

Severe anemia: a case report

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Abstract

Anemia refers to a hemoglobin or hematocrit level lower than the age-adjusted reference range in healthy children and adults. Anemia is not a specific disease entity but is a condition caused by various underlying pathologic processes. The clinical effects of anemia depend on its duration and severity. When a precipitous drop in the hemoglobin or hematocrit level occurs (eg, due to massive bleeding), the clinical presentation is typically dramatic and can be fatal if the patient is not immediately treated. Even then, mortality risk is very high. We report the case of a 76-year-old woman with clinical symptoms and laboratory confirmation of severe anemia with level of hemoglobin 24 g/l, and hematocrit 0.08. Anemia was a sign of malignoma of the stomach, later pathohistologically verified gastric adenocarcinoma. Aim of management is to prevent tissue hypoxia by maintaining an adequate circulating volume and oxiform capacity. However, as shown in this case, the very rapid correction of anemia and the circulatory volume does not decrease the risk of fatal outcome.

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Introduction

Anemia refers to a hemoglobin or hematocrit level lower than the age-adjusted reference range in healthy children and adults (1). The definition of anemia has attracted considerable interest recently because of epidemiologic studies that suggest that anemia may be associated with poorer outcomes in a variety of disorders (2). Anemia is not a specific disease entity but is a condition caused by various underlying pathologic processes. Anemia in cancer patients is multifactorial and may occur as a either a direct effect of the cancer, as a result of the cancer treatment itself, or due to chemical factors produced by the cancer (3). Upper GI endoscopy can be expected to reveal a cause in between 30 and 50% of patients (4). The clinical effects of anemia depend on its duration and severity (5). When a precipitous drop in the hemoglobin or hematocrit level occurs (e.g., due to massive bleeding), the clinical presentation is typically dramatic and can be fatal if the person is not immediately treated.

Even then, mortality risk is very high, as demonstrated in this case report. Fecal occult blood testing, upper endoscopy and lower endoscopy should be performed to identify bleeding lesions (5). A hematocrit of less than 15% can result in cardiac failure (6). In the largest consecutive series of patients with anemia, mortality rose as preoperative Hb fell, and postoperative Hb of 50–60 g/l was associated with a strikingly high mortality (6). Gastric cancer is rare before the age of 40, but its incidence steadily climbs thereafter and peaks in the seventh decade of life. Gastric cancer continues to be one of the leading causes of cancer-related death. The diagnosis of gastric cancer requires histopathologic assessment of tissue or cytologic assessment of gastric brushing/washes. Consequently, 80% to 90% of patients with gastric cancer present with locally advanced or metastatic tumors that have poor rates of respectability (7). Patients may present with anorexia and weight loss (95%) as well as abdominal pain that is vague and insidious in nature. Nausea, vomiting, and early satiety may occur with bulky tumors that obstruct the gastrointestinal lumen or infiltrative lesions that impair stomach distension. Ulcerated tumors may cause bleeding that manifest as he-

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matemesis, melena, or massive upper gastrointestinal hemorrhage (8,9), like in our case. Anemia is defined as a reduction in red blood cell (RBC) mass or blood hemoglobin (Hb) concentration resulting in a decrease in the oxygen-carrying capacity of the blood (10). Tissues cannot 'bank' oxygen. Blood can be thought of as a pipeline that delivers oxygen continuously from pulmonary alveoli to capillary beds. In healthy subjects, the oxygen delivery system exceeds resting oxygen needs by several times. In chronic anemia, the reduced capacity of the blood to carry oxygen is compensated for by: 1) an increase in cardiac output, 2) redistribution of blood flow and 3) increase in the 2, 3-DPG content of the red cells, which causes a shift to the right in the oxygen dissociation curve, so that at a given degree of oxygen saturation of Hb, oxygen is more readily given up to the tissues (11). As the oxygen content is diminished in anemia, the anemic patient can maintain the overall supply of oxygen to the tissues only by increasing cardiac output and thus reducing the cardiac reserve. If the coronary blood flow fails to deliver sufficient oxygen the heart muscle becomes relatively hypoxic, and there will be a fall in cardiac output and a reduction in systemic blood flow. Clinical signs of severe anemia are: fatigue, dyspnea, tachycardia, change in mental status, decreased UOP, hypotension, $\text{PaO}_2/\text{FiO}_2 < 200$. An extreme reduction in Hb concentration is found as blood is redistributed from the skin to internal organs. Pale conjunctivae, tongue, mucous membranes and nail beds evidence the altered perfusion. Pale optic fundi may be accompanied by retinal hemorrhages. As cardiac output increases, patients may experience tinnitus and palpitations. Rapid respiration and shortness of breath at rest should be considered as disturbing evidence of oxygen deficit and evidence of cardiac decompensation. Dizziness and fainting are common as anemia progresses, but apprehension, changes in mentation and leg cramps are indications of severe oxygen deprivation and presage coma and death, or course that may lead to organ failure (1, 11, 12, 13). When the amount of blood lost rapidly is equivalent to 30% of the blood volume, a subject may develop oligoemic shock (14). The clinical symptoms of shock are the 'three windows to the microcirculation: (a) Mental status/level

of consciousness (cerebral perfusion) – agitation, confusion, somnolence or lethargy, (b) Peripheral perfusion – cold and clammy skin, delayed capillary re-filling, tachycardia, (c) Renal perfusion – urine output ($< 0.5 \text{ mL/kg/h}$) (15). These clinical findings help to differentiate whether a patient is 'haemodynamically normal' or just 'apparently haemodynamically stable' but in compensated shock. Arterial blood gas can indicate lactate levels, and base deficit represents highly sensitive parameters for recognition of metabolic acidosis reflecting 'hidden shock' (15).

Case study

A 79-year-old female patient presented at our surgical department with one-month history of abdominal pain and melena. The family reported that the patient has had cholecystectomy one year ago. Abdominal pain has started 5 months after surgery. Upper and lower GI symptoms in the past 5 months presented with: a markedly decreased appetite, weight loss about 12 kg, increased fatigue and reduced activity, intermittent nausea or vomiting with black stools. She had the ultrasound (US) exam done which showed: presence of tumor mass between stomach and pancreas with retroperitoneal lymphadenopathy, and without metastatic lesions in the abdomen. Laboratory results before first hospitalization were normal, with Hct 0.36, WBC $8.8 \times 10^{12}/\text{L}$, PLT $297 \times 10^9/\text{L}$. Her family history revealed no significant medical illnesses. The physical examination on admission: pronounced pallor of the skin and mucous membranes, mild resting dyspnea, somnolence, malignant cachexia, normal breathing sounds, arrhythmic heart rate was 90 beats per minute, quiet tones, without murmurs, the arterial blood pressure was 75/35 mmHg. The abdomen was soft and non-distended without hepatosplenomegaly, deep palpation revealed palpable flank mass, 5 cm in diameter, in umbilical area. There was no evidence of edema in the extremities. Other physical findings were unremarkable. Additional laboratory studies were obtained, and a diagnostic procedure was performed. Admission laboratory results: sedimentation 10, RBC count $1.03 \times 10^{12}/\text{l}$, Hb 24 g/l, Hct 0.08, MCV 75.7, MCHC 308 g/l, Platelets $365 \times 10^9/\text{l}$, WBC count

12.5x10¹²/l. Electrolyte status revealed mild hypokalemia -3.2 mmol/l, sodium 138 mmol/l, calcium 1.67 mmol/l, with the proper values of urea, creatinine, bilirubin, AST, ALT, CPK and alpha-amylase. Urine findings, alpha-fetoprotein, CA 125 II, CA 19-9 XR were normal and values of ferritin 32.38 (4.63 to 204.00), slight iron deficiency - 6.5 µmol/l. High CEA value of 276.66 µg/ml (0.00 to 5.00), together with anamnestic data, were indications for gastroscopy. ECG demonstrated atrial fibrillation, rarely visible p-wave, ventricular response was 90/min, low amplitude, intermediate electrical axis, adequate progression of R waves in precordial leads, slight horizontal depression of 0.5 mm in D1, aVL and V4-V6. Based on the history and laboratory evaluation, a diagnosis of severe hemorrhage anemia was made, and the patient was started with replacement treatment. The patient received prompt volume restoration therapy including repeatedly RBC transfusions and fluid resuscitation. When Hct value increased to 0.24-0.26, upper GI endoscopy was performed. Endoscopy showed circumferent mucosal defect 2 cm in diameter which was suspected as a malignant tumor and later pathohistological examination verified gastric adenocarcinoma. Patient remained hemodynamically unstable with intermittent hematemesis and melena. She was admitted to intensive care unit and continuously monitored. The patient was transfused with several units of packed red blood cells. Fluids resuscitation to restore the blood volume and parenteral antiulcer medications were administered. She regained full conscious and started enteral nutrition. Fourteenth day after admission Hct was 0.26, Hb 88 g/l. After an external meal patient condition abruptly worsened. She became somnolent, dyspneic with chest pain, her arterial blood pressure and heart rate rapidly declined. She was severely hemodynamically unstable, and died despite adequate supportive treatment on the fourteenth day after admission.

Discussion

In this paper, we presented the case of a patient with gastric adenocarcinoma who developed severe anemia (Hb 24 g/l) due to bleeding from that lesion. The medical history and physical examination of this patient were important diagnostic clues,

followed by essential laboratory tests and endoscopic examination needed to confirm diagnosis. Hyperanemia is a severe form of anemia, in which the hematocrit is below 10%. Critical condition of patient reported in this case, required aggressive treatment in order to avoid fatal consequences of anemia and hypovolemia. In this case, patient had long history of chronic gastric bleeding which was well compensated until admission in hospital. Management is aimed at preventing tissue hypoxia by maintaining an adequate circulating volume of red cells. This requires a multidisciplinary approach including control of the relevant physiological parameters, rapid control of bleeding, maintenance of tissue perfusion, temperature control and blood component or pharmacological treatment to support coagulation. The effects of anemia must be separated from hypovolemia, although both can impede tissue oxygen delivery. Oxygen delivery in healthy adults is maintained even with hemoglobin levels as low as 6-7 g/dl. Hb around 10g/L had previously served as a trigger. Transfusion is necessary to minimize symptoms and risks associated with symptomatic chronic anemia when hemoglobin is at 6 g/dl. Trials of acute normovolemic hemodilution in healthy volunteers and surgical patients found the limit of critical oxygen delivery in humans at about 50 g/l (12, 13). The goal of early volume replacement is to delay or prevent the chain of events that leads to irreversible shock (13,15). In hemorrhagic shock, the main management strategies are the arrest of bleeding and the replacement of circulating volume. Fluids used are isotonic and hypertonic crystalloids, colloids (mainly gelatins and starch solutions) and blood products. Bleeding may be worsened by injudicious fluid administration as a consequence of a dilutional coagulopathy and of clot disruption from increased blood flow, increased perfusion pressure and decreased blood viscosity. Traditional guidelines generally employ early and aggressive fluid administration to restore the blood volume. Some studies have shown increased mortality rates with rapid infusion of fluids compared with standard infusion, and with immediate compared with delayed resuscitation (13). The concept of low-volume fluid resuscitation or 'permissive hypotension' avoids the detrimental effects of

early aggressive resuscitation, while maintaining a level of tissue perfusion that, although decreased from normal, is adequate for short periods (16). This approach is contraindicated in brain and spinal injuries and its effectiveness still needs to be confirmed in randomized clinical trials (12,15,16). Patients who have become anemic as a result of recurrent hemorrhage should be transfused unless it is reasonably certain that risk of further hemorrhage has abated. Decision about adequate treatment is always difficult. Whether to employ early and aggressive fluid administration or standard infusion to restore the blood volume? Bleeding recurs in 30–50% of peptic ulcers with non-bleeding visible vessels and adherent clots that are not treated with endoscopy and in 1–12% of patients treated with invasive inpatient therapy. Overall mortality rate for bleeding peptic ulcers remains about 6–7%. Invasive therapies clearly improve prognosis. Early transfusion in these settings seems prudent lest rebleeding prove fatal before endoscopic or surgical interventions can be undertaken. As earlier noted, our patient received prompt volume restoration therapy including repeatedly RBC transfusions and fluid resuscitation before upper GI endoscopy was performed. Red blood cells are indicated for patients with a symptomatic deficiency of oxygen-carrying capacity or tissue hypoxia due to an inadequate circulating red cell mass. They also should not be used as a source of blood volume, or oncotic pressure or to improve wound healing, or sense of wellbeing. The number of RBC units transfused is an independent predictor of worse clinical outcome (17). Circulatory overload, leading to pulmonary edema, can occur after transfusion of excessive volumes or at excessively rapid rates. This is a particular risk in the elderly and in patients with chronic severe anemia in whom low red cell mass is asso-

ciated with high plasma volume (6). Overloading is best prevented by close attention to the state of the patient's circulation (13). High infusion rates of blood products containing citrate can decrease calcium concentrations, particularly in patients with hypothermia or liver failure (who are unable to metabolize the citrate), so monitoring of serum calcium may be required. Hypothermia carries a risk of cardiac arrhythmia or cardiac arrest.

Conclusion

In conclusion, chronic upper GI tract bleeding resulting in severe anemia is the most common sign of upper GI tract neoplasm, in this case pathohistologically confirmed gastric adenocarcinoma. The clinical symptoms of anemia vary according to the individual's capacity to respond to blood loss or reduced red cell production. In this case, patient had history of chronic gastric bleeding which was well compensated. It is clear that the priority during initial treatment must be the maintenance of tissue oxygenation with appropriate use of fluid and blood components. Volume overloading is unusual but it does occur. Bleeding may be worsened by injudicious fluid administration. Clinicians should be cautious with the treatment of such patients because of possible development of fatal complications. Coagulation may be supported by controlling temperature and blood pH and by correcting coagulopathic deficiencies (12). This patient probably died due to transfusion-mediated coagulopathy which lead to pulmonary embolism or transfusion-related acute lung injury. Actual cause of death was never determined, because autopsy was not performed.

Competing interests

The authors declare that they have no competing interests.

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