Gingival Bleeding: Initial Presentation of Prostatic Cancer

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Although coagulation disturbances have been described as potential complications of prostatic cancer,[1–3] gingival bleeding is rarely the presenting symptom.[2] In fact, bleeding gums in an otherwise healthy patient is frequently considered to be trivial. This case illustrates how gingival bleeding uncovered a more ominous diagnosis of prostatic carcinoma.

CASE REPORT

A 72-year-old male patient of the Family Medicine Center telephoned the resident on call one Saturday morning, complaining of bleeding gums. The patient reported continuous oozing of blood from his gums for the past week. He was also alarmed by a 1-day history of painless hematuria. He denied hemoptysis, melena, hematemesis, epistaxis, or bruising. The patient was then encouraged to come to the hospital for further assessment. A more complete history was taken at that time. Findings on functional inquiry were normal except for a long-standing history of prostatism. The patient felt otherwise well and had no fatigue, dizziness, weight loss, or night sweats. Past medical history revealed a 2-year history of non–insulin-dependent diabetes mellitus, and a past episode of malaria, treated with quinine. There was no history of liver disease or prior surgery, and there was no family history of bleeding disorders. The patient's only medication was chlorpropamide, 125 mg daily. He specifically denied recent use of nonsteroidal anti-inflammatory medications. The patient was a retired administrative worker who enjoyed an active life. He was a nonsmoker and did not drink alcohol.

On examination, he was seen to be a healthy-appearing man who looked his stated age. Vital signs were stable, and there was no orthostatic drop in blood pressure. Examination of the head and neck showed diffuse oozing of blood from the gums without any obvious gingival inflammation. Fundoscopy revealed flame-shaped retinal hemorrhages. There was no scleral icterus or cervical lymphadenopathy. Inspection of the hands showed numerous splinter hemorrhages. The cardiovascular and respiratory systems were unremarkable. The liver edge was felt about 3 cm below the costal margin. The spleen could not be palpated. On rectal examination, the prostate gland was found to be hard and enlarged. Stool for occult blood was negative.

Initial blood work results included hemoglobin 12.8 g/L (128 g/dL), white cell count 6.4×10^9/L ($6.4 \times 10^3/\mu L$), and a greatly decreased platelet count of 26×10^9/L ($26 \times 10^3/mm^3$) (normal levels 250 to 400×10^9/L). The blood smear was leukoerythroblastic. The prothrombin time was elevated at 17.1 seconds, control 12.3 seconds, and the partial thromboplastin time was 30.3 seconds, control 28.7 seconds. Electrolytes were normal. Blood glucose was 9.2 mmol/L (166 mg/dL). The urea nitrogen was 7.2 mmol/L (20 mg/dL), and creatinine 112 μmol/L (1.3 mg/dL). The urine specimen was grossly bloody with proteinuria (+1). The electrocardiogram and chest x-ray results were within normal limits.

The greatly diminished platelet count and prolonged prothrombin time and partial thromboplastin time pointed to a combined thrombocytopenia and coagulopathy. The patient was treated immediately with vitamin K, 10 mg given subcutaneously, and two units of fresh frozen plasma. A bone marrow aspirate and biopsy were then attempted without success. The iliac crest was rock hard, and the trocar could not be advanced through the cortex.

The patient was then admitted to the hospital. As there was still active gingival bleeding, he received six units of

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platelets. The platelet count rose to 88 × 10^9/L (88 × 10^3 mm^3).

Further investigations initially focused on the liver. An ultrasonogram of the abdomen showed a large liver that was normal in texture with no splenomegaly or evidence of retroperitoneal lymphadenopathy.

Laboratory examination of the blood revealed asparate aminotransferase 0.62 μkat/L (37 U/L) (normal level 0.66 μkat/L; 40 U/L), alanine aminotransferase 0.27 μkat/L (16 U/L) (normal level 0.66 μkat/L; 40 U/L) gamma-glutamyltransferase 0.62 μkat/L (37 U/L) (normal levels 0.15 to 0.72 μkat/L; 9 to 43 U/L) alkaline phosphatase 10.25 μkat/L (615 U/L) (normal levels 0.33 to 1.67 μkat/L; 20 to 100 U/L), total protein 61 g/L (6.1 g/dL) (normal levels 60 to 76 g/L; 6.0 to 7.6 g/dL), and albumin 33 g/L (3.3 g/dL) (normal levels 39 to 50 g/L; 3.9 to 5.0 g/dL). It was concluded that the liver was not the cause of the bleeding.

Investigation then centered on blood coagulation. The fibrinogen level was decreased to 0.75 to 1.0 g/L (75 to 100 mg/dL) control 2.5 g/L (250 mg/dL). The thrombin time was 13.8 seconds, control 10.6 seconds. Fibrin degradation products were elevated to 40 to 80 μg/mL (normal levels 10 μg/mL). The hematologic picture was that of acute disseminated intravascular coagulation.

Finally, the unsuccessful bone marrow biopsy attempt and grossly elevated alkaline phosphatase level prompted an x-ray examination of the pelvis, which showed areas of very dense bone that were thought to represent osteoblastic bone lesions. A bone scan revealed markedly increased activity in the spine, ribs, and humerus suggestive of metastases. The acid phosphatase level was elevated at 1300 nkat/L (78 U/L) (normal level < 118 nkat/L; <7.1 U/L), and the prostatic acid phosphatase was likewise elevated at 1075 nkat/L (64.5 U/L) (normal level <20 nkat/L; <1.2 U/L), leading to a presumptive diagnosis of prostatic cancer.

The patient's course in hospital was that of continued slow gingival bleeding. He began passing blood clots through the urethra, a condition that eventually progressed to urinary retention, necessitating continuous bladder irrigation. His hemoglobin dropped to 85 g/L (8.5 g/dL). He was transfused with packed red blood cells and cryoprecipate.

Cystoscopic examination revealed a large, mildly obstructed prostate and a normal bladder. A transperineal biopsy specimen was reported to be negative for malignant cells. A repeat prostatic biopsy was planned for a confirmed tissue diagnosis, but the risk of bleeding was felt to be too great. The final diagnosis was still presumed to be advanced metastatic prostatic carcinoma. The patient was then started on diethylstilbestrol, 1 mg by mouth, three times a day. Shortly after starting this therapy, all bleeding ceased and the prothrombin time returned to normal. The patient was then discharged home in satisfactory condition.

DISCUSSION

Several reports in the literature have described an association between cancer of the prostate and disseminated intravascular coagulation,[1–3] but bleeding is a rare initial presentation of prostatic carcinoma. It has been estimated that approximately 13% of patients with prostatic carcinoma have chronic disseminated intravascular coagulation,[4] which usually manifests simply as abnormal coagulation values in an asymptomatic patient. Acute disseminated intravascular coagulation in a patient with prostatic carcinoma has been most commonly encountered in a clinical setting associated with sepsis, instrumentation, radiation, or chemotherapy.[1] In this case there was no such identifiable triggering mechanism.

The pathogenesis of acute disseminated intravascular coagulation is believed to involve the liberation of thromboplastins produced by the tumor cells, with resultant activation of the extrinsic coagulation pathway. This course eventually leads to a consumptive coagulopathy with thrombocytopenia and removal of coagulation factors from the circulation. The fibrinolytic pathway is secondarily activated with the conversion of plasminogen to plasmin. Plasmin serves to inactivate several clotting factors and promotes the breakdown of fibrinogen and fibrin to fibrin degradation products, which even further inhibit coagulation. The combination of thrombocytopenia, deficient clotting factors, hypofibrinogenemia, and circulating fibrin degradation products results in a bleeding diathesis.

Initially, the patient presenting with disseminated intravascular coagulation should be stabilized with replacement of the necessary blood components. Ultimately, the essential principle is to treat the underlying disease process. Hormonal therapy has long been the traditional treatment for metastastic cancer of the prostate. High-dose intravenous diethylstilbestrol has been successful in treating disseminated intravascular coagulation of acute onset in several patients with widespread cancer of the prostate.[5] In this case report it is interesting to note that the patient's bleeding stopped after standard oral doses of diethylstilbestrol.

More recently, ketoconazole, an antifungal agent, has been found to be extremely effective in reversing acute disseminated intravascular coagulation in patients with prostatic cancer.[6,7] The standard treatment regimen is a dose of 400 mg given orally every 8 hours. The drug exerts its antiandrogenic effects by inhibiting an enzyme in the testosterone synthetic pathway. Ketoconazole has a distinct advantage over diethylstilbestrol in that the former

drug reduces testosterone to castrate levels within 48 hours compared with 2 weeks for diethylstilbestrol. Ketoconazole, however, is indicated only for the emergency treatment of acute disseminated coagulation in patients with prostatic cancer, as long-term effects include hypoadrenalism and elevation of liver enzymes.

CONCLUSIONS

This case illustrates how an initial complaint of gingival bleeding represented an acute coagulopathy apparently triggered by an underlying prostatic carcinoma. It was important to recognize and treat the responsible disorder to stop the bleeding. Furthermore, the case emphasizes the point that beneath a seemingly straightforward complaint can lurk a complex and serious disease process.

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