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"HEMOPERITONEUM: AN UNUSUAL PRESENTATION OF CHRONIC GRANULOCYTIC LEUKEMIA IN A PEDIATRIC PATIENT."

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Hemoperitoneum: an unusual presentation of chronic granulocytic leukemia in a pediatric patient.

Abstract

Chronic granulocytic leukemia (CGL) is a rare hematologic disease in pediatric patients. It usually presents with insidious symptomatology. However, some cases may have an atypical presentation. We report herein the case of a 13 year-old female, admitted to the emergency department with acute abdomen. She had hyperleukocytosis of 500.0 x 1000 cells/mm^3 suggestive of CGL. A paracentesis performed due to abdominal compartment syndrome demonstrated hemoperitoneum. At laparotomy, a ruptured ovarian mass was found with multiple tumor implants in the serosal surface. Pathology revealed a CGL infiltrated ovary. The patient is currently stable, has finished adjuvant chemotherapy and is at 24 months of follow-up. To our knowledge, this is the first report of such a case.

Introduction

Chronic granulocytic leukemia (CGL) is a malignant disease characterized by leucocytosis in peripheral blood, with granulocytic cell overgrowth in the bone marrow, along with Abl-1 translocation from chromosome ^{9}, towards the BCR gen region on chromosome 22 (Philadelfia chromosome)[1]. The first clinical description of CGL appeared in 1845 by Bennet and Virchow[3]. It was not until a hundred years later that its associated chromosomal abnormality was characterized.

Most cases of CGL occur within the age range of 40 to 60 years. There is a slight male preponderance in cases presenting below age 20 years (1.5:1). The entity is

exceedingly rare in pediatric patients[1, 2] with an estimated annual incidence of one case per million in occidental countries. It accounts for 2 to 3% of leukemia cases in children and adolescents[2, 3]. Horibe et al. reported a series in which CGL represented 0.2% of leukemias between 1 and 4 years of age, 2.2% between 5 and 9 years, 3.7% between 10 and 14 years, and 8.3% between 15 and 19 years old [4].

CGL presentation may be chronic, accelerated and blastic[5, 6, 7]. The vast majority of cases are diagnosed at the chronic phase with insidious manifestations. Patients have weakness, pallor, and splenomegaly with abdominal distention and tenderness[2, 3].

Diagnosis is clinical, morphologic, cytogenetic, and molecular. Therapy is directed towards the chromosomal abnormality.

This atypical case illustrates the need to further refine our understanding regarding the biologic behavior of this entity[1, 2].

Other atypical forms of presentation include osteolytic bone lesions, and extramedullary infiltrates including skin, lymph nodes, breasts, orbital, paranasal sinuses, spinal cord, and gastrointestinal tract. As opposed to the common chronic onset GCL, most atypical cases occur in an accelerated form, and also, in atypical age groups[1, 3, 5, 6].

To our knowledge, this is the first reported case of hemoperitoneum due to a ruptured CGL-infiltrated ovary in a pediatric patient.

Case

We present herein the case of a 13 year-old female with a six months history of intermittent epigastric pain.

She was treated with ranitidine, omeprazole, butylhioscine, and aluminum / magnesium gel, with partial improvement.

She referred occasional headache with photophobia, dizziness, fatigue, weakness, pallor, diaphoresis, and 5 kg weight loss within four months. One week before admission she presented bone pain in face and limbs. She was brought to the emergency department with a 24-hour history of diffuse cramping abdominal pain and diarrhea.

On examination, she was pale, tachycardic (124 beats per minute) and polypneic (22 breaths per minute). A mobile and tender mass was found in the left infraclavicular region. No other lymphadenopathy was noted.

The abdomen was distended, tender, and hypoactive, with rebound tenderness. The spleen was palpable at the left iliac crest.

On rectal examination the mass was evident towards the left pelvic wall.

She was admitted and laboratory studies were as follows:

Blood count: Hb 8.6 gr/dL, Hct 27 %, Leu 508.2 x 1000 cells/mm3, with leukocyte differencial of neuthrophils 33%, bands 7%, lymphocytes 2%, monocytes 2%, myelocytes 6%, metamyelocytes 7%, blasts 43%, and platelet count of 622 x 103/mm3. Hematology-reviewed peripheral blood smear with hypochromia, anisocytosis +, immature forms in all stages of differentiation, and myeloid blasts.

Clotting time: PTT 32 seconds and PT 16.5 seconds, INR 1.31

Blood chemistry and serum electrolytes: Glucose 100 mg/dL, urea nitrogen 13.1 mg/dL, creatinine 0.67 mg/dL, sodium 138 mmol/L, potassium 3.4 mmol/L, chloride

105 mEq/L, calcium 9.3 mg/dL, ric Acid 6.2 mg/dL, phosphorus 4.9 mg/dL, lactate dehydrogenase 956 U/L.

These results suggested the diagnosis of chronic granulocytic leukemia. Hyperhydration and antibiotic treatment with ceftriaxone and metronidazole was started along with tyrosine kinase inhibitor, (Imatinib Mesylate), and hydroxyurea.

She developed abdominal compartment syndrome with an intravesical pressure of 27cmH2O, and a paracentesis confirmed the presence of hemoperitoneum. At laparotomy three liters of blood were found free in the peritoneal cavity, due to a very large and ruptured right ovarian tumor. Extensive tumor implants were identified adherent to the intestinal serosal surface as well as peritoneal walls and paracolic gutters. Massive splenomegaly was also present.

She underwent damage control, and surgical protocol for ovarian tumor was performed, including right oophorectomy, exploration of the left ovary without biopsy due to normal appearance, multiple biopsies of all peritoneal implants seen including the diaphragm, and partial omentectomy, appendectomy, and exhaustive cavity washing, plus splenectomy.

Postoperatively she remained in the ICU requiring multiple transfusions. Persistent bleeding at the surgical wound was controlled with Factor VIIa administration. She was hemodynamically stable and extubation was achieved, but bleeding recurred through the surgical wound and peritoneal drains, so she was taken back to the operating room for surgical revision. Hemoperitoneum was again found, with remaining tumor tissue implanted on the bowel serosa. Extensive cavity washing and removal of tumor implants was performed. Postoperative course was uneventful.

Histopathology confirmed the diagnosis of a CGL-inflitrated and ruptured ovary. Karyotype showed 46 XX t (9;22).

Currently the patient is stable, treated with tyrosine kinase inhibitors, with good clinical, hematological and cytogenetic remission.

Discussion

It is not uncommon for pediatric hemato-oncological patients to present episodes of acute abdomen. These can occur at diagnosis, during active treatment, or during follow up with disease recurrence. Possible causes include abdominal organ infiltration, solid organ rupture or torsion, neutropenic enterocolitis, extrinsic intestinal obstruction, intussusception, or abdominal sepsis among others.

Malignant hemoperitoneum refers to the presence of blood in the peritoneal cavity, due to a ruptured abdominal tumor [15].

Acute abdomen due to malignant hemoperitoneum is extremely rare [8], occurring in less than 5% of patients[9, 10].

Leukemic ovarian infiltration has been reported. Road and Madsen referred a 66% incidence of ovarian infiltration in postmortem pediatric patients with acute leukemia and lymphoma. However, all cases where in patients with acute leukemia, without any previous case described in patients with CGL[11, 12].

The diagnosis of malignant hemoperitoneum should be considered in patients with large abdominal masses, who develop distension, abdominal compartment syndrome, hypotension, decreased urine output, or anemia[13, 14]. Abdominal tumors may either rupture spontaneously due to fast enlargement, necrosis, and capsular infiltration, or they can do so secondary to chemotherapy-induced necrosis.

Ovarian masses may undergo torsion, leading to ischemia, necrosis, and rupture. Pediatric ovarian tumors are more prone to torsion when compared to their adult counterparts, due to longer and more lax fixation ligaments[17].

Malignant hemoperitoneum due to an ovarian tumor rupture as the presenting sign of acute leukemia is extremely rare. Lee et al[16] reported a series of 100 pediatric patients with ovarian tumors. Only 10 cases presented with acute abdomen and only two of them had hemoperitoneum.

Feyeresilova and Cepicky reported a case of an adult female patient with acute myeloid leukemia and hemoperitoneum, due to rupture of an endometrial ovarian cyst[18]. Habeck et al. described a case of acute abdomen secondary to rupture of a corpus rubrum, in a woman with acute lymphocytic leukemia[19]. CGL tends to be a diffuse and systemic disease, with localized infiltration being exceedingly rare. The surgical findings in this patient, as well as the histopathologic analysis of the specimens, confirm that the right ovary was diffusely infiltrated by CGL. The ruptured ovary produced the hemoperitoneum as well as the diffuse tumor infiltrates in the entire serosal surface of the peritoneum.

To our knowledge, this is the first reported case of malignant hemoperitoneum from a ruptured ovary with CGL infiltration, both in children and adults.

Conclusions

CGL is rare in children, particularly in this age group in which atypical presentations are more frequently reported. The clinician must be especially sensitive to the presence of these unusual manifestations in patients with CGL, including extramedullary infiltration which may, as this case illustrates, affect unusual organs such as ovary, producing a rare complication of hemoperitoneum and acute

abdomen due to ovarian rupture. Malignant hemoperitoneum should be part of the differential diagnosis in pediatric patients with large abdominal masses, who develop pain, distention, abdominal compartment syndrome, shock, low urine output, and/or acute anemia.

During the procedure, the primary tumor should be resected if feasible; otherwise, damage control surgery is indicated.

Bibliography

1. Spiers AS. Clinical manifestations of chronic granulocytic leukemia. Semin Oncol. 1995;4:380-395.
2. Millot F, Traore P, Guilhot J, et al. Clinical and biological features at diagnosis in 40 children with chronic myeloid leukemia. Pediatrics. 2005;1:140-143.
3. Vardiman JW. Chronic myelogenous leukemia, BCR-ABL1+. Am J Clin Pathol 2009;132:250-260.
4. Horibe K, Tsukimoto I, Ohno R. Clinicopathologic characteristics of leukemia in Japanese children and young adults. Leukemia. 2001;15:1256-1261.
5. Bathia R, Radich JP. Chronic myeloid leukemia. In: Hoffman, Hematology: Basic principles and practice. 5th ed. Churchill Livingston Elsevier; 2009:1109-1123.
6. Rosenthal S, Canellos GP, Devita VT, et al. Characteristics of blast crisis in chronic granulocytic leukemia. Blood. 1977;49:705-714.
7. Tsalkidis A, Gardikis S, Cassimos D, et al. Acute abdomen in children due to extra-abdominal causes. Pediatr Int. 2008;50: 315-318.
8. Nishimoto F, Okuno K, Kurakagi C, et al. Hemoperitoneum as the first manifestation of acute leukemia. Gynecol Obstet Invest. 2008;66:12-13.
9. Brisse H, Schleiermacher G, Sarnacki S, et al. Preoperative Wilms Tumor Rupture. A Retrospective Study of 57 Patients. Cancer. 2008;1:202 –13.
10. Kosloske AM, Mciver WJ, Duncan MH. Intraperitoneal Rupture of a Wilms Tumor. West J Med. 2005;5:694-696.

11. Demiroğlu H, Ozcebe OI, Akcan Y, et al. Ovarian relapse and cutaneous involvement in a case of acute lymphoblastic leukaemia. Acta Haematol 1994;1:56.

12. Reid H, Marsden HB. Gonadal infiltration in children with leukaemia and lymphoma. J Clin Pathol. 1980;33:722-729.

13. Baeza C, García L, Álvarez F, et al. Hemoperitoneo maligno, complicación infrecuente. Presentación de tres pacientes con tumor abdominal. Acta Pediatr Méx. 2000;14: 95 –98.

14. Covarrubias G, Rendón H, Cordero M. Tumores malignos en niños hospitalizados por una masa abdominal. Rev Mex Pediatr. 2005; 2:61-64.

15. Lida T, Suenaga M, Takeuchi Y, et al. Successful Resection of a Ruptured Hepatoblastoma Prior to Chemotherapy: Report of a Case. Surg Today. 2004;34:710-714.

16. Lee W, Yuan Ch, Lai Ch, et al. Hemoperitoneum is an initial presentation of recurrent granulosa cell tumors of the ovary. Jpn J Clin Oncol. 2007;2: 509 – 512.

17. Yoffe N, Bronshtein M, Branded J. Hemorrhagic ovarian cyst detection by transvaginal sonography: the great imitator. Gynecol Endocrinol. 1991;5:123 – 129.

18. Cepicky P, Feyereislova A. Hemoperitoneum due to rupture of an ovarian endometroid cyst as a first symptom of acute leukaemia. Acta Clin Belg. 1991;1:28-29.

19. Habek D, Cerkez I, Galic J, et al. Acute abdomen as a first symptom of acute leukemia. Arch Gynecol Obstet. 2004;270:122-123.