Case Report

Dental treatment of a rare case of pyoderma gangrenosum with aggressive periodontal disease

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Abstract

Background: Pyoderma gangrenosum (PG) is a rare neutrophil-mediated autoinflammatory dermatosis, which may involve the oral mucosa. Dental surgery represents a potential triggering factor for the onset of PG lesions. Here, we describe and discuss the dental management of a rare case of aggressive periodontitis in a PG patient, from multiple tooth extractions to prosthetic rehabilitation, including systemic steroid prophylaxis administration before surgery to prevent the potential onset of PG-related lesions. **Case report:** A 22-years-old male patient previously diagnosed with PG and affected by aggressive periodontal disease, underwent dental extractions, gingivoplastic surgery and prosthetic rehabilitation. The patient was pre-medicated with 8 mg intramuscular betamethasone 20 minutes before the oral surgical procedure. The tissues healed perfectly and no adverse effects were reported. **Practical implications:** In case of minor oral surgery, prophylactic corticosteroids might help to reduce the risks of PG-related lesions. The prosthetic devices should be planned in order to be as atraumatic as possible.

Introduction

Firstly reported in 1930 by Brunsting, pyoderma gangrenosum (PG) is to date regarded as a neutrophil-mediated autoinflammatory dermatosis [1,2]. PG is a rare skin disease with an incidence varying from 3 to 10 patients per million [3], which may affect individuals at any age with a peak at 20-50 years and with a slight predisposition for females [3,4]. PG involvement of the oral cavity is even more rare, with just few cases reported in literature [5]. In about half of the cases, a systemic disease associated with PG can be identified: more often, inflammatory bowel diseases, endocrine diseases, rheumatoid arthritis and hematological disorders [2,4]. Otherwise, PG can be idiopathic or can contribute to define rare syndromes, such as PAPA syndrome (Pyogenic Arthritis, Pyoderma gangrenosum and Acne).

The typical PG signs are sterile cutaneous pustules, in most cases localized at the legs, characterized by a neutrophilic granulocytes' infiltrate [6]. In the ulcerating PG subtype, pustules result in very painful ulcers with undermined purple borders and a central area of necrosis exuding pus, while in the vegetating PG subtype, the same pustules result in vegetating erosions [6]. Pustular forms of PG, either as bullous lesions ("bullous PG") or as multiple pustules ("pustular PG"), are sporadic [6]. Further extracutaneous lesions can involve the subcutaneous adipose tissue in form of panniculitis and the eye with corneal ulceration. Internal organs, such as bone or lungs, are rarely affected [6]. Infrequently, intraoral and lip ulcers have been also described in PG patients [5–7].

The diagnosis requires the presence of both the two major criteria (presence of clinical lesions and exclusion of other possible causative diseases, basing on medical history and clinical findings) and, at least, two additional criteria, which include microbiology testing and histological examinations, particularly pivotal for differential diagnosis [6]. Histology contributes to exclude other diseases rather than to confirm the diagnosis, as only 7% of the biopsies were reported to show specific features, such as neutrophilic infiltration of the dermis, signs of vasculitis and accumulation of immunoglobulins and/or complement factors beside the vessels [6,8]. Currently, the PG standard treatment consists of systemic steroids administration, although, in presence of resistant cases, dapsone represents an alternative therapy [6,8]. Topical steroids are particularly useful to manage oral ulcers [9].

Most patients report a triggering factor that initiated or worsened the disease. Indeed, the phenomenon of pathergy, which correlates to an abnormal response to stimuli such as mechanical traumas (surgery, stings, or bites), is a typical findings in PG [6,10]. When surgery is required, evidence suggests that a corticosteroid-based prophylaxis could reduce the risk of PG-related lesions triggered by surgical trauma [11,12], although no specific guidelines for PG patients receiving dental surgery are available to date. In 2007, a clinical case reported the onset of a PG lesion of the maxillary sinus following tooth extraction. The authors concluded that prophylactic corticosteroid could be of help in case of surgical interventions [12]. A further recommendation was recently reported by Bissonnette *et al.* [7] who stated that "surgical debridement of PG lesion should be avoided without concomitant medically-induced immunosuppression or pre-operative corticosteroids as surgery has been demonstrated to exacerbate cutaneous PG".

Given the rarity of this disease and the current limited availability of established guidelines for oral surgical procedures, this clinical case aims at reporting the dental management of a case of aggressive periodontal disease in a young patient with a previous diagnosis of PG, who required multiple dental extractions and gingivoplastic surgery and who was not under concurrent immunosuppressive therapy at the time of dental surgery. The surgical treatment was performed following intramuscular corticosteroid prophylaxis to reduce the potential risk of triggering PG-associated oral lesions. The subsequent prosthetic oral rehabilitation is also described, resulting altogether in a clinically successful outcome.

Case report

In October 2015, a 22-years-old male patient was referred by his general practitioner to our clinic (Clinica Odontoiatrica ASST Santi Paolo e Carlo, Università degli Studi di Milano) for periodontal evaluation. The patient was affected by hepatitis B and, three years before, received a diagnosis of cutaneous PG. Since then, he had a history of intermittent systemic steroid treatment based on the use of dexamethasone and dapsone. When he came to our clinic, he was under dapsone, further suspended by his specialist a few weeks later.

At the oral examination, the patient was partially edentulous, with few remaining, hopeless teeth characterized by grade III mobility (Miller Classification), severe gingival inflammation and bleeding on gentle probing. The patient had a very poor oral hygiene compliance and reported severe pain at tooth brushing (Figure 1 a). The panoramic radiograph showed severe loss of alveolar bone, consistent with the clinical picture (Figure 1 b).

The following treatment plan was formulated: extraction of all the remaining teeth in two stages (upper jaw and, subsequently, lower jaw) and the delayed fabrication of upper and lower total dentures.

At the time of dental extraction, the patient, who was not receiving any systemic treatment for PG since a few weeks, was pre-medicated with 8 mg intramuscular betamethasone 20 minutes before surgery. After a mouthwash with 0.2% gluconate chlorhexidine right before the intervention, local anesthesia was obtained by injecting mepivacaine 2% plus epinefrine 1:100.000. All teeth were extracted without the need of opening flaps or performing osteotomy. A first intention suture was achieved with silk. The patient received post-surgical instructions and was prompted to rinse with 0.2% gluconate chlorhexidine twice a day for 2 weeks and apply 1% chlorhexidine gel three times a day for two weeks on the wounds. The extracted teeth were preserved in 10% formalin for histological analysis. The sutures were removed one week after surgery and complete healing of the soft tissues was observed (Figure 2 a, b and c). At weekly follow-up visits, the patient did not complain of any peculiar pain or discomfort.

One month following the lower jaw extractions, the soft tissues appeared to have perfectly healed but, in the third quadrant, gingival remodeling resulted in a mucosal flap that would have hindered the correct

fabrication of the lower jaw denture. Therefore, gingivoplastic surgery of the affected area was performed (Figures 3 a and b) following the same pre-medication protocol with intramuscular betamethasone. First intention closure was achieved by means of a Vycril® 5/0 suture (Ethicon Inc, Somerville, New Jersey, US) (Figures 3 c) The patient was provided with the same post-surgical instructions as for tooth extractions. The removed gingiva was preserved in 4% formalin solution for histological analysis. Two weeks later, at suture removal, a small ulceration was observed at the site of a stitch. The lesion was treated with 1% chlorhexidine gel (Corsodyl®, GlaxoSmithKline plc, London, UK) application three times a day for two weeks on the wound and completely resolved in 3 weeks (Figure 3 d). The patient was therefore deemed ready to start the prosthetic phase.

Alginate impressions were obtained and custom-made impression trays fabricated. Definitive impressions were taken one week later with a polysulfide impression material (Permlastic Regular®, Kerr Italia srl, Scafati, Salerno, Italy). Two weeks later, the teeth mounted on a wax rim were tested and their fit was adjusted on the patient. After two more weeks, the dentures were finalized and delivered to the patient who expressed his great satisfaction.

In the next 3 months, follow-up visits were performed every two weeks, during which the base of the dentures was adjusted when required. The oral mucosa was carefully examined at each visit in order to detect potential traumatic lesions. At 3 months, a painful traumatic ulceration occurred in the inferior jaw, localized at the anterior left fornix. The denture base was corrected and the patient was instructed to apply 1% chlorhexidine gel three times a day for two weeks on the wound. Two weeks later, at control, the ulceration had fully resolved. At two-years follow up, the patient showed a healthy mucosa and a complete congruence of the dentures (Figures 4 a, b, c and d).

Dental histological examination, performed after tooth processing for ground sectioning [13] and further staining with Toluidine Blue and Pyronin Yellow revealed a normal architecture of both enamel and dentine (Figure 5 a and b), beyond areas of demineralization and carious lesions concerning some teeth. On the coronal portion of the root, calculus was evident. When visible, the periodontal ligament, lining the apical portion of the root, did not show any inflammatory cells infiltration (Figure 5 c). The histological examination of the gingival tissue, performed after including the soft tissue biopsies in paraffin and staining

the sections with Hematoxylin & Eosin, showed a dense, mixed inflammatory infiltrate with a large prevalence of neutrophils and lymphocytes (Figures 5 d).

Discussion

The present case-report describes the management of a patient affected by PG and aggressive periodontal disease, requiring multiple extractions and prosthetic rehabilitation. Few reports exist concerning the oral manifestations of PG, that can be considered a very rare clinical finding (for review see Curi et al. [9] and Bissonnette et al. [7]). Hernandez-Hernández-Martín et al. reported the case of a 84-years-old woman presenting a PG oral ulcer [14] not associated with skin lesions, which resolved a few weeks later by treatment with oral steroids. A case of oral involvement related to PG was reported in a 65 years old woman with skin lesions and a deep ulceration of the tongue and it was successfully treated with mycophenolate mofetil. [15] Irregular, painful, large oral lesions in patients with PG have been reported to involve tongue, palate, lips, buccal mucosa, gingiva and tonsils [4,16–20]. Concerning the involvement of periodontal tissues, Paramkusam et al. [5] reported of a 42-years old woman with a dermatologic diagnosis of PG and under treatment with corticosteroids, dapsone, cyclosporine, and metrogyl DG gel, who presented skin lesions and a solitary ulcer localized at the right anterior hard palate. The latter was associated with the presence of severe periodontal lesions of the upper anterior teeth (1.2 and 1.3), which showed grade III mobility. [5] The patient underwent tooth extraction of 1.2 and 1.3 and was instructed to apply metronidazole ointment three times a day over the lesion and to rinse using a chlorhexidine-based mouthwash three times a day, besides taking systemic prednisolone and dapsone [5]. After 2 weeks, a new ulcer appeared on the left retromolar area, which healed, together with the palatal lesion, 6 weeks later. [5] Marzano et al. reported of a case of severe periodontal disease in an 18-year-old Pakistani man affected by PG, consisting in loss of bone support of most of his teeth and jaws atrophy [1]. In the previous and the present cases, however, a conclusive dissertation is not possible whether the aggressive periodontal disease is a manifestation or a consequence of PG rather than an independent and concomitant condition. Nonetheless, despite PG oral involvement is an uncommon finding [5], dental practitioners are asked to recognize and manage such patients and, when required, to perform accurate periodontal treatments, dental extractions and oral rehabilitations. The rarity of PG largely hindered the development of guidelines for performing oral surgical procedures in these patients, to date still anecdotal. Since surgery has been identified as triggering factor for PG lesions due to pathergy, when a surgical intervention becomes

necessary, currently available evidence (mainly related to non-oral and extensive surgeries) suggests that a steroid treatment, in form of concomitant medically induced immunosuppression or pre-operative corticosteroids, be used [12,21,22]. A recent systematic review of post-surgical PG referring to breast, cardio-thoracic, or abdominal surgeries concluded that a careful follow-up of wound healing is needed, and, in case of breast surgery, perioperative prednisone may prevent PG-related lesions at the surgical site [22]. Although specific guidelines do not exist for oral surgery in PG patients, it seems reasonable to adopt the same standards. Tallon and co-workers described a maxillary sinus PG lesion developed following tooth extraction in a patient and suggested that prophylactic corticosteroid for essential surgical interventions should be used [12]. Such suggestion is consistent with most clinical reports on minor oral surgery (like oral biopsies or tooth extractions) in patients with PG [11]. In the case report by Paramkusam et al. [5], the authors opted for a medication with prednisolone and dapsone soon after tooth extractions. In other studies [14,23], at the time of mucosal biopsy, the patients were already under steroid treatment for their systemic condition. In a further case where patient had PG-like lesions requiring oral biopsy [9], but no specific intervention was detailed.

Basing on the existing literature [11,12,22] and in absence of established guidelines for oral surgical procedures, the current clinical case was managed by administrating a steroid-based prophylaxis consisting in intramuscular betamethasone before oral surgery to prevent potential post-surgical PG lesions, under the rationale that PG is an autoinflammatory dermatosis that can be triggered by surgical trauma and that it is responsive to steroid therapy. The risk of developing PG lesions following surgery has been documented in the literature and, consistently, as mentioned above, the available knowledge supports the use of peri-operative steroid therapy when surgical interventions are needed in these patients [11,12,22]. Biologically, indeed, glucocorticoids induce anti-inflammatory and immunosuppressive effects, by interfering with key inflammatory pathways (NF-κB and AP-1) [24] and, particularly, by inhibiting neutrophil activation, chemotaxis, adhesion, transmigration, apoptosis, oxidative burst, and phagocytosis [25]. Moreover, primary intention wound closure was obtained and topical application of antiseptic agent (chlorhexidine) prescribed to prevent wound infection. Such protocol resulted, in our case, in successful healing and lack of complications, thus supporting the usefulness of prophylactic corticosteroids used to decrease the risks of

PG-related lesions before oral surgery, when the patient is not already under concurrent immunosuppressive therapy, as already suggested by Tallon et al. [12]. Nonetheless, the prosthetic rehabilitation was carefully followed-up on a long-term basis, in order to detect potential lesions or trauma. The histological findings showed the presence of a large number of neutrophils and lymphocytes within the gingival soft tissues, a typical finding in periodontal diseases. From a histological point of view, it is not possible to differentiate among chronic and aggressive periodontitis, as both forms share similar histological features, i.e. an inflammatory infiltrate characterized by neutrophils, lymphocytes and plasma cells. Over the time, inflammation results in different degrees of periodontal destruction with variable clinical outcomes (from pathological periodontal pockets to tooth mobility and, eventually, tooth loss), based on a still not well-defined individual susceptibility of the host. The intraoral clinical condition of our patient, together with the soft tissue histological findings, the young age and the severity of periodontal destruction, support the diagnosis of an aggressive form of periodontal disease. The latter might have been sustained by the systemic condition of the patient, although conclusive dissertations about a correlation between PG and aggressive periodontitis remain under debate.

Future directions for dental practitioners cannot be exempted from including an accurate and periodical oral examination of PG patients, aiming at excluding both mucosal lesions and/or periodontal diseases, whose outcomes would greatly benefit by early diagnosis and treatment. In particular, a well planned periodontal supportive therapy to prevent oral diseases acquires, in these patients, overwhelming importance, in the perspective of preserving oral health, reducing the number of diseased teeth and the need of tooth extraction at a young age (as it occurred in our case) and, globally, maintaining a patient's satisfactory quality of life.

Conclusions

Dentists should be aware of the potential oral involvement of PG in forms of mucosal ulcers and/or periodontal disease. Dental treatment is not exempted from risks; especially dental surgery may represent a potential triggering factor for PG lesions. As in our case, when minor oral surgery, in particular, is required, prophylactic corticosteroids may be of help to decrease the risks of PG-related lesions, especially when the patient is not already under immunosuppressive therapy. Nonetheless, follow-up visits are pivotal, in order to check carefully the post-surgical mucosal healing, the congruence of prosthetic rehabilitation and to intercept potentially early lesions.

Future research, including clinical trial on larger population, should focus on better elucidate the efficacy of this approach in preventing lesions' occurrence.

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Figure legends

Figure 1. Patient's oral condition of aggressive periodontal disease. Clinical image (a) and panoramic radiograph (b) at baseline.

Figure 2. Healing of tissues after dental extraction: frontal view (a) and occlusal views of upper (b) and lower (c) dental arches.

Figure 3. Pre-prosthetic surgery at III dental quadrant. Clinical pictures of gingival flange before intervention (a); gingivoplastic surgery with gingival tissue removal (b) and first intention suture (c); healing of soft tissue after surgery (c).

Figure 4. Prosthetic oral rehabilitation (two-year follow up). Total upper and lower dentures after finalization (a and b, respectively), and the patient wearing the prostheses (c and d).

Figure 5. Histological aspect of the hard and soft tissues. Enamel and dentine structure were preserved (a); figure (b) highlights the typical dentinal tubules. Periodontal ligament showed the absence of inflammatory infiltrate (c), which was detectable within the gingival tissue, instead (d). Toluidine Blue and Pyronin Yellow staining (a, b, c), Hematoxylin and Eosin staining (d).