INTRODUCTION

Dental implants are currently widely used to replace missing teeth with a high success rate, although biologic and prosthodontic complications still exist. The biologic complications include peri-implant mucositis and peri-implantitis. In a systematic review, Atieh et al. demonstrated that the rates of peri-implant mucositis and peri-implantitis were 30.7% and 9.6% at the implant level, respectively. It is noteworthy that reactive lesion formation around dental implants could be another biologic complication that needs to be taken into great consideration. Despite less attention paid to these lesions, the presence of such lesions could result in the removal of dental implants and in implant failure.

Pyogenic granulomas (PG), peripheral giant cell granulomas (PGCG), and peripheral ossifying fibromas (POF) are more likely gingival reactive lesion formation around teeth. All of these reactive lesions present as exophytic and asymptomatic nodules unless they become traumatized. The clinical features are almost similar, and histopathologic study is required for a definite diagnosis.

In the present systematic review, we reviewed the literature on the reported implant-associated reactive lesions, and age, sex, histopathologic features, rates of recurrence, and treatment outcomes are discussed.

MATERIALS AND METHODS

In the present systematic review, we conducted an electronic search of PubMed Central, Scopus, Google Scholar, and Science Direct using the following key words: reactive lesions AND dental implant.
peripheral giant cell granuloma AND dental implant, pyogenic granuloma AND dental implant, peripheral ossifying fibroma, AND dental implant. Hand search of the bibliographies of selected articles was also done. The search strategy was confined to full-text English-language published until May 2017. Only case reports or case series were included.

The full text of each article was reviewed by two authors independently. Articles with insufficient information were excluded. Data obtained from all the cases assessed in detail and those requiring information were extracted. Data on patients’ sex and age, histopathological features, radiographic information, rates of recurrence, modalities of treatment, and treatment outcomes were collected.

3 | RESULTS

In the present review, 19 articles were retrieved, which reported on 27 lesions in 25 patients in total (2 patients presented with 2 independent lesions). The literature search strategy diagram is shown in Figure 1. Histopathologically, nine cases were diagnosed as PG, 15 cases as PGCG, and one case was diagnosed as POF + PGCG, which was considered PGCG. All reported lesions had an exophytic appearance. Some lesions presented radiographic changes (underlying bone loss), but only one implant revealed mobility that was not osseointegrated. The mean age of the patients was 51.28 ± 14.48 years. Most of the lesions occurred in the mandibular gingiva (70.37%), and particularly in the posterior mandible (66.66% of all lesions). The total recurrence rate was 33.33% (9 lesions).

3.1 | Peripheral giant cell granuloma cases

The clinical features of the PGCG cases are shown in detail in Table 1. In the present study, 16 PGCG cases around dental implants were found. The mean age of cases was 51.87 ± 14.55 years. Posterior mandibular gingiva was the most affected site (68.75%). Radiographic changes were seen in 13 cases (81.25%). The most common performed treatments were excision and curettage. Six cases (37.5%) showed recurrence; three of those six cases had multiple recurrence. The literature review showed the total five implants (31.25%) removed due to severe underlying bone loss in patients who presented with recurrence. Poor oral hygiene (4 cases), not fully seated prosthesis, and unscrewed healing abutment were suggested as possible causal factors. In one case, the existence of metallic particles was noted in the tissue specimen histopathologically (Table 1).

3.2 | Pyogenic granuloma cases

The clinical features of pyogenic granuloma cases are shown in detail in Table 2. In total, 11 PG cases reported in nine patients were found in our study. Five patients were female and four were male. The mean age of the patients was 52.92 ± 11.55 years. The posterior mandibular gingiva was the most affected site (63.63%). Radiographic changes (underlying bone loss) were found in five lesions. Recurrence was reported in three cases (27.27%). The recurrence reported in one case was due to using electrocauterization twice, but no recurrence was reported when the lesion was excised using CO₂ laser. Multiple recurrences were reported in two other cases following curettage, restoration removal, and laser therapy, and eventually, removal of all implants was carried out. The failure rate of implants due to PG was 27.27%.

Poor oral hygiene (2 cases), pregnancy, hormonal replacement therapy, and oversized healing abutment were suggested as possible causal factors. The presence of particulate metallic foreign material was reported in the tissue in one of the cases, histopathologically.

4 | DISCUSSION

PGCG and PG are both reactive/inflammatory lesions that are usually found around both teeth and dental implants. POF are also reactive/inflammatory process. In the present study, we performed a systematic review on the association of such oral reactive lesions with dental implants. To the best of our knowledge, this is the first systematic review to do so. PGCG are confined to the oral cavity (commonly in gingiva and alveolar mucosa), and their exact etiology is still unknown. It is believed that the source of PGCG is either the periosteum or periodontal ligament, and giant cells are derived from osteoclasts. There is female predilection for PGCG, with a peak incidence in the first five decades of life, but some studies have
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<th>Sex/age (years)</th>
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<th>Radiographic findings</th>
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<th>Number of recurrences</th>
<th>Final outcome</th>
<th>Type of supra-structure</th>
<th>Duration of follow up (months)</th>
<th>Possible causing factor</th>
</tr>
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<tr>
<td>Hirshberg et al.</td>
<td>Male/31</td>
<td>Posterior mandible</td>
<td>Unknown</td>
<td>Mild horizontal bone loss</td>
<td>Excision &amp; curettage/after recurrence: Excision with laser</td>
<td>1</td>
<td>Good</td>
<td>Ceramometal crown</td>
<td>24</td>
<td>Unknown</td>
</tr>
<tr>
<td></td>
<td>Male/69</td>
<td>Anterior maxilla</td>
<td>14 months</td>
<td>Mild horizontal bone loss</td>
<td>Excision &amp; curettage/after recurrence: Excision with laser</td>
<td>1</td>
<td>Implant removal</td>
<td>Ceramometal crown</td>
<td>N/A</td>
<td>Unknown</td>
</tr>
<tr>
<td></td>
<td>Female/44</td>
<td>Posterior mandible</td>
<td>6 years</td>
<td>Mild horizontal bone loss</td>
<td>Excision &amp; curettage</td>
<td>3</td>
<td>Implant removal</td>
<td>Ceramometal crown</td>
<td>N/A</td>
<td>Unknown</td>
</tr>
<tr>
<td>Bischof et al.</td>
<td>Female/56</td>
<td>Posterior mandible</td>
<td>2 years</td>
<td>Marginal bone loss</td>
<td>Excision &amp; curettage</td>
<td>0</td>
<td>Good</td>
<td>Plastic healing cap</td>
<td>36</td>
<td>Unscrewed healing cap/ poor oral hygiene</td>
</tr>
<tr>
<td>Cloutier et al.</td>
<td>Male/21</td>
<td>Posterior mandible</td>
<td>6 years</td>
<td>Severe bone loss</td>
<td>Excision &amp; curettage</td>
<td>0</td>
<td>Implant removal</td>
<td>Screw retained non-cemented fixed prosthesis</td>
<td>12</td>
<td>Unknown</td>
</tr>
<tr>
<td>Hernandez et al.</td>
<td>Female/45</td>
<td>Posterior mandible</td>
<td>34 months</td>
<td>Bone loss</td>
<td>Excision &amp; curettage</td>
<td>5</td>
<td>Implant removal</td>
<td>Screw retained non-cemented fixed prosthesis</td>
<td>N/A</td>
<td>Unknown</td>
</tr>
<tr>
<td></td>
<td>Female/36</td>
<td>Posterior maxilla</td>
<td>27 months</td>
<td>Bone loss</td>
<td>Excision &amp; curettage</td>
<td>4</td>
<td>Implant removal</td>
<td>Screwed ceramo-metalic crown</td>
<td>N/A</td>
<td>No calculus on implant crown, but calculus on adjacent tooth</td>
</tr>
<tr>
<td></td>
<td>Female/62</td>
<td>Posterior mandible</td>
<td>3 months</td>
<td>Bone loss</td>
<td>Excision &amp; curettage</td>
<td>0</td>
<td>Good</td>
<td>Healing abutment</td>
<td>Unknown</td>
<td>Unknown</td>
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<tr>
<td>Ozden et al.</td>
<td>Female/60</td>
<td>Posterior mandible</td>
<td>6 year</td>
<td>Horizontal crestal bone loss</td>
<td>Excision &amp; curettage</td>
<td>0</td>
<td>Good</td>
<td>Fixed prosthesis</td>
<td>12</td>
<td>Not fully seated prosthesis (poor marginal adaptation)</td>
</tr>
<tr>
<td>Olmedo et al.</td>
<td>Female/64</td>
<td>Anterior maxilla</td>
<td>12 years</td>
<td>Concave shaped bone loss</td>
<td>Excision &amp; curettage</td>
<td>0</td>
<td>Good</td>
<td>Fixed prosthesis</td>
<td>24</td>
<td>Metal-like particles in the tissue</td>
</tr>
<tr>
<td>Penarrocha-Diago et al.</td>
<td>Female/54</td>
<td>Posterior mandible</td>
<td>3 years</td>
<td>Slight bone resorption</td>
<td>Excision &amp; curettage &amp; implantoplasty</td>
<td>0</td>
<td>Good</td>
<td>Cemented fixed prosthesis</td>
<td>12</td>
<td>Unknown</td>
</tr>
<tr>
<td>Ogbureke et al.</td>
<td>Male/44</td>
<td>Posterior mandible</td>
<td>3 months</td>
<td>No radiographic appearance</td>
<td>Excision</td>
<td>0</td>
<td>Good</td>
<td>Cower screw</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
<tr>
<td>Pacifici et al.</td>
<td>Male/60</td>
<td>Anterior maxilla</td>
<td>5 years</td>
<td>Large radiolucency</td>
<td>Excision &amp; curettage</td>
<td>0</td>
<td>Good</td>
<td>Crown</td>
<td>19</td>
<td>Poor oral hygiene</td>
</tr>
<tr>
<td>Brown et al.</td>
<td>Male/46</td>
<td>Posterior mandible</td>
<td>10 months</td>
<td>No radiographic appearance</td>
<td>Excision (excision &amp; curettage after recurrence)</td>
<td>1</td>
<td>Good</td>
<td>Not mentioned (cower screw)</td>
<td>12</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

(Continued)
shown equal prevalence for both sexes.\(^8\)\(^{10}\) PG affect both the oral cavity and skin, and 75\% of oral PG occur in the gingiva.\(^7\)\(^5\) PG in the gingiva show a female predilection, and most cases occur in the third decade of life.\(^1\)\(^1\)\(^2\) Some authors have shown equal sex predilection in older patients with PG.\(^1\)\(^1\) In the current review, no sex predilection was found for PGCG, while PG cases showed a slight female predilection (55.55\%).

Dental implants are most commonly used in older patients; therefore, it is expected that associated reactive lesions be seen at advanced age compared to those seen around natural teeth.

The usual and common site of involvement with PGCG in dentulous/edentulous patients (but with no implant) is the posterior mandibular gingiva/alveolar ridge,\(^8\)\(^1\)\(^0\) while PG are usually seen in the anterior maxillary gingiva.\(^1\)\(^2\) In our systematic review, we found the posterior gingival region the most common location of involvement for both PGCG and PG cases. Difficulty in getting access to the posterior region for good oral hygiene performance could be an explanation for the increased risk of reactive lesions in this area.\(^1\)\(^3\) Hernandez et al. suggested occlusal forces as a risk factor for development of reactive lesions around implants in the posterior area.\(^1\)\(^4\)

All of the cases in the present review had an exophytic appearance similar to classic cases of PGCG and PG, but Kaplan et al. reported that some reactive lesions might present as peri-implantitis without nodular tissue formation.\(^1\)\(^5\) One implant was not osseointegrated, whereas all the others were associated with no mobility. Therefore, it can be suggested that reactive lesion development around dental implants does not affect osseointegration, but might play a role in crestal bone loss, which consequently could lead to implant failure.\(^4\)

The possible contributing factors in PGCG development around teeth include trauma, tooth extraction, food impaction, ill-fitting restorations, orthodontic appliance, and poor oral hygiene.\(^8\)\(^9\) Chronic low-grade irritations, trauma, hormonal factors, poor oral hygiene, and some medications (i.e., cyclosporine) have been considered as possible factors for the development of PG around the teeth.\(^1\)\(^1\) The exact etiology for the development of such lesions around dental implants has still not been established; however, there could be predisposing factors. In the present review, poor oral hygiene, prosthesis with poorly-adapted margins, oversized and unscrewed healing abutment, pregnancy, hormonal replacement therapy, and non-osseointegrated implants were found as possible causal factors for the development of such reactive lesions around dental implants (Tables 1 and 2). The presence of particulate foreign materials might act as an irritant factor, as reported by Olmedo et al. in two cases of PGCG and PG associated with dental implants.\(^1\)\(^6\) Burbano et al. reported the presence of five types of dental cement particles in human peri-implantitis biopsies using scanning electron microscopy.\(^1\)\(^7\) In a study by Wilson et al., light microscopy studies showed chronic inflammatory lesions dominated by plasma cells in human specimens in response to the titanium and dental cement particles.\(^1\)\(^8\) Interestingly, scanning electron microscopy of the same lesions confirmed the
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<th>Final outcome</th>
<th>Type of supra-structure</th>
<th>Duration of follow up (months)</th>
<th>Possible causing factor</th>
</tr>
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<tr>
<td>Olmedo et al.</td>
<td>Female/75</td>
<td>Posterior mandible</td>
<td>2 months</td>
<td>No radiographic appearance</td>
<td>Excision &amp; curettage</td>
<td>0</td>
<td>Good</td>
<td>Crown screw</td>
<td>0</td>
<td>Metal-like particles in the tissue</td>
</tr>
<tr>
<td>Dojcinovic et al.</td>
<td>Male/32</td>
<td>Posterior maxilla</td>
<td>6 months</td>
<td>No radiographic appearance</td>
<td>Excision &amp; curettage</td>
<td>0</td>
<td>Good</td>
<td>Healing abutment</td>
<td>18</td>
<td>Oversized healing abutment</td>
</tr>
<tr>
<td>Johnson et al.</td>
<td>Female/49</td>
<td>Posterior mandible</td>
<td>1 year</td>
<td>Not mentioned</td>
<td>Excision</td>
<td>0</td>
<td>Implant removal as a consequence of malposition</td>
<td>Healing abutment</td>
<td>N/A</td>
<td>Hormonal replacement therapy/implant malposition</td>
</tr>
<tr>
<td>Etoz et al.</td>
<td>Female/55</td>
<td>Posterior mandible</td>
<td>1 month</td>
<td>No radiographic appearance</td>
<td>Excision &amp; curettage</td>
<td>0</td>
<td>Implant removal of not osseointegrated implant</td>
<td>Crown</td>
<td>N/A</td>
<td>Non-osseointegrated implant/bone splitting</td>
</tr>
<tr>
<td>Trento et al.</td>
<td>Female/33</td>
<td>Posterior mandible</td>
<td>6 years</td>
<td>-</td>
<td>Excision &amp; curettage</td>
<td>0</td>
<td>Good</td>
<td>Ceramic screw retained crown</td>
<td>6</td>
<td>Pregnancy</td>
</tr>
<tr>
<td>Kaya et al.</td>
<td>Male/34</td>
<td>Anterior maxilla</td>
<td>7 years</td>
<td>Horizontal bone loss</td>
<td>Excision &amp; implant decontamination with erbium-doped yttrium aluminium garnet laser</td>
<td>0</td>
<td>Good</td>
<td>Metal-supported porcelain restoration</td>
<td>24</td>
<td>Unknown</td>
</tr>
<tr>
<td>Jane-Salas et al.</td>
<td>Male/52</td>
<td>Posterior maxilla</td>
<td>3 years</td>
<td>Bone loss</td>
<td>Excision &amp; curettage + irrigation with chlorhexidine 0.5%</td>
<td>0</td>
<td>Good</td>
<td>Crown</td>
<td>12</td>
<td>Poor oral hygiene/History of periodontitis/calculus</td>
</tr>
<tr>
<td>Geferer et al.</td>
<td>Female/55</td>
<td>Posterior mandible (right)</td>
<td>6 months</td>
<td>Horizontal bone loss in the grafted area</td>
<td>Excision (without removing restoration)/after recurrence: removing restorations</td>
<td>3</td>
<td>Implant removal</td>
<td>Crown</td>
<td>N/A</td>
<td>Lack of attached gingiva and simultaneous exposure of implant threads</td>
</tr>
<tr>
<td></td>
<td>Female/55</td>
<td>Posterior mandible (left)</td>
<td>15 months</td>
<td>Excision &amp; curettage &amp; CO₂ laser</td>
<td>Implant removal</td>
<td>2</td>
<td>Implant removal</td>
<td>Crown</td>
<td>N/A</td>
<td>Lack of attached gingiva and simultaneous exposure of implant threads</td>
</tr>
</tbody>
</table>

N/A: not applicable.
presence of foreign bodies surrounded by inflammatory cells. X-ray spectrometer revealed particulate titanium and dental cements. Precise histopathological or electron microscopic studies could be helpful to identify the presence of any metallic particles in such lesional tissues. Because poor oral hygiene is one of the factors that could be associated with the development of such reactive lesions around dental implants, maintaining good oral hygiene and appropriate plaque control is highly recommended. Gefrerer et al. presented a case with two discrete PG around dental implants which were associated with neither wrong associated prosthesis nor overloading. They assumed the lack of attached gingiva and the simultaneous exposure of implant threads as probable risk factors for the development of PG. Mucosal displacement around dental implants by muscle contraction might cause chronic mucosal irritation, which could result in the development of a reactive lesion. Cloutier et al. considered the exposure of rough implant surface as a source of chronic irritation, which resulted in the formation of reactive lesions.

In teeth-associated PGCG, superficial erosion and local destruction of underlying cortical bone was seen in 26%-28% of cases, which could manifest radiographically. PG rarely result in underlying bone loss. In our study, 81.25% of PGCG cases and 50% of PG cases around dental implants demonstrated underlying bone loss.

Surgical excision from the periosteum and the elimination of any possible local irritant factors are the treatment of choice for PGCG and PG. Superficial removal could lead to recurrence. Using neodymium-doped yttrium aluminum garnet laser, carbide dioxide (CO2) laser, diode laser, and erbium-doped yttrium aluminum garnet (Er:YAG) laser have also been suggested as other treatment modalities. The role of decontamination of implant surfaces as an adjunctive treatment has also been considered. In the present review, only two cases were surgically excised using CO2 laser and Er:YAG laser, along with decontamination of the surface of the implant with Er:YAG laser. In some cases, laser was used as an adjunctive for initial treatment, or used for the treatment of recurrent lesions.

The recurrence rate for PGCG is varied, but has been shown in most of the studies to be 15%-20%. The recurrence rate for PG has been reported as 16%. In our systematic review, the rate of recurrence for PGCG and PG associated with dental implants were 37.5% and 27.27%, respectively, and there was no sex predilection. Therefore, it seems that the recurrence rate for inflammatory/reactive lesions associated with dental implants is higher than those that are not implant related. As dental implants are screw type and the elimination of all diseased tissues is more difficult, that would explain the higher rate of recurrence of such lesions formed around dental implants. However, limited access could prevent complete removal of the lesion, which might result in implant removal or implant failure.

In our study, there were two cases of implant failure (31.25%) for PGCG due to recurrent lesions and severe bone loss. For PG cases, 27.27% of cases in our literature review were associated with implant failure, and lack of osseointegration was found to be the reason in one of those cases. Implant malposition (not considered as a consequence of reactive lesions) was mentioned to explain another case of implant failure.

In conclusion, the reactive lesions associated with dental implants are considered important biologic complications that could lead to implant failure and removal. It is recommended that all tissues around dental implants are removed, even peri-implantitis lesions, for histopathological studies in order to provide better management and prevent recurrence and implant failure. The maintenance of good oral hygiene and appropriate plaque control, placement of prosthesis with well-adapted margins, and preservation of a sufficient amount of peri-implant keratinized tissue might prevent the development of these reactive lesions around dental implants.

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REFERENCES


