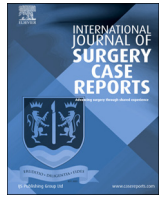


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Oral management in a patient with Gardner-Diamond Syndrome: A case report

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ABSTRACT

INTRODUCTION: Gardner-Diamond Syndrome (GDS) is rare. It is characterized by the spontaneous formation of painful erythematous skin lesions that develop into ecchymoses within 24 h and then disappear progressively over days to weeks. The complications can be serious.

PRESENTATION OF CASE: A 35-year-old man with GDS was admitted to the oral surgery department for dental infectious focus eradication. Clinical and radiological examinations indicated extraction of tooth 17. It was performed with local anaesthesia, cardiac monitoring, and verbal reassurance therapy. After delivering anaesthesia, two intra-oral hematomas and a bruise quickly developed. Cardiovascular manifestations and a spontaneous painful right temporal erythematous skin lesion appeared in the next 24 h. The patient was briefly hospitalized in the cardiovascular medicine department. Over the next 21 days, some hematomas regressed, another expanded, and a new cervico-thoracic ecchymosis developed.

DISCUSSION: The surgical and post-surgical complications in this clinical case raise several points concerning the oral management of patients with GDS. We propose to apply: verbal reassurance therapy during surgery; presurgical haematological evaluation and postsurgical daily haematological follow-up; and atraumatic surgery with intra- and post-surgical haemostatic precautions. Systematic antibiotic prophylaxis and non-steroidal anti-inflammatory drugs may also be useful. Other possibilities include desmopressin acetate, corticosteroids, antihistamines, plasmapheresis, and immunosuppressive agents; however, few cases have been treated with these strategies.

CONCLUSION: This case highlights the difficult management of patients with GDS who require oral surgery. Further studies are needed to improve the oral surgical procedures in these patients and to establish a systematic management algorithm.

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1. Introduction

Gardner-Diamond Syndrome (GDS) (also known as autoerythrocyte-sensitization syndrome, psychogenic purpura, or painful-bruise syndrome) is a rare condition that mainly occurs in young adolescents and females [1]. It typically starts with cutaneous pruritus that associates with fever, asthenia, myalgia, arthralgia, severe headache, abdominal pain, and dizziness. The pruritus precedes by a few hours the spontaneous formation of painful erythematous skin lesions. Over the next 24 h, these lesions turn into ecchymotic patches, which then disappear progressively

over days to 2 weeks [2]. GDS associates with psychiatric disorders: its acute episodes are frequently linked to psychological/physical stress [1,2]. While the lesions occur most commonly on the upper and lower extremities, face, and trunk, mucocutaneous lesions, particularly intra-oral haemorrhages, are also common [3–5]. GDS may be underpinned by immunological mechanisms, specifically immune autosensitization to the phosphoglyceride on red-blood cell membranes and the development of antiphosphatidylserine and anticardiolipin plasma IgEs. Alternative hypotheses suggest that it is caused by capillary dysfunction and platelet disorders [3,6–10]. Laboratory analyses and sometimes skin biopsies are needed to confirm the diagnosis and exclude other diseases, including disseminated intravascular coagulation, idiopathic thrombocytopenic purpura, von Willebrand disease, Henoch-Schönlein purpura, dermal angitis, Pfeifer-Weber-Christian disease, systemic lupus erythematosus, and Ehlers-Danlos syn-

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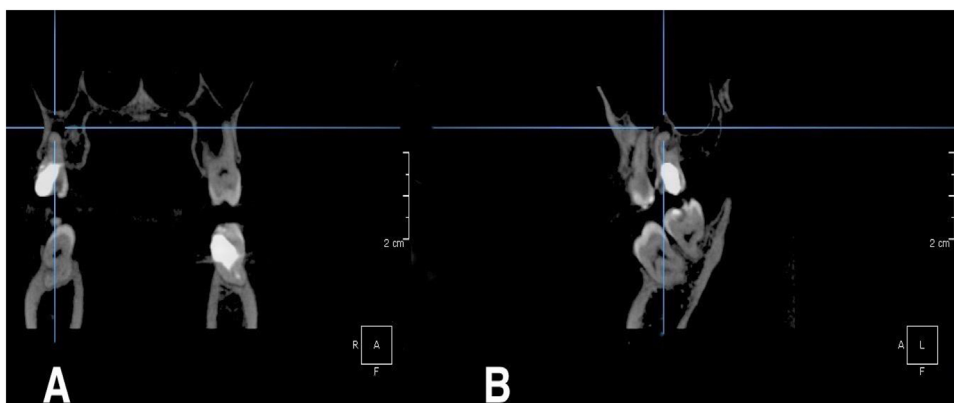


Fig. 1. Cone-beam computerized tomography showing a peri-apical cyst on the upper-right second molar. A. Coronal section. B. Sagittal section.

drome. Munchausen Syndrome, domestic violence, child abuse, and dermatitis artefacta should also be excluded [1,11,12]. The literature describes several treatments, including psychotherapy, reassurance therapy, selective serotonin-reuptake inhibitors (SSRIs), and tricyclic antidepressants (TCAs). Adjunct treatments with corticosteroids, antihistamines, hormonal contraceptives, and immunosuppressive drugs have also been described, although their efficacy is more uncertain [1].

This work has been reported in line with the SCARE criteria [13].

2. Presentation of case

A 35-year-old man with GDS was admitted to the oral-surgery department of the University Hospital of Nancy, France to eliminate a focus of dental infection so that a humanized monoclonal antibody (mepolizumab) treatment could be administered for his severe asthma. Indeed, the diagnosis was already made by hematologist. His medical history indicated he had an anxious personality, nasal polyps, multiple epistaxis episodes, pulmonary embolism, haematuria, subconjunctival haemorrhage, multiple thoracic-pain episodes, recurrent sinus tachycardia and hypertensive crisis, an apparent haemorrhage during third-molar surgery, and a tramadol allergy. Moreover, he had an aregenerative hypochromic normocytic anaemia related to recurrent bleeding that required regular intravenous iron infusion.

Clinical examinations revealed a 2-cm-diameter right soft-palate haematoma and palpation/percussion pain on the upper-right second molar (tooth 17). It was suspected that this tooth had an inflammatory apical lesion. According to French Society of Oral Surgery recommendations, dental panoramic radiography was performed. While it showed that the patient had endodontic treatment on tooth 17, it did not reveal an apical lesion in tooth 17. This confirmation was obtained by cone-beam computerized tomography, which revealed a lesion at the level where the proximal vestibular root curved to its last apical third (Fig. 1). Since the patient urgently required anti-asthma treatment and endodontic retreatment associated with anatomical difficulties, dental extraction was proposed to the patient, who consented. The recent blood-test results were normal.

The surgery was performed by an oral surgeon in an oral-surgery office under local anaesthesia with articaine and adrenaline (concentration 1/100000) to limit haemorrhagic risk. The patient also underwent cardiac monitoring and verbal-reassurance therapy. Immediately after anaesthesia, two right inner-cheek haematomas developed, a small one on the anterior cheek and a medium-sized one on the posterior cheek, where the retractor was positioned. A 1-cm-diameter peri-apical bruise also developed quickly at the injection site (Fig. 2). Despite the mild avulsion, oroantral commu-



Fig. 2. Immediately after anesthesia, two intra-oral hematomas of the right anterior (1) and posterior cheek (2) where the retractor was positioned, and a peri-apical bruising at the injection site (3).

nication was observed due to proximity to the sinus. Absorbable haemostatic gauze (Pangen®) was inserted into the socket, a cross-suture with 3/0 polyglycolic acid absorbable wire was placed, and an upper-right silicone haemostatic gutter that the patient was asked to wear for 48 h was made.

The patient was prescribed the following medications for the next 7 days: a amoxicillin/clavulanic acid (1000 mg/125 mg) mixture t.i.d to limit infection of the oroantral communication; 1 g acetaminophen per 6 h and 20 mg oral nefopam hydrochloride per 4 h to control pain; oral tranexamic-acid solution that had to be applied *via* a sterile compress for 5 min three times a day; and chlorhexidine 0.20% as a mouth wash after every meal. The patient was also advised to consume a soft diet for 7 days to avoid gingival trauma. The patient had good adherence to his treatment.

The 24-h follow-up revealed sinus tachycardia (118 beats/min), high blood pressure (154/98 mmHg), and surgical-site pain that scored 8 on the visual analogue pain scale. Clinically, a spontaneous, painful, 4-cm long, 1-cm wide, right-temporal erythematous skin lesion that appeared 16 h after surgery was noted. While the haematoma on the inner right-anterior cheek and the peri-apical bruising had disappeared, the right-posterior cheek and soft-palate haematomas remained (Fig. 3). Short hospitalization in the cardiovascular medicine department was advocated. The biological variables at admission were normal. Cardiac monitoring was established and intravenous acetaminophen and nefopam hydrochloride infusion was prescribed. The vital signs normalized rapidly and the pain dropped significantly, allowing the patient to return home.

On postoperative day 14, the patient presented with moderate upper-right oral-cavity pain and normal granulation tissue on the extraction site. The right-posterior cheek haematoma had almost

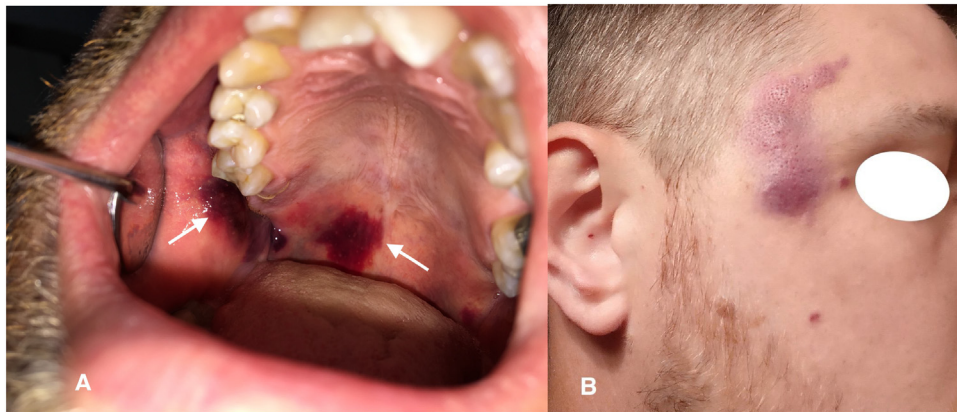


Fig. 3. At 24 h, persistence of medium-sized hematoma of the inside right posterior cheek and right soft palate (A). Appearance of spontaneous and painful right temporal erythematous skin lesion (B).

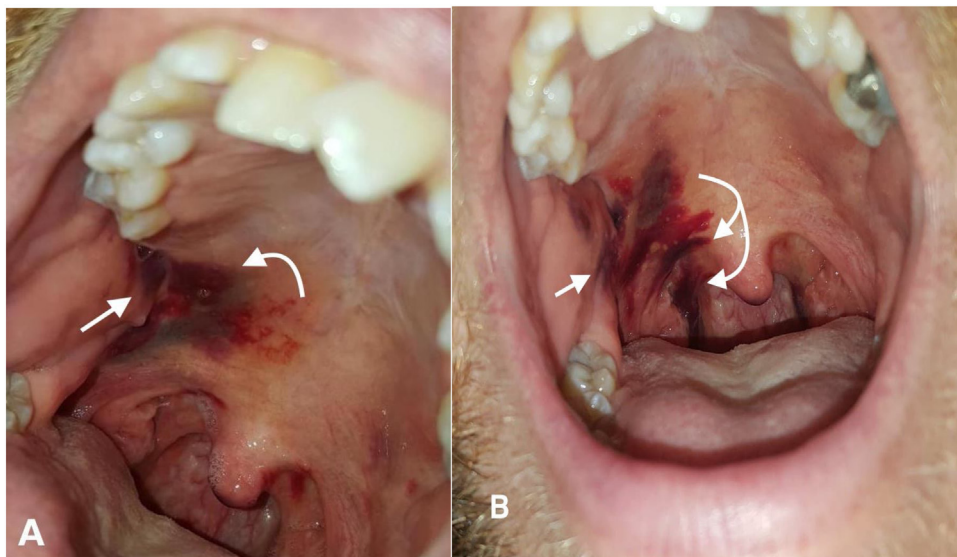


Fig. 4. The haematoma on the inner right-posterior cheek had almost disappeared at postoperative day 14 (A) and was unchanged at 21 days (B). Lateralization of the right soft-palate haematoma was observed at postoperative day 14 (A) and its expansion to the anterior and posterior tonsillar pillar was noted at postoperative day 21 (B).

disappeared but lateralization of the right soft-palate haematoma was observed (Fig. 4A).

On postoperative day 21, the patient had almost no pain and the extraction site exhibited fibrous connective tissue with peripheral keratinized epithelium. The right-posterior cheek haematoma was unchanged but the right soft-palate haematoma had expanded towards the anterior and posterior tonsillar pillars (Fig. 4B). A remarkable left cervico-thoracic ecchymosis that was resembled a bead necklace was also observed (Fig. 5).

3. Discussion

The surgical and post-surgical complications observed in this clinical case raise several points concerning the oral management of patients with GDS.

First, preoperative precautions are required. One relates to the patient's psychological state: the appearance of GDS lesions is promoted by psychological or physical stresses, including surgery [1,2], and can be effectively prevented by psychotherapy, reassurance therapy, SSRIs, and TCAs [1]. To address this, our patient was under psychiatric follow-up and SSRI treatment (already since his diagnosis) and the oral surgeons provided continual verbal reassurance during the surgery. Another precaution relates to the patient's

haematological status: GDS can cause haemorrhage, and indeed, our patient had chronic anaemia because of this. Therefore, it is recommended that GDS patients should undergo preoperative haematological evaluation and daily follow-up of haemoglobin levels for at least 3 days after oral surgery. Thirdly, given our patient's postoperative pain, right temporal lesion, and cardiovascular complications, it may be advisable to schedule ambulatory surgery or short-term hospitalization, as is already recommended for congenital haematological diseases [14–16].

Second, GDS patients should be managed as atraumatically as possible during surgery. Our patient newly developed two intra-oral hematomas and a bruise immediately after anaesthesia. This could be explained by the psychological stress of the surgery and/or possible weakening of the capillary walls due to kinin-kallikrein system dysfunction [7]. Therefore, atraumatic surgical techniques and instruments should be used. Notably, we also applied local haemostatic agents, tension cross sutures, and a silicone haemostatic gutter to limit the bleeding: indeed, no intra-oral haemorrhage from the surgical site was observed. This strategy was inspired by that used for inherited bleeding disorders such as Glanzmann thrombasthenia [15].

The third point relates to postoperative precautions. Our patient systematically applied tranexamic acid to the surgical site. This



Fig. 5. On postoperative day 21, the patient also had a left cervico-thoracic ecchymosis that was resembled a bead necklace.

probably helped prevent postoperative haemorrhages. This drug has already proven its efficacy in patients with acquired or hereditary bleeding disorders [16]. We also provided systemic antibiotics for 7 postoperative days. However, prophylactic antibiotics should perhaps also be considered because the pain and stress of surgery could yield new acute episodes that could rapidly lead to local infection. Moreover, the presence of a temporary bacteremia secondary to the surgical act could yield inflammatory cytokines and cellular degradation products that damage the inner lining of the blood-vessel walls. This hypothesis has been proposed for Henoch-Schönlein purpura, a differential diagnosis of GDS; as a result, Echavarría-García et al. recommended that Henoch-Schönlein purpura patients should routinely receive systemic antibiotic prophylaxis before dental procedures. However, they did not discuss postoperative antibiotics [17]. Finally, the patient's postoperative pain was poorly controlled. Non-steroidal anti-inflammatory drugs, which effectively prevent inflammation and pain after oral surgery, may be a more suitable choice [18].

Specific treatments may also be suitable for GDS. Intranasal desmopressin acetate (DDAVP) has successfully reduced the ecchymosis duration/severity of a GDS patient with a platelet disorder [9]; it has also been used for several Von Willebrand-disease cases (a GDS differential diagnosis) [16]. Moreover, since autoimmunity may participate in GDS [6], corticosteroids could improve GDS symptoms and antihistamines (e.g. tripeleminamine) might have beneficial effects. Moreover, plasmapheresis has deterred new attacks for several weeks in GDS. Other immunosuppressive agents have also been employed [1,19,20]. However, the usefulness of these therapies in oral management of GDS remains uncertain due to the small number of cases reported.

4. Conclusion

GDS causes physical and mental discomfort and potentially serious complications. Our dental-extraction case shows that oral management in GDS can be complex. It is important to make health professionals aware of this pathology and to conduct further studies to establish a systematic management algorithm. In the meantime, in the absence of guidelines, patients with GDS should be considered at high bleeding risk. Moreover, pre and postoperative medical follow should be instituted.

Declaration of Competing Interest

All authors declare that there are no financial and personal relationships with other people or organisations that could inappropriately influence their work.

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Ethical approval

Exception from ethical approval because the study was a case report. The patient provided written consent to undergo the procedures described in this case report and for his data and images to be published.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author's contribution

Conception and design of the study, or acquisition of data: A. Bellot, R. Curien, A. Derache, B. Delaitre, R. Longo, B. Phulpin.

Drafting the article or revising it critically for intellectual content: A. Bellot, R. Curien, R. Longo, Y. Zevering, J. Guillet, B. Phulpin.

Final approval of the version to be submitted: A. Bellot, R. Curien, A. Derache, B. Delaitre, R. Longo, Y. Zevering, J. Guillet, B. Phulpin.

Registration of research studies

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Guarantor

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