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Concurrent diagnosis of severe haemophilia A and acute lymphoblastic leukemia in a child: First report in Greece

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Abstract

Haemophilia A is a congenital bleeding disorder resulting by deficiency of coagulation factor VIII and Acute Lymphoblastic Leukemia (ALL) Is the most common cancer type in children. The concurrence of hemophilia and ALL in pediatric patients is quite rare. We report a case of a 2.5 year old boy, with an uneventful past history, which presented with pallor, petechiae, ecchymoses and lethargy to the emergency department. A full blood count on admission revealed severe leukocytosis, anemia and thrombocytopenia. Diagnosis of ALL was confirmed and the patient was put on chemotherapy. Excessive bleeding from the site of entry of the central venous catheter led to complementary testing, which revealed very low levels of Factor VIII and severe Haemophilia A was also diagnosed. The patient suffered from minor gastrointestinal bleeds and a severe intrabdominal hemorrhage due to an abcess eruption during his treatment for ALL. To date, very few cases of ALL and Haemophilia have been reported in children, and due to this rarity there are no guidelines concerning the adjustments in treatment in this small population of patients.

Abbreviations: ALL: Acute Lymphoblastic Leukemia; APT: Activated partial thromboplastin time; PT: Prothrombin time; CT: Computed Tomography.

Introduction

Hemophilia A is a congenital bleeding disorder resulting by deficiency of coagulation factor VIII, with a prevalence of approximately 23 per 100.000 live male births [1]. Acute Lymphoblastic Leukemia (ALL) is the most common cancer type in children. The concurrence of hemophilia and ALL in pediatric patients is even more rare and particularly challenging due to the specific clinical problems it poses. We report the first case in Greece of concurrent diagnosis of Acute Lymphoblastic Leukemia and severe Hemophilia A in a child.

Case Presentation

A 2,5 year old boy presented to the emergency department with pallor, petechiae, ecchymoses and lethargy. Past history was uneventful, except for iron deficiency anemia at one year of age, which was corrected by oral iron supplementation and minor nose bleeds since that age, that were never assessed for treatment. Family history was at the time reported normal. Physical examination revealed a systolic murmur, tachycardia and splenomegaly, without apparent mucosal bleeding. A full blood count on admission revealed severe leukocytosis, anemia and thrombocytopenia (WBC 212.9 K/μl, Hb 5.2 g/dl, PLT 16 K/μl). Activated partial thromboplastin time (APTT) Was severely prolonged at >100 sec (normal range 25-35) And prothrombin time (PT) Within normal ranges (12.7 sec). Immunophenotyping of a bone marrow aspirate confirmed the diagnosis of Acute Lymphoblastic Leukemia. After placement of a central venous catheter, the patient displayed excessive bleeding from the site of the catheter's entry and was transfused with platelets and fresh frozen plasma. Mother revealed at that point that a maternal uncle was suffering from haemophilia, and further testing confirmed low FVIII levels (lower than 1%), Setting the diagnosis of severe Haemophilia A. The patient started treatment for leukemia according to the ALL-IC-BFM 2009 protocol. He received prophylactic factor VIII products and on demand, as well as other blood products, in order to treat one episode of nose bleed and three episodes of minor gastrointestinal bleeding due to treatment-related colitis.

After the end of treatment the patient remained hospitalized due to prolonged febrile neutropenia. He received empiric antibiotic therapy and was regularly transfused with blood products supportively, due to bone marrow aplasia. He also received replacement therapy of factor VIII. Due to recurrent abdominal pain, an ultrasound was performed, revealing a widening of the intestinal wall, attributed to neutropenic colitis. On the fifteenth day of his hospitalization, in the presence of persistent pain, an abdominal Computed Tomography (CT scan) was performed, which revealed a cystic formation resembling an abcess behind cecum. A few days later, the patient presented with acute severe abdominal pain, hypotension and tachycardia. The patient was transfused with platelets and packed red blood cells and factor VIII replacement therapy was administered. After stabilization of his vital signs, a CT scan revealed the formation of a hematoma in front of the secum and intrabdominal hemorrhage. Due to bradycardia and hypovolemic shock, the patient was finally intubated and transferred to the Pediatric Intensive Care Unit, where he remained for a week. He underwent a partial colectomy with colostomy, which was restored three months later. At present, the patient remains in good clinical condition and in complete remission regarding his ALL. He is also on replacement therapy for haemophilia.

Discussion

Haemophilia A is an X-linked congenital bleeding disorder resulting by deficiency of coagulation factor VIII, with a prevalence of approximately 23 per 100.000 live male births [1]. Acute Lymphoblastic Leukemia is the most common cancer type in children. This is the first report in Greece of simultaneous diagnosis of Haemophilia A and Acute Lymphoblastic Leukemia in a child. Our literature search revealed 17 cases of patients under the age of 16 to be diagnosed with Haemophilia and Leukemia up to this day [2,7].

Of these patients, twelve were diagnosed with Haemophilia A, four with Haemophilia B and for one patient this information was not provided. Regarding the type of Leukemia, eleven of them presented with Acute Lymhoblastic Leukemia, four of them with Acute Myeloid Leukemia, one had Burkitt Leukemia and for one patient the type of leukemia was not provided. For patients with non-HIV and non-hepatitis C related cancers, it is unclear whether the prevalence of cancer in haemophiliacs is higher than that of the healthy population [3,8].

The concurrence of Haemophilia and Leukemia in pediatric patients is quite rare and particularly challenging due to the specific clinical problems it poses. Treatment-related events, such as chemotherapy – induced thrombocytopenia and infection, increase the risk of bleeding in a patient that already has bleeding diathesis. Inevitably, measurements of platelets should be frequently performed, but there are no guidelines as to the threshold of platelet count under which the patient with hemophilia needs to be transfused [8]. During cancer treatment several procedures need to be performed, such as central venous catheter placement, bone marrow biopsies and lumbar punctures, increasing the risk of hematoma formation. Current guidelines recommend preparing for such procedures with adequate factor replacement and blood product transfusions to prevent life-threatening hemorrhage or spinal hematomas [8]. For patients with prolonged chemotherapy or radiotherapy induced thrombocytopenia, continuous prophylactic replacement therapy is also recommended [8]. Screening for inhibitors is also crucial and should not be omitted in these patients [8].

Conclusion

It is well established that the concurrence of Haemophilia and Leukemia is quite rare in the pediatric setting. When treating these patients, pediatricians and hematologists should bear in mind the increased risk of breakthrough bleeding during chemotherapy and necessary procedures and follow recommendations regarding their management.

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