Acute promyelocytic leukemia presenting as an extradural mass

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Acute promyelocytic leukemia is potentially a highly curable type of leukemia that usually presents with pancytopenia, coagulopathies and bleeding. We describe a case of an unusual presentation of acute promyelocytic leukemia. A 53 year-old male was admitted complaining of pain and weakness in his legs. He presented at examination a spastic paraparesis with a sensitive level at the eighth thoracic medullar (T8) segment. Magnetic resonance imaging showed a posterolateral extradural mass from T6 through T8 segments with medullar compression. A complete blood count showed anemia, thrombocytopenia and the presence of promyelocytes and blasts. Marrow examination was compatible with the diagnosis of acute promyelocytic leukemia by cytogenetics and polymerase chain reaction for the PML-RARα gene. He was treated with all-trans-retinoic acid therapy plus daunorubicin and presented an all-trans-retinoic acid syndrome. Despite hematological remission, the patient presented neurologic deterioration and had to be treated with radiotherapy (total dose 3000 cGy) of the extradural lesion. The patient evolved with severe sepsis and died without any recovery from his neurologic deficit. Extramedullary infiltration is a very rare complication in acute promyelocytic leukemia. Most cases are related to relapse after initial treatment with all-trans-retinoic acid. The skin and the central nervous system are the most frequently involved sites. This is possibly the first case reported of this condition in which the patient had a symptomatic extradural mass.

Keywords: *Leukemia, promyelocytic, acute; Sarcoma, myeloid; Spinal cord neoplasms; Case reports*

Introduction

Acute promyelocytic leukemia (APL) is a particular type of leukemia that usually presents with pancytopenia, coagulopathies and bleeding and is characterized by the presence of a translocation between chromosomes 15 and 17 [t(15;17)(q22q21)] identified by cytogenetics and a *PML-RAR* gene by PCR. APL is a highly curable disease with a combination of all-trans-retinoic acid (ATRA) and an anthracycline (idarubicin or daunorubicin), the currently used treatment,[1] inducing complete remission in almost all patients. Extramedullary disease at presentation of APL is extremely rare. We describe a case of an unusual initial presentation of APL as an extradural lesion.

Case report

A 53-year-old male was admitted to the emergency department. He complained of four-month progressive fatigue, and pain and weakness of his legs for about one week. He had been taking diclofenac (a NSAID) for the pain but without relief. He presented neither fever nor other symptoms (weight loss, night sweats). On examination, spastic paraparesis was confirmed with a sensitive level at the eight thoracic medullar (T8) segment. He was slightly pale and had a gingival hemorrhage, ecchymosis of the left thigh and hepatomegaly. Spinal magnetic resonance imaging (MRI) showed a posterolateral extradural mass from T6 through T8 segments with medullar compression (Figure 1). A complete blood count showed anemia (hemoglobin 10.6 g/dL), thrombocytopenia (12 x 10^9/L) and white blood count of 7.5 x 10^9/L (with 4.8 and 1.3 absolute promyelocyte and blast counts, respectively). Fibrinogen was below normal limits (1.04 g/L: normal range: 1.8-3.0 g/L), the international normalized ratio was 1.86 (normal range: 0.8-1.2) and the partial thromboplastin time was within normal limits. Electrolytes and the hepatic and renal functions were within the normal range. Uric acid (588 µmol/L) and lactate dehydrogenase (712 UI/L: normal ≤ 610 UI/L) were both elevated. A bone marrow biopsy showed hypercellularity with a massive infiltration of promyelocytes (with palisades of Auer rods) compatible with the diagnosis of APL. Qualitative polymerase chain reaction (PCR) for the *PML-RARα* gene was positive and a cytogenetic examination identified a t(15;17)(q22q21) abnormality.

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The authors declare no competing financial interest

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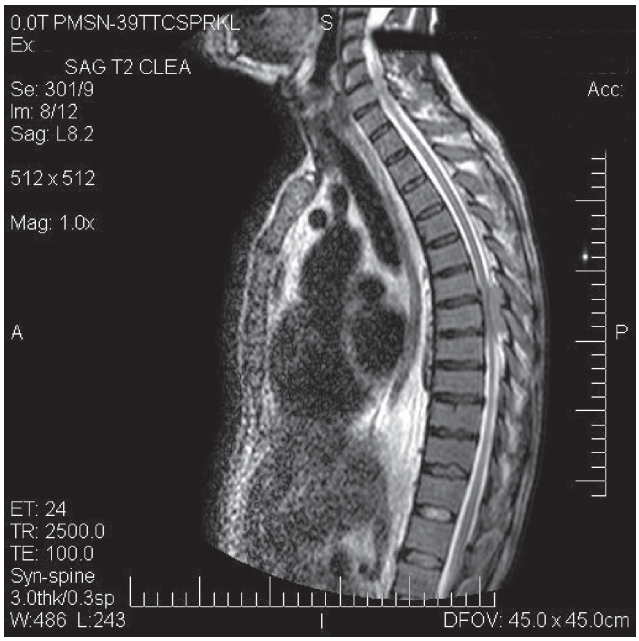

Figure 1 – T2-weighted sagittal magnetic resonance image showing a hyperintense extradural lesion at the eighth thoracic spinal segment

ATRA therapy (45mg/m^2/day) combined with daunorubicin (60 mg/m^2) on days 2, 4, 6 and 8 was initiated. The patient evolved with ATRA syndrome that was controlled with dexamethasone, and febrile neutropenia, treated with ceftazidime and amikacin. Despite chemotherapy and ATRA, the patient presented deterioration in the weakness of his legs and lost bladder sphincter control. Radiotherapy for the extradural lesion (total dose of 3000 cGy) was attempted but no clear clinical improvement was noticed. Nephrotic syndrome was noted, probably due to treatment with ATRA, which was interrupted. The patient evolved with hematological remission of APL but persistence of the extradural mass. Soon after hematological remission was achieved, he presented with respiratory distress that evolved to hypotension and shock. Pneumonia was diagnosed which was treated with vancomycin and imipenem. Despite intensive care with ventilation support, the patient died of sepsis without any recovery from his neurologic deficit.

Discussion

APL, described in 1957, is a particular subtype of acute myeloid leukemia (AML). Classically, APL presents as pancytopenia and a hemorrhagic/disseminated intravascular coagulation syndrome. It accounts for 10 to 15% of all AML cases in the United States[1] but it seems to be more frequent in Mexico, Central and South America, Spain and Italy.[2] Once a highly fatal disease during induction therapy, mainly due to bleeding disorders, now it is the most curable AML subtype, mainly due to introduction of ATRA therapy in association with anthracycline-based chemotherapy.[1] More recently, arsenic trioxide has also proved to be useful in APL treatment, especially in relapsed patients.[1] Risk stratification for relapse includes white blood cell and platelet counts at diagnosis, as described by the PETHEMA (Programa para el Estudio de la Terapéutica en Hemopatía Maligna) and GIMEMA(Gruppo Italiano Malattie EMatologiche dell'Adulto) groups. While high risk patients presented a 5-year disease-free survival of 73%, low risk and intermediate risk showed a 5-year disease-free survival of 87% and 90%, respectively.[3] Our patient was classified as intermediate risk. It is important to mention that the early death rate in APL patients has decreased due to use of ATRA soon after diagnosis. This patient died of infection not directly linked to induction therapy but, instead, because of a long immobilization/bed rest, a known risk factor for nosocomial pneumonia, due to his neurological symptoms.

Extramedullary infiltration is a very rare complication in patients with APL.[4,5] The majority of cases reported are related to relapse after initial treatment, with the central nervous system and skin being the most frequently involved sites.[6,7] Factors associated with extramedullary relapse include age less than 45 years, high white blood cell count and the bcr3 isoform of *PML-RARA*.[7] Association of ATRA treatment with extramedullary relapse is controversial.[5,6] Much more uncommon is the description of cases with extramedullary involvement at presentation.[4,8,9] In the literature, there is only one previous report of a extradural spinal mass that was identified one month before the diagnosis of APL.[10] In that particular case, laminectomy was possible as the patient did not present any signs of APL at the time of surgery. The patient was in complete remission after chemotherapy, radiotherapy and autologous bone marrow transplantation (ABMT). However, a MRI 5 months after ABMT suggested a small residual mass. In our case, laminectomy was not possible because the patient had a coagulopathy. Radiotherapy was ineffective to induce significant mass reduction and to alleviate neurologic symptoms.

In summary, this patient, who presented with an extradural mass at diagnosis of APL, died of clinical complications of leukemia treatment but also due to failure to ameliorate his neurological symptoms. Laminectomy should be performed as soon as possible as radiotherapy alone seems to be ineffective in some cases.

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References

1. Tallman MS, Altman JK. Curative strategies in acute promyelocytic leukemia. Hematology Am Soc Hematol Educ Program. 2008: 391-9.
2. Sanz MA, Grimwade D, Tallman MS, Lowenberg B, Fenaux P, Estey EH, et al. Management of acute promyelocytic leukemia:

recommendations from an expert panel on behalf of the European LeukemiaNet. Blood. 2009:113(9):1875-91.

3. Sanz MA, Montesinos P, Vellenga E, Rayón C, de la Serna J, Parody R, et al. Risk-adapted treatment of acute promyelocytic leukemia with all-trans retinoic acid and anthracycline monochemotherapy: long-term outcome of the LPA 99 multicenter study by the PETHEMA Group. Blood. 2008;112(8):3130-4.
4. Wiernik PH, De Bellis R, Muxi P, Dutcher JP. Extramedullary acute promyelocytic leukemia. Cancer.1996;78(12):2510-4. Comment in: Cancer. 1997;80(3):518-9. Cancer. 1997;79(11):2263-4.
5. Evans GD, Grimwade DJ. Extramedullary disease in acute promyelocytic leukemia. Leuk Lymphoma. 1999;33(3-4):219-29.
6. Vega-Ruiz A, Faderl S, Estrov Z, Pierce S, Cortes J, Kantarjian H, et al. Incidence of extramedullary disease in patients with acute promyelocytic leukemia: a single-institution experience. Int J Hematol. 2009;89(4):489-96.
7. de Botton S, Sanz MA, Chevret S, Dombret H, Martin G, Thomas X, Mediavilla JD, Recher C, Ades L, Quesnel B, Brault P, Fey M, Wandt H, Machover D, Guerci A, Maloisel F, Stoppa AM, Rayon C, Ribera JM, Chomienne C, Degos L, Fenaux P; European APL Group; PETHEMA Group. Extramedullary relapse in acute promyelocytic leukemia treated with all-trans retinoic acid and chemotherapy. Leukemia. 2006;20(1):35-41.
8. Liso V, Specchia G, Pogliani EM, Palumbo G, Mininni D, Rossi V, et al. Extramedullary involvement in patients with acute promyelocytic leukemia: a report of seven cases. Cancer. 1998;83(8):1522-8.
9. Worch J, Ritter J, Fruhwald MC. Presentation of acute promyelocytic leukemia as granulocytic sarcoma. Pediatr Blood Cancer. 2008;50(3):657-60.
10. Zuiable A, Aboud H, Nandi A, Powles R, Treleaven J. Extramedullary disease initially without bone marrow involvement in acute promyelocytic leukaemia. Clin Lab Haematol. 1989;11(3):288-9.

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