Conus medullaris syndrome and acute colonic pseudo-obstruction in a child with acute lymphoblastic leukemia

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A 5$^{3/12}$-year-old boy with Philadelphia chromosome (+) pre-B acute lymphoblastic leukemia (ALL) without extramedullary involvement did not achieve remission after induction therapy. His family stopped therapy, but he was readmitted eight months later due to pyoderma, pneumonia and active leukemia with leukocytosis. During cytoreductive and antibiotic therapy, he developed progressive abdominal distension, pain, globe vesicale, tachypnea, and respiratory alkalosis. Bowel sounds could not be auscultated. Dilation, mainly in the large intestine, was detected radiologically. His neurological examination revealed absence of superficial reflexes and hypoesthesia along with normal motor strength and deep tendon reflexes in the lower extremities, consistent with conus medullaris syndrome, which was thought to give rise to acute colonic pseudo-obstruction.

Key words: conus medullaris syndrome, cauda equina syndrome, acute colonic pseudo-obstruction, acute lymphoblastic leukemia.

Central nervous system (CNS) involvements in acute lymphoblastic leukemia (ALL) mostly present as leptomeningeal infiltration (pia and arachnoid)[1], and rarely as space-occupying masses (intracranial, spinal) [2] . Spinal cord involvement in ALL is encountered as localized intradural, intramedullary or epidural mass[2,3]. However, cauda equina syndrome (CES) or conus medullaris syndrome (CMS) due to leukemic infiltration in ALL is rare. CMS develops due to damage to the lower sacral segments of the spinal column, giving rise to fecal and urinary incontinence and loss of sensation at S2, S3 and S4 dermatomes.

Herein, CMS complicated with acute colonic pseudo-obstruction (ACPO) in a child with ALL is presented.

Case Report

A 5$^{3/12}$-year-old boy with Philadelphia chromosome (+), pre-B ALL without CNS involvement did not achieve remission after induction chemotherapy (M3 bone marrow) (Table I). The family refused to continue the therapy. Eight months later, however, the patient was readmitted because of fever. Body temperature was 37.5°C, with a respiration rate of 47/min and a pulse rate of 127/min. Physical examination revealed multiple cervical lymphadenopathies, bilateral rales in lungs, hepatosplenomegaly, and an infected burn lesion on the dorsum of the right foot.

Hemoglobin was 71 g/L, leukocyte count (white blood cells [WBC]) 243 x 10^9/L and platelet count 34.5 x 10^9/L, and L1 type lymphoblasts were detected in bone marrow (68%) (Table I). Lactate dehydrogenase (LDH) was 1054 U/L, uric acid 6.58 mg/dl, aspartate aminotransferase (AST) 704 U/L, alanine aminotransferase (ALT) 995 U/L, and direct/total bilirubin 1.25/1.8 mg/dl. Chest radiograph revealed bilateral paracardiac infiltration. Hydration, allopurinol, bicarbonate, antibiotics (cefoperazone-sulbactam, amikacin, teicoplanin, cotrimoxazole, clarithromycin), and hydroxyurea were started. The WBC count and liver function tests gradually normalized

Table I. Some Laboratory Findings of the Patient

Laboratory finding	At the first admission	At the second admission
Leukocyte count (x10^9/L)	190	240
Hemoglobin (g/L)	100	71
Platelet count (x10^9/L)	26	34.5
Lymphoblast percentage (peripheral blood and bone marrow) (%)	98/100	57/68
Flow cytometric findings	CD3: 23%, CD22: 71%, CD10: 47%, CD19: 72%, CD5: 24%, CD7: 25%, HLA-DR: 74%, CD8: 22%, CD34: 40%	-
Cytogenetics	46, XY, t(9;22)(q34;q11)(2)/ 46,XY(3) Ph (+): 40%	-
BCR/ABL fusion gene (RT-PCR)	+	-
Cerebrospinal fluid	Protein: 15 mg/dl; glucose: 39 mg/dl; no cells in cytologic examination	Protein: 20 mg/dl; glucose: 65 mg/dl; no cells in cytologic examination

and fever disappeared; however, constipation, progressive abdominal distension, pain, globe vesicale, tachypnea, and respiratory alkalosis were established on the 13th day of admission. No bowel sounds could be heard. Abdominal X-ray showed bilateral diaphragmatic elevation and dilation of the bowel segments, mainly of the large intestine (Fig. 1a). Abdominal computed tomography revealed dilation of the large intestine and globe vesicale. Neurological examination revealed absence of bilateral cremasteric reflexes, decrease in superficial anal reflex and hypoesthesia in the perianal and gluteal regions. Motor strength examination in the lower extremities and deep tendon reflexes were normal. CMS and ACPO were considered. Spina bifida and thickening of the conus medullaris and cauda equina were detected on lumbosacral magnetic resonance imaging (MRI) (Figs. 1b, 1c). However, no contrast could be injected since his general condition deteriorated during the procedure. Cerebrospinal fluid (CSF) examination revealed normal biochemistry and no cells. Intrathecal cytosine arabinoside (30 mg), prednisolone (10 mg) and methotrexate (12 mg) were administered. Gas flow started within 24 hours and abdominal pain, abdominal distension and globe vesicale disappeared within the following two days. One week later, perianal and gluteal hypoesthesia mildly reversed, and weak cremasteric reflexes emerged. Meanwhile, he developed varicella infection with fever so acyclovir therapy was started. The levels of the liver function tests increased temporarily. Voriconazole was added due to *Candida tropicalis* growth in blood culture. Nevertheless, disseminated intravascular coagulation and cardiac arrest developed and the patient died.

Discussion

Cauda equina syndrome (CES) and CMS develop due to damage to the lower sacral segments of the spinal column. Fecal and urinary incontinence and loss of sensation at S2, S3 and S4 dermatomes develop with and without motor deficit, respectively. The difference between CES and CMS is that muscle weakness of the lower extremities and paralysis develop before the sphincter defect in CES, while paraplegia and paraparesis are absent in the beginning of CMS[5] . Our patient was consistent with CMS, since there was no motor deficit in the lower extremities.

In a postmortem study, leukemic infiltration of the CNS was shown to be more common in ALL (81%) than in acute myeloid leukemia (AML) (46%), involving mostly the cauda equina (38%) followed by cerebral leptomeninges (34%). Spinal involvement due to leukemia has been reported most often with AML, and 50% of the patients with spinal leukemic involvement did not display any symptoms[4] .

Our investigation of the English literature revealed only one case of ALL (a 22-year-old female with T-ALL) who presented with CES as isolated CNS involvement (relapse)[3],

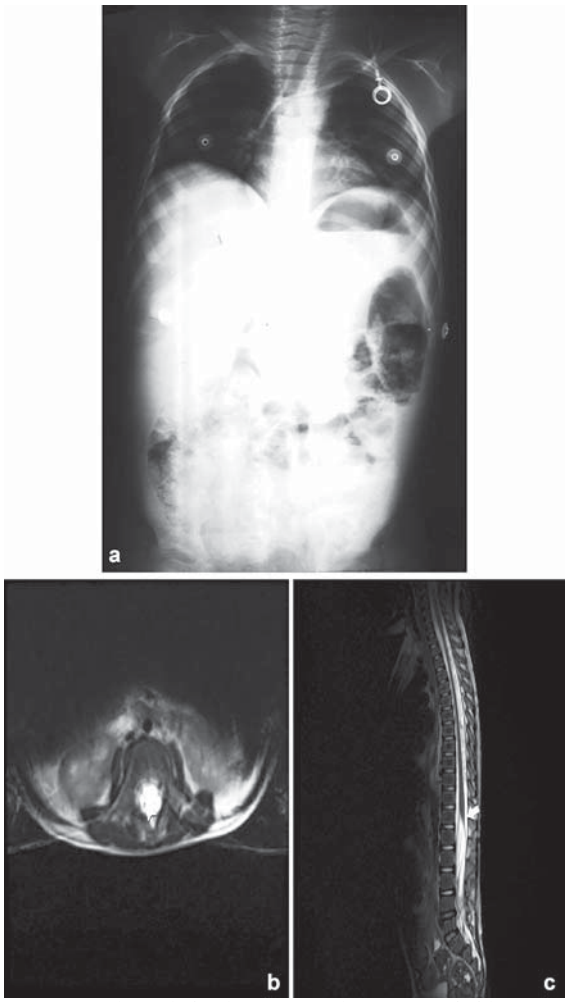

Fig. 1a. Bilateral diaphragmatic elevation and dilatation of the intestinal segments, mainly in the large intestine, on direct abdominal X-ray. **1b.** Milimetric nodular defective appearence (arrow) at the conus medullaris level T11- T12 on T2-weighted axial MRI. **1c**. Thickening of the conus medullaris and cauda equina seen on T2-weighted sagittal MRI.

but there was no adult or pediatric ALL case indicating CNS involvement as CMS. Thus, to our knowledge, our case can be considered the first such case in the literature.

Leukemic involvement of the CNS presented with intriguing laboratory findings in this patient in that the CSF biochemistry and cytology were normal, and given the presence of neurologic findings, this situation was considered as presence of infiltration of the dura or the superficial arachnoid membrane (arachnoid trabeculae and walls of veins); thus, absence of cell migration into the CSF[5]. In addition, it was demonstrated that malignant cells could be determined in only some 50% of the patients after a single CSF examination, whereas this rate reached 90% after repeated examinations for leptomeningeal carcinoma and hematological malignancies[1]. As our patient had to be treated immediately, repeated CSF examinations before therapy were not possible. Furthermore, high CSF protein is encountered in only 50% of patients with leptomeningeal leukemia; protein level in the remaining 50% is normal[5].

Gadolinium MRI was reported to be as sensitive as cytologic examination of the CSF and very valuable, especially when CSF findings were normal[6]. On the other hand, in CES, MRI findings may be completely normal [7]. Leptomeningeal metastases, infectious or granulomatous meningitis, infarcts, operations, and arachnoiditis due to irritation of intrathecal chemotherapy drugs within 12 hours lead to clustered/non-clustered thickening of the nerve roots at the spinal cuff and pathological contrast augmentation on MRI [8,9]. Our patient's MRI showed thickening of the conus medullaris and cauda equina. However, presence of pathological contrast enhancement could not be tested, since the contrast agent could not be administered. Since our patient had received his last intrathecal therapy eight months before his last admission, arachnoiditis due to intrathecal medications was unlikely[8].

Acute colonic pseudo-obstruction (ACPO) is a disorder presenting with excessive enlargement and obstruction of the colon without mechanical obstruction and carries a high risk of mortality because of complications such as ischemia and perforation. Early diagnosis and prompt cause-oriented and supportive therapy and neostigmine are important to decrease the mortality[10].

In ACPO, an imbalance of autonomic innervation of the colon causes parasympathetic suppression or sympathetic over-stimulation. While vagal innervation of the colon up to the splenic flexura is provided by the nervus vagus, parasympathetic innervation of the left colon is provided by the sacral plexus. Sympathetic innervation of the large intestine is provided by celiac and mesenteric sympathetic ganglia[10]. We think that leukemic involvement of the cauda equina caused ACPO in our patient. Dramatic disappearance of pseudocolonic obstruction

and globe vesicale, which are also signs of CMS, following intrathecal chemotherapy, despite persistence of other signs of CMS to varying degrees, suggested that CMS and therefore ACPO were related to the leukemic infiltration of this region. Obviously, repeated intrathecal therapies along with other necessary therapies such as systemic chemotherapy and radiotherapy, which could not be administered to our patient, were required for the full recovery of CMS.

This patient is presented because of the rarity of CMS with normal CSF findings and with a consequent complicating ACPO in ALL.-

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