Unusual Post-Extraction Hemorrhage in a Cardiac Patient: A Case Report

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Abstract

In patients with cyanotic congenital heart disease (CCHD), the need for antibiotic prophylaxis for infective endo-carditis is well known among dentists, but not many dentists are aware of the associated hemorrhagic tendencies in such patients. We report a case of post-extraction hemorrhage in a patient with Eisenmenger's syndrome and discuss the importance of more elaborate hematologic evaluation in patients with CCHD before oral surgery.

MeSH Key Words: *Eisenmenger complex/complications; oral hemorrhage/adverse effects; tooth extraction/adverse effects*

An untreated ventricular septal defect may result in Eisenmenger's syndrome, which is defined as "elevation of pulmonary arterial pressure to the systemic level caused by increased pulmonary vascular resistance with reversal or bi-directional shunting through a large intracardiac or extracardiac congenital heart defect."[1] In Eisenmenger's syndrome, deoxygenated venous blood returning to the heart is pumped out into the systemic circulation without passing through the lungs for oxygenation, which results in central cyanosis.[2] Chronic hypoxia, caused by cyanosis, results in increased erythropoietin secretion by the kidneys and, subsequently, polycythemia.[3] The type and magnitude of hematologic abnormalities in patients with cyanotic congenital heart disease (CCHD) are directly proportional to the degree of polycythemia.[3]

Cardiac patients usually undergo dental treatment only after a physician's consent, and treatment follows established protocols for infective endocarditis antibiotic prophylaxis and withdrawal of anticoagulants, which are set, reviewed and updated periodically by scientific authorities. However, these measures alone cannot ensure safe extraction in a patient with CCHD. Review of the literature reveals that excessive bleeding can occur in such patients for reasons other than the use of acetylsalicylic acid and anticoagulant therapy. Hematologic abnormalities can be thrombocytopenia, accelerated fibrinolysis or decreased production of

coagulation factors leading to increased prothrombin time and thromboplastin time.[4] This case report highlights a hemorrhagic tendency encountered in a patient with a ventricular septal defect with Eisenmenger's syndrome. With an increasing number of patients with Eisenmenger's syndrome surviving to adulthood,[5,6] it is more likely that dentists will encounter such patients in their practice, underlining the importance of their awareness of this condition.

Case Report

A 30-year-old man presented with bleeding from the lower left molar region over 2 days. The patient was known to have congenital heart disease. Two days earlier, a local dentist had extracted his lower left first molar after routine antibiotic prophylaxis for infective endocarditis. However, the dentist did not order any hematologic investigations. Bleeding occurred that evening and the patient noticed blood-tinted saliva and droplets of blood oozing from the extraction socket. The next day, the patient returned to the dentist, who debrided and sutured the socket area. The patient appeared normal after this treatment, but had a recurrent episode of bleeding after a few hours. He then reported to our department for evaluation.

The patient was of moderate build, fairly well nourished and with vital signs within normal limits. There was clubbing of fingers. Liver, spleen and lymph nodes were not palpable and no signs of pedal edema or ascites were observed.

Table 1   **Summary of hematologic investigations**

Investigation	Normal range[a]	Patient's value	Evaluation
Hemoglobin	8.1–11.2 mmol/L	15.45 mmol/L	Increased
PCV	0.40–0.54 L/L	0.80 L/L	Increased
TLC	$4.0–11.0 \times 10^9$/L	3.6×10^9/L	Normal
RBCs	$4.5–6.5 \times 10^{12}$/L	9.9×10^{12}/L	Increased
Platelet count	$150–400 \times 10^9$/L	96×10^9/L	Decreased
Bleeding time	1–6 min (Ivy method)	5 min	Normal
PT	< 3.0 (INR)	3.13 (INR)	Increased
aPTT	25–35 s	43.0 s (control 32 s)	Increased
Biochemical investigations			
AST	5–40 U/L	61 U/L	Increased
ALT	5–40 U/L	27 U/L	Normal
ALP	40–140 U/L	689 U/L	Increased

[a]*For males.*

ALP = alkaline phosphatase; ALT = alanine transaminase; aPTT = activated partial thromboplastin time; AST = aspartate transaminase; PCV = packed cell volume; PT = prothrombin time; RBCs = red blood cells; TLC = total leucocyte count.

An intraoral periapical radiograph of the region ruled out the presence of root fragments. The extraction area was again debrided under local anesthesia without adrenaline, irregular bony margins were smoothened and the area was closed with interrupted sutures. Pressure packs and local hemostatic hemocoagulase were used to control bleeding and the patient was discharged. The patient reported again the next day with bleeding from the same area. Examination revealed petechiae over the skin of his arms and thorax. Ethamsylate was administered and the bleeding was controlled temporarily. The patient was referred for cardiac consultation and hematologic tests were ordered. The next day, the patient had another episode of bleeding and was admitted to hospital.

Cardiologist's Report

The patient had grade III carpopedal clubbing and central cyanosis. He had a grade III left parasternal heave with a right ventricular fourth heart sound and an accentuated pulmonary component in the second heart sound along with pansystolic murmur with tricuspid regurgitation. An electrocardiogram suggested right ventricular hypertrophy, right axis deviation and secondary ST-T changes. It revealed a large (2.2 cm) ventricular septal defect; right-to-left shunting; a right ventricular thickness of 1.3 cm; and grade II tricuspid regurgitation. Cardiac catheterization revealed a pulmonary-to-systemic flow ratio of 0.8 and a pulmonary vascular resistance of 520 dynes $\times$ s $\times$ cm^{-5}.

Hematologic Investigation

Tests revealed a high hemoglobin concentration (15.45 mmol/L), a high red blood cell count (9.9×10^{12}/L), a packed cell volume of 0.80 L/L, a prothrombin time of 3.13 (INR), an activated partial thromboplastin time of 43 s (with a control of 32 s) and a reduced level of platelets (96×10^9/L) (**Table 1**). Biochemical investigations revealed an increased level of aspartate transaminase (61 U/L) and

alkaline phosphatase (689 U/L). White blood cell counts were normal.

Subsequently, 2 units of fresh frozen plasma were infused, after which the bleeding stopped completely.

Discussion

Hemostatic abnormalities in patients with CCHD are well documented. Bleeding tendency is usually mild to moderate and is characterized by easy bruising, petechial hemorrhage and gingival bleeding.[7] In patients with congenital cardiac defects, infective endocarditis prophylaxis and determination of bleeding tendency are the most important factors that dental practitioners must consider.[8]

In Eisenmenger's syndrome, pulmonary hypertension causes the heart to circulate deoxygenated blood resulting in chronic hypoxia. Hypoxia triggers the secretion of erythropoietin from the kidneys, which causes erythrocytosis and subsequent polycythemia and an increase in the hematocrit[3] (**Fig. 1**). Because bleeding in patients with CCHD has a systemic cause, the use of a topical hemostatic agent results in only temporary cessation of bleeding, as observed in our case; hence the role of local hemostatics is limited.

In CCHD, abnormal hemostasis has a multifactorial etiology. It may be caused by a decrease in the coagulation factors synthesized in the liver, i.e., vitamin-K-dependent factors II, V, VII, IX and X, which can be explained by deficient synthesis resulting from hypoxic damage to the liver and sluggishness of microcirculation caused by high blood viscosity[9] (**Fig. 1**). This explains the elevated levels of liver enzymes and the increase in prothrombin time and activated partial thromboplastin time observed in our patient. It also emphasizes the need for specific assays (**Box 1**), which had not been performed in our patient. Our patient's abnormal hemostasis was a result of deficient clotting factors, which was corrected by transfusion of fresh frozen plasma.

In patients with CCHD, platelets have both qualitative and quantitative abnormalities. Platelet count and hematocrit are inversely related; thus an increased hematocrit is associated with thrombocytopenia.[3,9] Low platelet counts are attributed to either shortened half life of the platelets[3] or decreased production of platelets as megakaryocytes escape fragmentation in lungs owing to a right-to-left shunt.[10] An elevated PCV and reduction in platelet count was found in our patient (**Table 1**).

In patients with CCHD, polycythemia occurs with overproduction of platelet microparticles, probably due to high shear stress caused by increased blood viscosity, which might play an important role in the coagulation abnormalities identified in such patients.[11] In their study of 33 patients, Bhargava and others[12] concluded that there was reduction in platelet adhesiveness to glass and impaired availability of platelet factor 3 in nearly 50% of patients and poor clot retraction in 84% of patients. There is also a deficit in the platelet adhesion receptor glycoprotein Ib, which can also contribute to hemostatic complications.[13] Qualitative platelet defects associated with CCHD include abnormal aggregation of platelets in response to adenosine diphosphates, epinephrine and collagen, which is directly related to the degree of polycythemia.[3] Tests to confirm these findings were not performed in our patient, as temporary cessation of bleeding indicated that the hemostatic defect was not due primarily to platelet abnormalities but to a coagulation defect. However, tests to rule out qualitative platelet defects are recommended in CCHD patients (**Box 1**).

A variant of von Willebrand disease, characterized by a deficiency of the high molecular weight forms of the von Willebrand factor in plasma, has also been reported.[3,11,12] Cyanosis, turbulent blood flow and pulmonary vascular disease appear to be independently associated with a reduction in or the absence of large von Willebrand factor multimeric forms.[14,15] It remains to be determined whether the von
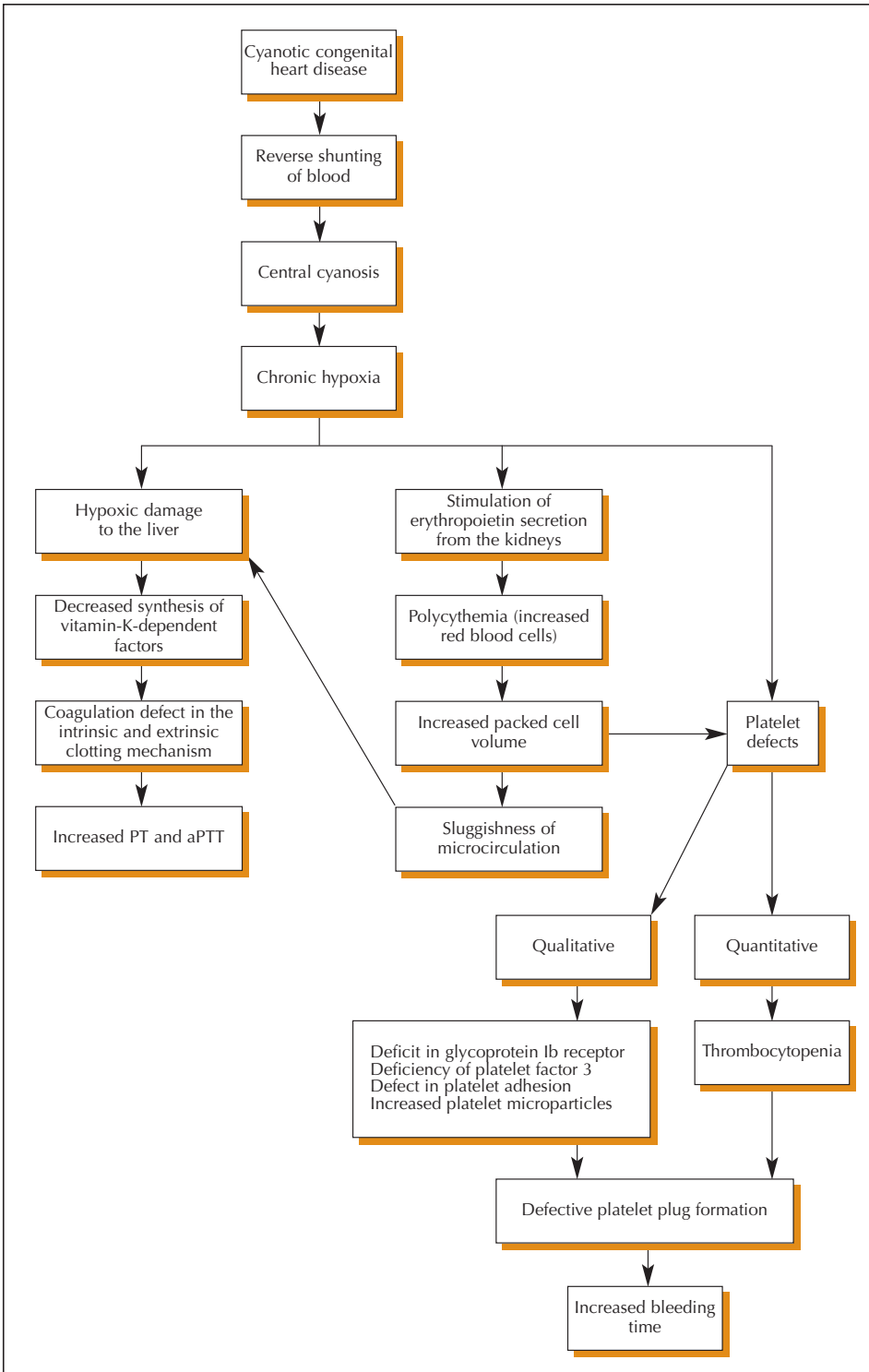

Figure 1: *Clinicopathologic processes responsible for abnormal hemostasis in patients with cyanotic congenital heart disease. (Disseminated intravascular coagulation and abnormality in von Willebrand factor also contribute to hemostatic abnormalities.) aPTT = activated partial thromboplastin time; PT = prothrombin time*

Willebrand abnormality has a central role in the clinical hemostatic disturbance experienced by patients with CCHD.[7] Although rare, specific tests to rule out von Willebrand disease are recommended in CCHD patients after consultation with a physician.

Abnormal hemostasis resulting from a state of consumptive coagulopathy or disseminated intravascular coagulation has also been observed in some patients with elevated D-dimer levels. D-dimers are specific degradation products of cross-linked fibrin[16] and indicate prior thrombin generation and subsequent lysis. Chan and others[17] observed an increase in thrombin generation and consumptive coagulopathy as indicated by high levels of thrombin–antithrombin complexes in cyanotic and acyanotic heart disease patients. Therefore, assessment of D-dimer and antithrombin levels can be performed to rule out disseminated intravascular coagulation and increased fibrinolytic activity.

In most patients, preoperative abnormalities in screening tests predict a subclinical hemorrhagic tendency,[9] but normal test results do not exclude the possibility of a major postoperative bleeding diathesis.[18] This emphasizes the need for specific tests (**Box 1**), which should be performed with a physician's consent in patients with continuous postoperative bleeding tendency after minor orosurgical procedures despite normal screening tests or before any major orosurgical procedure.

In the management of such patients, nonsteroidal anti-inflammatory drugs, such as acetylsalicylic acid, should be avoided, as they block the cyclooxygenase pathway and inhibit platelet aggregation, thus enhancing intrinsic hemostatic defects caused by existing platelet abnormalities in patients with CCHD.[8] Corticosteroids and anticoagulants also increase the risk of bleeding, and these drugs should be avoided.

Before a major orosurgical procedure, if the hematocrit is high, prophylactic phlebotomy is recommended, with a physician's consent, to reduce the hematocrit level to below 65%. This improves hemostasis and decreases the risk of post-surgical hemorrhage.[19] Units of phlebotomized blood should be stored for potential autologous transfusion in the future. In addition to bringing the hematocrit under control, prophylactic platelet transfusion can be performed; if it does not stop bleeding, fresh frozen plasma can be infused. Aprotinin, epsilon aminocaproic acid, tranexamic acid and desmopressin can also be used to control bleeding in CCHD patients.

In patients with Eisenmenger's syndrome, dental extractions and other minor orosurgical procedures should be performed under conscious sedation.[20]

Conclusion

This article emphasizes the need for and the importance of preoperative hematologic screening in patients with CCHD to prevent postoperative bleeding by predicting subclinical hemorrhagic tendencies. A detailed case history, symptoms of CCHD and abnormalities in such screening tests as complete blood count, hematocrit, prothrombin time and activated partial thromboplastin time should alert the dentist to such tendencies. In view of the nature of the problem, a team approach involving the dentist and the physician in the management of such patients is necessary to provide them with better and safer care. ❧

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