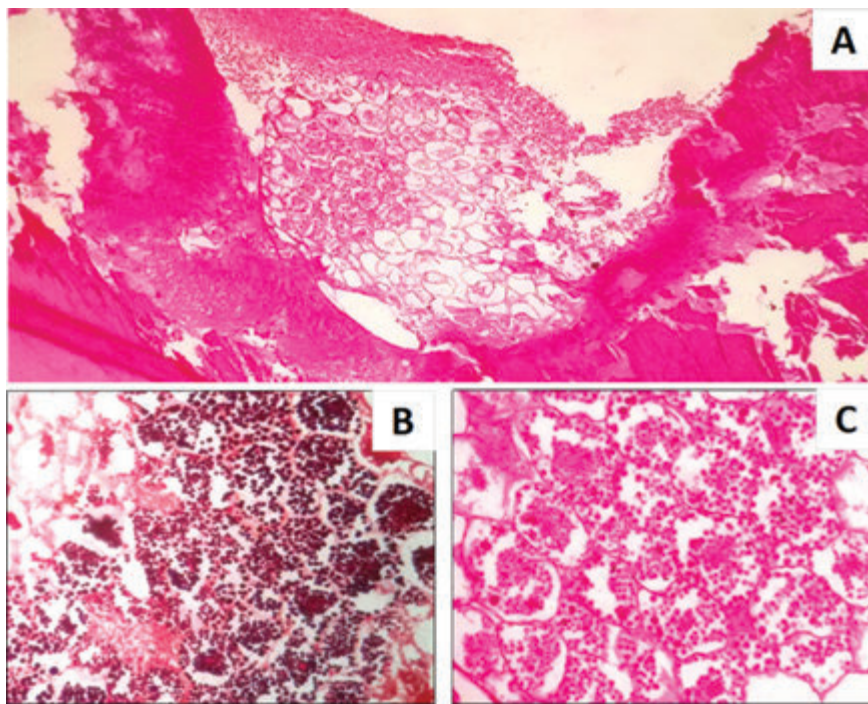
numerous microbial colonies suggestive of osteomyelitis. An isolated area of the biopsied specimen showed multiple hyaline rings arranged in a honeycomb pattern with the presence of eosinophilic starch granules within the thin cellulose envelopes. The cellulose rings and starch grains were PAS positive (Figure 3A). Following the removal of the sequestrum, the socket healed without any complications.

#### Case 4

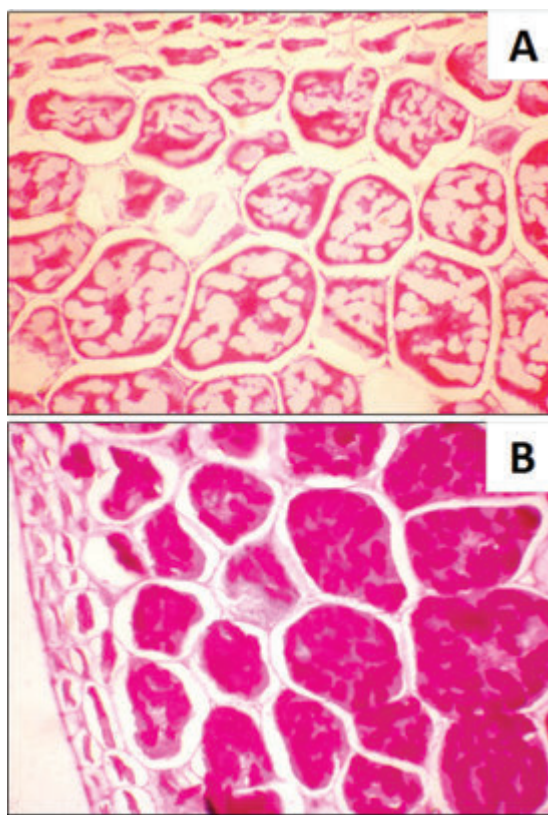
A 60-year-old male patient presented with a chief complaint of pain and discharge in the upper left back tooth region since 2 years. On intraoral examination, the bone was exposed in relation to 24, 25 with whitish yellow in color. The exposed bone was submitted for histopathological analysis. The decalcified section revealed devitalized mature bone fragments with an irregular border, empty lacunae surrounded by numerous microbial colonies suggestive of osteomyelitis. Adjacent to the bone fragments were multiple hyaline rings with degenerated starch like material. The vegetable matter was surrounded by devitalized bone, microbial colonies, and sparse collagen fibers. The cellulose rings were PAS positive (Figure 3B). The patient is currently under treatment for the osteomyelitis.

#### Case 5

A 28-year-old male patient presented with a chief complaint of growth and pain in the right lower back tooth region since 2 weeks. There was a diffuse swelling at the angle of the mandible. Intraoral examination revealed an erythematous proliferative growth involving grossly decayed 46, 47 and 48. In addition, a mixed radiolucent-radio-opaque lesion was evident immediately below the soft tissue proliferation. Incisional biopsy was done for both the soft and hard tissues along with the extraction of 48 and all the specimens were sent for histopathological analysis. The microscopic analysis of the soft tissue consisted of a predominantly myxoid tissue. The bone specimens were more conclusive consisting of hypercellular highly pleomorphic chondrocytes embedded in lacunae of varying dimensions. The features were suggestive of chondrosarcoma. In addition, the decalcified section of 48 showed features of cross sections of dentinal tubules and pulp chamber with few odontoblasts and cementum resembling a tooth. Also, multiple hyaline rings with disintegrated starch material and vegetable matter were noted adjacent to the tooth structure. Focal areas of microbial colonies were also noted. The cellulose rings were PAS positive (Figure 3C). The



**Figure 1.** A) Vegetable granuloma embedded in a grossly decayed tooth surrounded by microbial colonies (PAS, 4x); B) Spherical gram positive particles within the hyaline rings (Gram stain, 40x); C) PAS stained vegetable granuloma showing positivity in the cellular rings and in the spherical particles (PAS, 40x).



**Figure 2.** A) Vegetable granuloma present in peripheral ossifying fibroma with characteristic hyaline rings (Hematoxylin & Eosin, 40x); B) PAS positivity demonstrating the abundant starch within the hyaline rings (PAS, 40x).

patient underwent surgical excision for the chondrosarcoma and is currently under follow up.

### Case 6

A 25-year-old male patient reported with a complaint of pain, swelling and pus discharge from upper left posterior teeth region since 3 months. He had undergone an extraction of decayed 26 three months ago. On extra oral examination, there was mild swelling causing asymmetry on the left side of the face. Intraoral examination revealed pus discharge from the extraction site in relation to 26. Buccal cortical plate expansion was seen from 24 to 27 regions obliterating the buccal vestibule. The swelling was oval shaped bony hard and well defined and measured 3×2 cm in diameter. Excision of the lesion was done. The histopathological sections showed sheets of odontogenic epithelial cells that formed prominent intercellular bridges. Areas of extracellular, eosinophilic, and amyloid-like material with formation of concentric calcifications (Liesegang rings) were also present. Histopathological features were suggestive of the calcifying epithelial odontogenic tumor (CEOT). The stroma also showed hyaline rings as double layered refractile membranes appearing as round or irregular structures enclosing amorphous material consistent with degenerated starch cells in the dense chronic inflammatory infiltrate. The cellulose envelope was PAS positive. Post-surgical follow up did not reveal any recurrences.

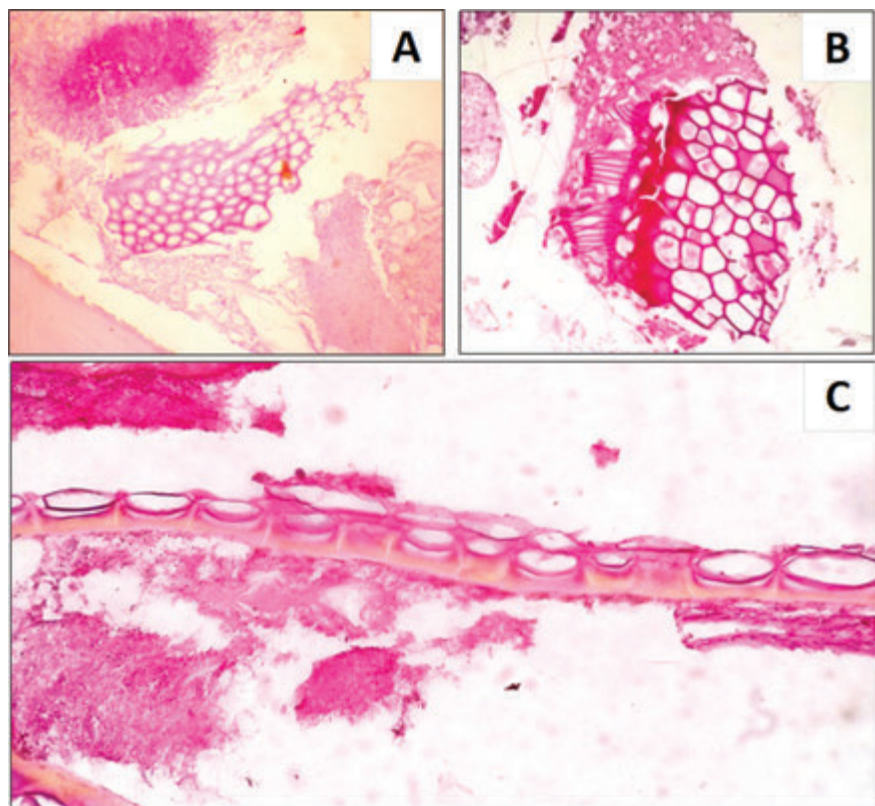
### Discussion

Various terminologies have been used to describe vegetable granuloma. Chou *et al* coined the term *hyaline ring granuloma* which best describes its histopathological features.<sup>5-7</sup> Etiopathogenesis of vegetable granuloma remains controversial. The most accepted theory of pathogenesis is that the lesions result from implantation of a foreign body of vegetable origin causing a granulomatous reaction.<sup>1</sup> The vegetable material consists of a hyaline ring bordering an amorphous eosinophilic deposit. The hyaline ring is made of cellulose and the amorphous material consists of starch.<sup>1,2</sup> Following implantation, the starch is rapidly digested by host's immune system, but the cellulose membrane remains intact, eliciting an inflammatory response.<sup>1-5</sup> In most of the cases, the patient gives a history of trauma or previous surgery in relation to the lesional site. The most common intraoral site of vegetable granuloma includes a peri-

apical region of grossly decayed or endodontically treated tooth, extraction socket and edentulous alveolar ridge of denture wearers.<sup>8-10</sup> Case reports of vegetable granuloma co-existing with inflammatory cysts and tumors have also been reported.<sup>11-14</sup> Few reported cases in the literature with clinical and histopathological findings supporting the foreign body pathogenesis are summarized in Table 1.<sup>6,8-10</sup> Alternative theories for the pathogenesis of vegetable granuloma are summarized in Table 2.<sup>7,11,15</sup>

The etiologic agent in most of these reported cases were legumes (pulses). The histopathological features are identical to the structure of a legume seed consisting of honeycombed structure (cotyledon) enclosing starch grains.<sup>1</sup> In the present case series, the clinical presentation is varying from peripheral lesion to central lesion as reported in literature.<sup>4</sup> Our cases include periapical granuloma, peripheral ossifying fibroma, osteomyelitis, calcifying epithelial odontogenic tumor, and chondrosarcoma. Case 1 presented with a grossly decayed tooth containing multiple hyaline rings with lentil seed like amorphous eosinophilic material (starch) superimposed with the

gram positive organism. The coexisting pericoronitis and decayed tooth could have favored the deposition of food particles within the tooth as well as the periodontium.<sup>8</sup> Among our cases, 4 cases as mentioned below showed similar histological features with no evidence of starch with PAS positive cellulose envelope. This feature provides evidence that the disintegration of starch grains are in process in a long-standing lesion.<sup>1</sup> In the second case, the vegetable particle could have triggered the host response resulting in the formation of peripheral ossifying fibroma. The primary biopsy did not reveal any vegetable matter, thus the recurrence could have been due to the host response to the persisting vegetable matter. There is also a possibility of the peripheral ossifying fibroma being the primary pathology and the vegetable granuloma being an accidental finding.<sup>9</sup> In cases 3 and 4, the vegetable matter coexisted with osteomyelitis, which could have been a coincidental findings or secondary to the implantation of a vegetable matter in a freshly extracted socket. The CEOT in case 6 was associated with tooth socket facilitating the implantation of the foreign body



**Figure 3.** A) Vegetable granuloma associated with osteomyelitis exhibiting characteristic hyaline rings (PAS, 4×); B) Vegetable granuloma associated with osteomyelitis showing cellulose outline without any starch granules (PAS, 4×); C) Vegetable granuloma associated with chondrosarcoma exhibiting a linear arrangement of the hyaline rings (PAS, 40×).

easily. Also, the chondrosarcoma in case 5 was associated with the decayed tooth (open cavity) which facilitated the lodging of the vegetable matter. Similar histopathological features of vegetable granuloma were observed in 2 cases of fibrous hyperplasia reported by Luiz AG<sup>2</sup> and in ameloblastoma reported by Manjunatha BS.<sup>3</sup>

While case 3 showed feature of osteomyelitis associated with the tooth socket, which resulted in the implantation of a foreign body. Starch presented in the form of floating granules within the thin cellulose envelopes, boiled legumes are said to loosen and get separated from the shell breaking up the honey comb structure, leaving clusters of eosinophilic starch granules.<sup>1</sup> The cellulose envelope and starch grains showed PAS positivity.

The diagnosis of the vegetable granuloma is made only in the presence of starch granules, with cellulose envelopes that appear as hyaline rings with or without granulomatous reaction. The hyalinized structures in the reported cases were positive for PAS supporting the hypothesis of McMillan *et al.* Cellulose derived from the implanted plant food material accounts for PAS positivity.<sup>1</sup> In the present cases, 4 cases (dental caries, peripheral ossifying granuloma, osteomyelitis, and CEOT) showed the presence of inflammatory cells surrounding the granuloma. Giant cells were not found in any of the cases. Variations in the number of hyaline structures were seen between reported and reviewed cases of pulse granuloma.<sup>16</sup>

There are various histopathological patterns of pulse granuloma, while we have observed only 2 patterns, others include:<sup>1</sup> i) the lumen of the hyaline rings presenting with either chronic inflammatory cells or multinucleated foreign-body giant cell; ii) hyaline rings with eosinophilic, fibrillary material and ellipsoid structures; iii) granular, basophilic material replacing the *hyaline* ring; iv) droplet calcification within the lumen of the hyaline ring. lentil cells in various stages of disintegration; v) filamentous material surrounded by multinucleated foreign-body giant cells within a chronically inflamed connective tissue stroma. This may be representative of the vegetable seed coat.

Oral pulse granuloma has been reported in association with many other lesions and conditions such as follicular ameloblastoma,<sup>3</sup> apical periodontitis,<sup>8-10</sup> endodontically treated tooth,<sup>8-10</sup> chronic periostitis,<sup>8-10</sup> keratinizing cystic odontogenic tumor,<sup>1</sup> pericoronitis, in post extraction tissue reaction and as part of a cyst wall,<sup>12</sup> as a complication of periodontal surgery or associated with deep periodontal pockets due to compromised periodontal health.<sup>16</sup> Extra-oral sites include lungs, gastrointestinal tract, skin, gallbladder, and fallopian tubes.<sup>17</sup>

The possible special stains employed to demonstrate the individual component of vegetable granuloma are Periodic acid Schiff (PAS) reagent, stains the cellulose envelope and starch granules due to the presence of glycol group. Alcian blue at pH 2.5, the cellulose envelope stains positive due to the presence of carboxyl group. Von

Kossa's can be used to stain calcium evident in the advanced or degenerative stage. Van Gieson's stains the collagen condensed at the periphery of the vegetable matter.<sup>3</sup>

Other investigative modalities include demonstrating the birefringence of the vegetable particle under a polarized microscope<sup>1-3</sup> and ultrastructural demonstration of microfibrils and architecture of the legume seed using a scanning electron microscope.<sup>2,18-20</sup>

## Conclusions

The vegetable granuloma may have diverse clinical presentations and histopathological features and the final diagnosis is based on the identification of the vegetable matter with or without surrounding granulomatous tissue. Here, we report 6 cases of oral vegetable granuloma with unique clinical and histopathological presentation. It is vital that the clinician biopsies the lesional tissue to rule out other granulomatous lesions like Sarcoidosis, Tuberculosis and Wegner's granulomatosis. In most of the cases the vegetable matter is associated with other oral pathologies, thus it vital to determine the primary pathology. If vegetable granuloma was the primary pathology, then the clinical lesion will regress following the removal of the irritant (vegetable matter). In these cases, biopsy of the lesional tissue containing the vegetable matter is both diagnostic and therapeutic.

**Table 1. Cases supporting the foreign body pathogenesis of oral vegetable granuloma.**

Authors	Features noted	Proposed pathogenesis
Lewars (1970) <sup>8</sup>	Chronic periostitis; it occurs in the buccal sulcus of full lower denture wearers	Foreign-body reaction
Adkins (1972) <sup>9</sup>	Radiolucent areas in edentulous portions of the jaws	Granulomatous reaction due to a foreign body, e.g.: oils from dental instruments, dressings or food debris
Rannie (1975) <sup>10</sup>	Foreign material in his cases resembled legume cells	Foreign-body reaction to legume
King (1978) <sup>6</sup>	Compared oral lesions to condition in pulmonary tissue resulting from aspiration of vegetable particles	Foreign-body reaction

**Table 2. Alternative theories for pathogenesis of oral vegetable granuloma.**

Authors	Proposed theories	Evidence supporting the theory
Dunlap and Barker <sup>7</sup>	Giant cell hyaline angiopathy; acute vasculitis followed by the vessel walls becoming thickened, hyalinized and acellular	Hyaline rings are positive for collagen stain and are birefringence under polarized microscope comparable to that of collagen
Chen <i>et al.</i> <sup>11</sup>	Pooling of extravasated proteins followed by fibrosis	Immunoperoxidase revealed the presence of serum proteins in hyaline bodies in a dentigerous cyst and residual apical periodontal cyst Hyaline bodies also stained for collagen and <i>frayed collagen fibrils</i> (observed ultrastructurally).
Hase <i>et al.</i> <sup>15</sup>	Infective processes	Positive for bacterial organism ( <i>Torulopsis glabrata</i> )

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