Case Report

Cauda Equina Involvement in Acute Myeloid Leukemia Relapse

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Although central nervous system (CNS) involvement in acute myeloid leukemia has been described in about 2 to 4%, it still represents a major therapeutic problem, particularly cauda eqina involvement that is clinically significant and unusual. Here, a 22-year-old man, with underlying AML (M_2-Subtype, FAB classification) and cytogenetic analysis resulted in 45, x, -y, t(8;21) (q22;q22)[15] whose presenting symptoms of low back pain and incontinence, 10 months after first remission, was reported. This was followed by peripheral and bone marrow relapse. The magnetic resonance image (MRI) findings revealed leukemic infiltration at S1-S5 of the spinal cord canal with associated soft tissue component at presacral area encasing bilateral S1-S5 exiting root with heterogeneous enhancement in bone marrow of S2-S4. The therapeutic and prognosis implications of spinal cord involvement by leukemia were discussed. Because of severe morbidity, the patient developed bone marrow failure and died from sepsis.

Keywords: *Cauda equina involvement, Acute myeloid leukemia, Relapse*

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CNS involvement is a well recognized complication of acute leukemia. Particularly about 20 to 40% of those cases are acute lymphoblastic leukemia (ALL). On the contrary, about 2 to 4% is acute myeloid leukemia (AML), with the hypothesis that CNS represents a sanctuary for leukemia blasts that eventually repopulate in the bone marrow. Meningeal involvement is more common than spinal cord involvement, which is clinically significant and unusual. CNS prophylactic therapy in AML is still controversial because the number of AML patients with CNS involvement is small and it is a rare complication. The authors need more information about the therapeutic possibilities in such restricted subset of AML patients[1].

The cauda equina is formed by the nerve roots below the level of spinal cord termination end (conus medullaris). Cauda equina syndrome resulting in significant morbidity during the clinical course of leukemia is very rare[2]. This report shows a patient with AML who developed cauda equina syndrome as a manifestation of CNS, relapsed 10 months after first remission.

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Case Report

A 22-year-old-man was referred to a specialist because of malaise and prolonged coughing for three weeks, and an imparted blast cell in a peripheral blood smear.

On his admission, a physical examination revealed moderate pallor. No lymphadenopatly was palpable. Liver and spleen were not palpable either. Laboratory evaluation revealed hemoglobin 5.9 gm/dl, hematocrit 18.2%, white blood cell count 8.9 x 10^9/L, Platelet count 61 x 19^9/L, and 58% lymphocytes, 19% polymorphonuclear, 2% bands, 2% monocytes and 19% blasts in the peripheral blood (59% myeloblasts, 16%, promyelocytes, 9% myelocyte, 2% metamyelocyees, 2% polymorphonuclear leukocytes, 7% lymphocytes, 2% monocytes and 3% normoblasts in the bone marrow). Some blasts displayed Auer rod as a slender azurophillic giant granule in the cytoplasm. Flow cytometry revealed CD 11b 48.3%, CD 13 80.2% CD 33 70.8%, CD 117 20.5%, CD 34 54.1%, CD 15 45.6% CD 14 20.5%, CD 19 18.0%, CD 10 7.0%, CD 7 7.3% and HLA-DR 26%. Cytochemistry examination revealed

myeloperoxidase (MPO) positive in blasts 76.6%, tranadenyl tranferase (tdt) 18.0%. Cytogenetic evaluate diagnostic results showed 45, x, -y, t(8;21) (q22;q22)[15].

Thai universal coverage of induction chemotherapy for AML protocol consisted of cytosine arabinoside (100 mg/m^2) on day 1 to day 7. Doxorubicin 30 mg/m^2 on day 1 to day 3 was started every month and bone marrow evaluation presented fewer than 5% blast after four cycles of induction therapy.

At that time, he had not received bone marrow transplantation because of shortage of suitable donors. The post-remission therapy regimen consisted of cytarabine 3 gm/m^2 every 12 hours on day 1, 3, and 5 was started for two cycles and maintained with a combination of 6-thioguanine and cytarabine for 5 days every 2 months[3-5]. After his complete remission for 10 months, he complained about localized pain around the buttock that traveled down the right thigh and leg. Lower limbs muscle power had not significantly decreased and reflexes were still present. Lumbosacral spine films revealed to be normal. Three weeks later, the pain was continuous and more severe. It was coexistent with urinary incontinence, difficulty urinating and unconscious defecation. Because of pain at the right groin, the patient suffered when walking, had right lower limb weakness, and had a decreased in right lower limb joint reflexes. In addition, anal sphinctor tone and sensation of perine were detected.

Lumbosacral MRI was urgently done. It revealed leukemic infiltration at S1-S5 level of spinal cord canal extending along bilateral S1-S5 associated soft tissue component filling from the spinal cord through bilateral neural foramina from level of S1-S5 with encasing bilateral S1 to S5 exiting nerve roots and sacral plexus. In addition, it showed heterogeneous enhancement in bone marrow of S2-S4 (as Fig. 1, 2).

Before going to irradiation, the bone marrow study was repeated. It revealed 43% myeloblast (M2) and 33% myeloblast in a peripheral blood smear. Lactase dehydrogenase was 333 (140-271) Ū/L. The reinduction protocol consisting of idarubicin and cytarabine (3 + 7) was started, combined with 3,000 rads local radiation therapy in 10 fractionated doses. At the end of combination therapy, the right groin pain disappeared completely and he walked with normal gait but urinary and defecation incontinence persisted. Lumbar puncture was performed and it revealed clear colorless appearance of cerebrospinal fluid (CSF) with no cells. Protein and sugar CSF were 25 and 72 mg/dl respectively.

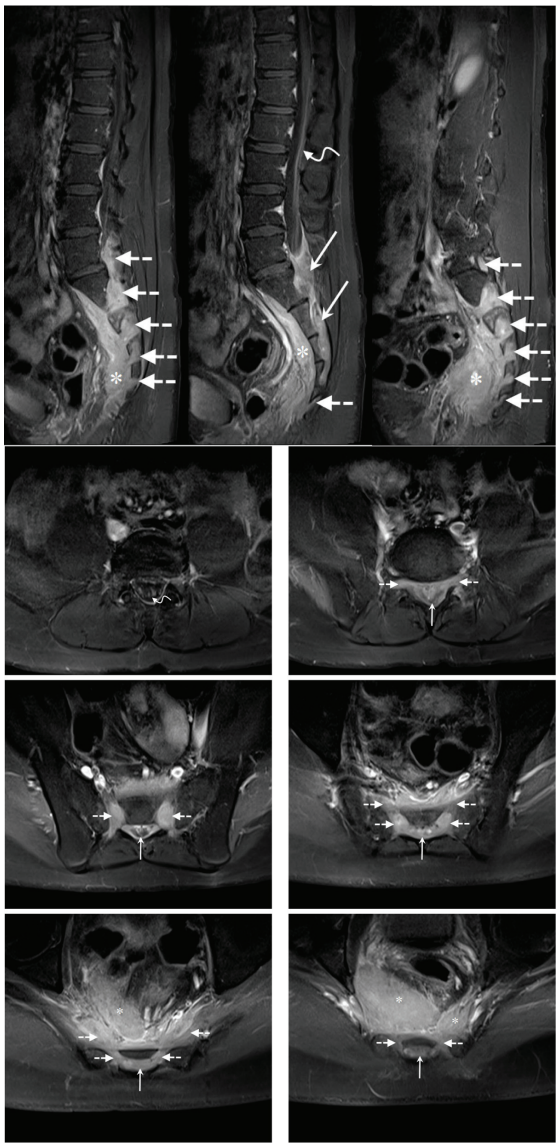

Fig. 1 Post contrast-enhanced sagittal T1 weighted images with fat suppression (from left to right) and post contrast-enhanced axial T1 weighted images with fat suppression (from level of cauda equina and L5 to S4 exiting nerve roots):
There is heterogeneously enhanced soft tissue filling entirely in the spinal canal from S1 down to S5 levels (arrow)
The enhanced soft tissue in spinal canal extends through bilateral neural foramina from level of L5 nerve roots to S5 nerve roots, causing encasement of these nerve roots and sacral plexus (dash arrow)
The enhanced soft tissue also continues with a lobulated presacral soft tissue mass (asterisk)
Enhancement of nerve roots in cauda equine is also noted (curved arrow)

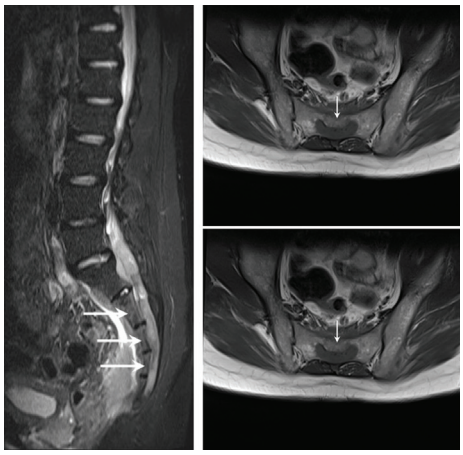

Fig. 2 Non contrast-enhanced sagittal T2 weighted image with fat suppression and non contrast-enhanced axial T1 weighted images (at S2 and S3 vertebral bodies): There is heterogeneous signal intensity of bone marrow in S2 down to S4 vertebral bodies (arrow), which could be due to leukemic cell infiltration

After two cycles of re-induction therapy the complex karyotype still revealed 45, x, -y, t(8;21)(g22;q22)[2]/46, xy[20], the patient developed hematuria and bleeding per rectum that aggravated the anemia and thrombocytopenia. This time, bone marrow remission was attained. The patient refused treatment with further steps of therapy and needed to stay at home. Within a short time, a second bone marrow relapse occurred. The patient deteriorated and died from sepsis.

Discussion

CNS involvement in patients with AML is quite uncommon, but it still represents a major therapeutic problem, whether it occurred during hematologic remission or relapse[1]. It was found that 46% of all AML patients, which autopsy material of the brain and the spinal cord of adults, had leukemia involvement of the CNS (39% of M1 + M2 subgroups and 69% of M4 + M5 subgroup) but only 40% of these patients exhibited signs of CNS involvement. The most frequent localization of leukemia infiltration was the cauda equina (38%) followed by the cerebral leptomeninges (34%)[6]. However, the cauda equina syndrome and conus medullaris syndrome in childhood owing to AML is rare[6].

This literature review studies[2,6-10] displayed 27 patients that found a mass of granulocytic sarcoma (chloroma) giving rise to spinal cord compression. It was associated with 3.1 to 9.1% of AML cases[9]. They were seen more often in men than women[11]. They rarely occur alone without peripheral blood or bone marrow evidence of leukemia[9]. In the review, they occurred in three undiagnosed patient[6,9,12]. Eight AML cases presented as a mass that compressed the spinal cord[7,8,12-17]. Three patients with initial presenting symptom of acute leukemia developed spinal cord involvement[6,7,18]. This occurs even when both are present at diagnosis[6,8]. Four patients who presented cauda equina syndrome showed diffuse infiltration of the cauda equina by myeloblast[6,8,19]. One patient had mass lesion and diffuse infiltration[6]. One in three patients had underlying myelodysplastic syndrome (MDS) and chronic myeloid leukemia (CML) in blastic crisis[1,4,6,15]. There were three cases in AML with current extra-medullary and leptominingeal relapse[6]. A very rare case with underlying AML (M5) presented with severe pain in her arms, legs and back. Autopsy revealed massive leukemic infiltrated peripheral nerves[10].

Their MRI displayed thickened and clumped nerve roots at a pathological level. Infiltration throughout the spine compressed the cauda equina. It enhanced the cauda equina with tumors and circumferential epidural lesion narrowing the thecal sac[6,20].

Conus medullaris syndrome in leukemia, is closely related to cauda equina syndrome. This is due to damage in the lower sacral of the spinal cord through infiltration by leukemic cells. It is characterized by urinary and fecal incontinence with loss of sensation over S2, S3 and S4 dermatomes. Cauda equina syndrome symptomatology presented weakness and paralysis of lower limbs, preceded with loss of sphincter tone. However, paraparesis often follows loss of sphincter tone, presented in conus medullaris syndrome[6]. Over 68% of patients with cauda equina syndrome complained of urinary, fecal and/or erectile problems. Of those patients, 18.2% presented with disturbed or decreased anal tone and/or distended bladder, 50% presented with paraparesis, paraplegia and leg weakness, 65% presented with pain in the lower back, perine, scrotum, buttock and lower limbs, 45% presented with hypo-hyper aesthesia in the lower limbs or perine and anal region, 30% presented with hypoesthesia in S1-S3 dermatomes and 20% presented with neurological defects involving cranium or upper limbs[6]. Isolated CNS relapse is extremely uncommon while systemic relapse precedes CNS relapse by four to 207 days[2,21].

CSF cytology was normal at diagnosis, as stated in the present report. On the other hand, the superficial arachnoid membrane or dura may be infiltrated. It was reported that the sensitivity of the MRI was equivalent to that of CSF and considered to be of diagnostic value especially when CSF was negative[6]. In the presented report, the development of the symptoms of cauda equina syndrome during post-remission therapy with diffuse cauda equina infiltration, a diagnostic biopsy was not performed. The MRI documented obvious leukemia involvement of the cauda equina.

Patients with extramedullary involvement are considered to adversely affect the prognosis for adults with t(8,21). It has been reported that the presence of CD56, CD19, CD7 on the blast of AML patients with t(8;21) (q22;q22) led to a significant reduction of complete remission and survival duration[22] and in patients with AML who have chromosomal abnormalities that influence the incidence of CNS involvement, remission and survival rate[16]. Striking point in review, chemotherapy and radiotherapy were not successful in curing all the diseases. It revealed that 50% of patients improved, in recovery or in remission, while 43.7% of cases reported deteriorated and died[6].

The management of spinal cord involvement in leukemia patients remains an inconclusive issue with poor results because of the risk of bone marrow relapse. Therefore, a systemic chemotherapy is necessary to prevent marrow receding in isolated CNS involvement or to treat marrow involvement[1]. Chemotherapy with high dose Ara-c (3 gm/m^2) has proven effective in acute leukemia and lymphoma. It has achieved a high degree of penetration into CSF and maintained potentially cytotoxic concentration of the drug (over 0.2u mol/L) in the CSF for the entire duration of chemotherapy[1]. The combination therapy, surgery in a mass lesion, chemotherapy with high dose Ara-c, and radiation therapy achieve a high incidence of complete neurological remission that correlates with a longer survival time of patients. This was based on clinical findings and guidelines for treatment of CNS involvement AML[1,11].

In conclusion, this reports a rare coexistence of cauda equina syndrome with an unusual presence in an AML patient. Low back pain and incontinence[23], as a component of cauda equina syndrome or conus medullaris syndrome, may be overlooked. It can introduce itself as symptoms of cauda equina involvement. Regarding the risk of CNS involvement in all leukemia patients, physicians should carefully evaluate at routine neurologic examination. Failure to detect blasts in CSF should not lead the physician to exclude leukemic involvement. The MRI is a non-invasive technology that displays leukemic involvement in patients who present with cauda equina syndrome or conus medullaris syndrome. This could make physicians handle such clinical problems early and improve the outcomes[1,11].

Potential conflicts of interest

None.

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การเกิดโรคกลับด้วยอาการกลุ่มรากประสาทคล้ายหางม้าในผู้ป่วยโรคมะเร็งเม็ดเลือดขาวเฉียบพลันชนิดมัยอีลอยด์: รายงานผู้ป่วย

จิตสุดา บัวขาว, อมเรศ ตาลเศวต

รายงานผู้ป่วยชายไทยอายุ 22 ปี ได้รับการวินิจฉัยเป็นโรคมะเร็งเม็ดเลือดขาวเฉียบพลันชนิด มัยอีลอยด์ (Myeloid) [M2] หลังการรักษาจนอาการและอาการแสดงหายไป ผู้ป่วยมาด้วย อาการปวดหลัง ปวดขา กลั้นอุจจาระปัสสาวะไม่ได้ พร้อมตรวจพบการเกิดโรคกลับจากเลือดและไขกระดูก ภาพถ่ายทางรังสีด้วยคลื่นแม่เหล็กไฟฟ้าพบการแทรกตัวของเซลล์มะเร็งเข้าไขสันหลังระดับ S1-S5 กระจายไปถึงเส้นประสาท S1-S5 ทั้งซ้ายและขวา และบริเวณด้านหน้าของกระดูกซาคัม (SACRUM) จนถึงเนื้อไขกระดูกระดับ S2-S4 รายงานนี้อภิปรายถึงการเกิดโรคกลับอาการแสดงทางระบบประสาทไขสันหลังที่ส่งผลต่อการรักษาและการพยากรณ์โรค ผู้ป่วยได้เสียชีวิตจากการติดเชื้อในกระแสโลหิต