Abstract

The present review describes the elementary lesions observed in the oral cavity in cases of bleeding syndromes and disorders of blood erythroid series. It has been identified and described diseases of the red series (anaemias, polycythaemias) and coagulation disorders (involving both platelet and plasma coagulation factors) that can cause manifestations in the mouth and briefly described these events. Pale mucous, xerostomia, atrophic glossitis, angular cheilitis, ulcers, gingival bleeding, petechiae, ecchymoses or swelling are common oral manifestations, some of them being non-specific symptoms of coagulation disorders and disorders of blood erythroid series. Whether it occurs early, late during the disease or as an effect of the treatment, oral manifestations are non-pathognomonic and must be considered in their clinical and laboratory context. Patients’ dental treatment should be based on the basic hematologic disease for each particular case.

Keywords: Hemorrhagic Disorders, Anemia, Oral Manifestations

Introduction

During the past 10 years a growing attention has been given to interdisciplinary therapies and patients whose diseases involve several medical specialties. Oral pathology of hemopathies has long been neglected by dentists and patients were treated for their basic disease in hematology clinics, intraoral manifestations of the disease not being considered a priority. It is absolutely essential that your dentist should know the types of bleeding disorders and oral manifestations that may occur in each of them. This way, such complications can be prevented and diseases can be treated early to prevent any inconvenience. Dental procedures like extractions and periodontal surgery are invasive procedures, commonly associated with posttreatment bleeding, which stop by itself in most cases, if the patient does not suffer from bleeding disorders. A small but significant number of people presents clotting problems, for which, even minimally invasive interventions may lead to increased risk of bleeding.

Excessive bleeding is not only uncomfortable for the patient, but can interfere with other medical procedures (eg suturing the wound) and can sometimes compromise the patient’s general health.

Lately, more and more people suffer from congenital or acquired blood disorders as a result of medications, diseases of other organs or alcohol [1]. Dental management of these patients should include an accurate knowledge of these conditions by the dentist and his collaboration with the haematologist.
Oral manifestations of hemopathies have been understood by dentists and hematologists in different ways, according to the evolution, diagnostic methods and therapeutic advances of the disease.

Diagnosis of oral manifestations in coagulation disorders and diseases of the red series is very important for the dentist and the daily practice. The dentist must recognize elementary lesions that occur in the oral cavity of patients with haematological background; make the differential diagnosis of these lesions to those that occur in other diseases and syndromes at intraoral level; develop a treatment plan that takes into account possible complications that may be associated with bleeding disorders or anemia [1,2].

For remote diagnosis of hemorrhagic syndrome it is useful to review and acknowledge the basic patterns of different oral lesions in association with modified blood counts: bleedings in case of thrombopenia, pallor and glossitis in case of anemia, gingival hyperplasia in polyglobulia, Hunter glossitis in Biermer anemia, etc [3]. Studies in recent years do not contain an adequate approach of this subject, only in the past decade there is an interdisciplinary interest among dental medicine and hematology, results being only a few.

This review presenting the main diseases of the erythroid series and major blood coagulation disorders, their intraoral manifestations and therapeutic features for the major types of dental procedure.

**Oral manifestations in blood red series pathology**

Hemopathies of the red series (erythrocytes) are divided according to their increase or decrease in anemia, respectively erytremia (polycythemia or erythroblastosis).

**Iron deficiency anemia** is the most common type of anemia [4]. In the oral field, manifestations are frequently seen in the pale mucous membranes, xerostomia, aphthae lesions, atrophic glossitis, purplish-red inflammation areas, with adjacent pale gums [5]. Atrophic glossitis manifests through a depapillated and erythematous tongue [4], which can be taken by mistake as migratory glossitis (in this case depapillated and erythematous areas are surrounded by a keratotic halo) [6]. In some cases of iron deficiency anemia, tongue can have a slight increase in sensitivity to acid, spicy foods, etc, patients accusing a sensation of stinging. Iron deficiency anemia is often associated with atrophic glossitis, angular cheilitis and commissural ulceration [2,7]. Angular cheilitis can get suprainfected with Candida albicans and/or other germs and mucous dehydration can occur [8].

**Plummer-Vinson syndrome** is also called Paterson-Kelly syndrome. It is a complex syndrome caused by chronic iron deficiency [9]. It is characterized by atrophic glossitis and occasionally keratotic lesions on the oral mucosa. Dysphagia and oropharyngeal mucosal atrophy may be associated [3,10].

**Thalassemia** is a constitutional anemia involving defects in the synthesis of α and β polypeptide chains of hemoglobin. Depending on the globin chain which has the quantitatively synthesis defect, thalassemias are divided into two main groups: α thalassemia and βthalassemia [7]. Oro-facial appearance of patients with thalassemia is known as Cooley facies: bosselation of frontal and parietal bones, increase of the maxillary bone which causes abnormalities of tooth implantation, sometimes having monstrous aspects and modified occlusion (open bite, overjet or other forms of malocclusion) [11]. Oral mucosa is pale most of the times [11,12]. In cases of α thalassemia, patients are asymptomatic, but may sometimes have mild anemia, expressed at oral level by mucosal pallor [12,13].

**Biermer pernicious anemia (megaloblastic anemia)** it occurs when a deficiency of vitamin B12 exists. Intraorally, the pathognomonic sign is Hunter glossitis, which is the progressive atrophy of the filiform and fungiform papillae [14,15]. They make the dorsal tongue look shiny red and smooth [15]. Tongue atrophy can be installed progressively and sometimes complicate by cracks and/or ulcerative lesions or blisters which become painful and sensitive to food contact [2,15,16]. Depapillation of the entire surface of the tongue can be distinguished from other types of glossitis [6]. Hunter glossitis is an important sign in Biermer anemia, and can occur at any time during the disease [17]. If anemia comes first, this is suggestive for the diagnosis of Biermer anemia and permits early treatment [14,18].

**Aplastic Anemia** is a disease characterized by pancytopenia due to the reduced amount of hematopoietic tissue in the bone marrow. The severity of symptoms depends on the degree of cytopenia [19]. At mouth level, gums bleeding and petechiae are mostly observed. Mucosa is pale, dry and atrophic; dorsal tongue is smooth, fine and painful; angular cheilitis may be present [20]; sometimes we can notice mucosal ulceration, superinfection with Candida albicans or viral infection, the latter being due to immunosuppression (neutropenia, lymphopenia) [8,20].

**Sickleemia** is a chronic hemolytic anemia related to the sickling phenomenon of erythrocyte (red blood cells lose their normal shape, which get the aspect of „sickle”) under low oxygen tension [1]. In this version of hemoglobin, glutamic acid in position 6 of the normal
Coagulation disorders (acquired or inherited) may cause fibrinolysis, then phenomena of bleeding appear. One or more of these phases, with the balance tilting physiological fibrinolysis phase. If there are defects in phase of coagulation factors (the actual clotting) and harmony: vascular phase, platelet phase, activation out in four stages which succeed in a perfect functional harmony: vascular phase, platelet phase, activation phase of coagulation factors (the actual clotting) and physiological fibrinolysis phase. If there are defects in one or more of these phases, with the balance tilting toward fibrinolysis, then phenomena of bleeding appear. Coagulation disorders (acquired or inherited) may cause a number of oral manifestations which include: petechiae, hematoma of the tongue, spontaneous gingival bleeding or prolonged gingival bleeding after surgical intervention [37]. Minimal trauma such as tooth brush or chewing gum may cause prolonged bleeding in time, even if the depth of the wound is not significant [37].

**Vascular phase** of hemostasis consists in a process of local vasoconstriction which reduces vascular gap size. If the vascular phase is altered (generally by an abnormality of the blood vessel wall), bleeding occurs more frequently at skin level, which expresses by petechiae, ecchymosis, or both. Vascular defect causing the hemorrhage may be inherited or acquired [3,36].

**Platelet phase** comprises the following stages: adhesion, platelet aggregation and thrombocyte secretion. Abnormal bleeding associate with thrombocytopenia (low platelets) or thrombasthenia (altered platelet function) and include: bleeding gums and mouth, prolonged bleeding after surgical intervention [38]. Glanzmann’s thrombasthenia is an extremely rare abnormality that occurs introraorally by gingival bleeding, purpura and mucosal petechiae [39].

**Clotting** occurs through two separate pathways that interact, the intrinsic and the extrinsic pathway. The extrinsic pathway is activated by external trauma that causes blood to escape from the vascular system. This pathway is quicker than the intrinsic pathway. It involves factor VII. The intrinsic pathway is activated by trauma inside the vascular system, and is activated by platelets, exposed endothelium, chemicals, or collagen. This pathway is slower than the extrinsic pathway, but more important. It involves factors XII, XI, IX, VIII. Both pathways meet and finish the pathway of clot production in what is known as the common pathway. The common pathway involves factors I, II, V, and X [40].

Defects in coagulation stage can be conventionally divided into two categories, first patients with acquired defects of certain factors (prothrombin, VII factor, IX factor, X factor), which occur following the treatment with anticoagulants, the deficiency of vitamin K and as a result of liver disease (globin synthesis disorders). The second categories, the patients with congenital defects of one or more coagulation factors. In this group of patients we can observe introraoral purple on the tongue and palate, intraoral hematoma, lips, tongue and oral mucosa ecchymosis, spontaneous or posttraumatic bleeding gums, prolonged bleeding after extraction. Hemarthrosis and arthropathy can also occur (most often in patients with hemophilia) in the temporomandibular joint [35,36,37].

**Fibrinolysis phase** – Gingival bleeding.
Dental management of patients with bleeding disorders

The management of patients with coagulation disorders depends largely on the disease ethiopathogenesis, its severity and the type of dental intervention to be carried out. If the dental procedure is minimally invasive and the haematological disorder is compensated, dental maneuvers can be performed without an increased risk.

If the patient has a severe blood disorder, he needs, as far as possible, to treat the basic haematological disease and subsequently ensure a rigorous hemostasis [41].

Control of pain. In patients with coagulopathy, truncal peripheral anesthesia is counterindicated because there is a very high risk of developing a hematoma [42]. Plexus and intraligamentous anesthesia are preferred in case the treatment can not be carried out without anesthesia. If possible, it's advisable to use anesthetic with vasoconstrictor. Patients who undergo intensive treatment in hematology clinics must be fully anesthetized, and the intervention will be made intraoperatively.

Oral Surgery. Surgical procedures involve a high risk of bleeding, and the additional measures required to achieve hemostasis that must be used are: wound suture, using a local hemostatic, pressure to the wound level, using local thrombin, topical fibrin glue [43] or vasoconstricter can be used individually or together [44,45,46]. Treatment should be delayed until the patient has normal blood levels, and the haematologist gives its consent on the intervention [46]. If the basic haematological condition persists, a preinterventional balancing can be achieved using substitution treatment with platelet concentrate, fresh plasma, concentrations of coagulation factors [45].

Periodontal Procedures. Periodontal health is of critical importance in patients with coagulation disorders, to which gingival hyperemia and gums bleeding may occur. Periodontitis can cause tooth mobility and may require the need for extractions, difficult to achieve in these patients [47].

Endodontic and restorative treatment. Restorative procedures do not imply bleeding in patients with coagulopathies. However, we should take care not to harm the gums by different procedures: application for rubber dam clamp, subgingival grinding etc. Endodontic treatment is preferable to extraction in these patients whenever possible [37].

Prosthetic treatment. This treatment should not represent an increased risk of bleeding, trauma being minimal if treatment stages are carried out with observance and attention.

Choice of drug therapy. Many prescription drugs in dental practice interfere with hemostasis. In addition, other drugs like non-steroid anti-inflammatory agents may potentiate the effect of oral anticoagulants by affecting the platelet function, increasing the risk of bleeding [48]. Penicillin, Erythromycin and Miconazole also potentiate the effect of Coumadin [49]. The dentist must consider the patient's current medication and consult with his hematologist to prescribe these drugs.

In conclusions the oral manifestations in hemopathies may have different characteristic features, depending on the background of haematological diseases and related complications.

Hematologists and dentists should focus their attention on oral lesions when dealing with patients suffering from hemopathies, this fact being useful for early recognition and treatment of various oral diseases that arise due to haematologic diseases. The dentist must be very familiar with the types of hemopathies and their oral manifestations and be prepared to face an intraoperative bleeding, to achieve efficient haemostasis and correct postintervention treatment and the patients' dental treatment should be based on the basic hematologic disease for each particular case.

Bibliography


