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Misdiagnosed as Ankylosing Spondylitis: An Unusual Case of Acute Promyelocytic Leukemia with Myeloid Sarcoma

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ABSTRACT

Introduction:
Acute promyelocytic leukemia (APL) accounts for 7-8% of adult acute myeloid leukemia cases. Extramedullary manifestations in APL are rare at initial diagnosis and exhibit unique biological characteristics.

Case presentation:
This study aimed to report a unique case of a 31-year-old male who initially presented with lower back pain and was misdiagnosed with Ankylosing Spondylitis. Subsequent development of cervical lymphadenopathy led to further investigation, revealing myeloid sarcoma and APL with Promyelocytic Leukemia/Retinoic Acid Receptor Alpha translocation. The patient underwent standard all-trans-retinoic acid therapy, followed by consolidation chemotherapy. Despite a relapse, the patient achieved complete remission after treatment with arsenic trioxide and a bone marrow transplant, which is uncommon for APL patients.

Conclusion:
This case underscores the importance of considering hematologic malignancies in patients with atypical presentations and highlights the role of genetic testing in confirming diagnoses. The successful use of a bone marrow transplant in this case suggests potential benefits for selected APL patients with extramedullary involvement and relapse.

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Introduction

Acute promyelocytic leukemia (APL) is a distinct subtype of acute myeloid leukemia (AML), accounting for approximately 7-8% of adult AML cases (1,2).

It was initially described in the 1950s as a hyperacute and highly fatal disease with a mean survival of less than a week. However, significant therapeutic advancements—particularly with all-trans-retinoic acid (ATRA) and arsenic trioxide (ATO)—have dramatically improved patient outcomes (3-6). Modern treatment regimens have led to 10-year survival rates approaching 90%, positioning APL as one of the most curable forms of leukemia. Extramedullary manifestations (EM) of APL at initial diagnosis are uncommon and pose unique diagnostic and therapeutic challenges (7,8).

Studies indicate that EM occurs in approximately 3-5% of APL patients, with an increased incidence following ATRA therapy. The EM presentations are highly variable, with the central nervous system being the most frequently affected site, followed by the skin. The EM has been reported less commonly in the lymph nodes, testis, nasopharynx, spine, lung, pleura, and heart. Myeloid sarcoma, a rare extramedullary tumor of immature myeloid cells, is a particularly challenging presentation, often mimicking other malignancies or inflammatory conditions, thereby delaying diagnosis and treatment (9-13). This case was notable due to its atypical presentation with lower back pain and cervical lymphadenopathy, initially misdiagnosed as Ankylosing Spondylitis (AS). While hematopoietic stem cell transplantation (HSCT) is not a standard treatment for APL, its use in this case resulted in complete remission without further relapse, highlighting its potential role in selected APL cases with extramedullary involvement.

Case Presentation

A 31-year-old male presented in 2019 with complaints of lower back pain. Initially, he consulted an orthopedic specialist, followed by a rheumatologist, who diagnosed him with AS and initiated Methotrexate (MTX) therapy. Subsequently, the patient developed cervical lymphadenopathy, which was suspected to be a side effect of MTX. However, despite the discontinuation of MTX, the lymphadenopathy persisted and expanded, necessitating an excisional biopsy.

In July 2019, a Complete Blood Count (CBC) revealed normal results, including a white blood cell count of 7.9 × 10^9/L, platelets count of 201 × 10^9/L, and hemoglobin count of 13.3 g/dL. These findings were atypical in the context of suspected malignancy; however, a biopsy conducted in August 2019 indicated the presence of a lymphoproliferative disorder, characterized by the infiltration of diffusely arranged lymphoid-type mononuclear cell clusters. Immunohistochemical analysis suggested a diagnosis of myeloid sarcoma, with positive markers for CD45, Ki67 (25% of tumoral cells), CD43 (in some tumoral cells), and myeloperoxidase (MPO) (in some cells). Subsequent bone marrow aspiration revealed 20% blasts among total cells, with an immunophenotypic profile of CD117+, CD13+, CD33+, MPO+, CD34-, and HLA-DR. Molecular studies confirmed the presence of the Promyelocytic Leukemia/Retinoic Acid Receptor Alpha (PML/RARα) translocation [t(15;17) (q22;q21)], consistent with APL.

Treatment and follow-up

The patient began chemotherapy with ATRA, the standard treatment for high-risk APL, in November 2019.

His symptoms, including lymphadenopathy, back pain, and CBC abnormalities, improved significantly. Following induction therapy, consolidation chemotherapy was administered to prevent relapse. In January 2020, maintenance treatment commenced, consisting of ATRA (45 mg/m^2), MTX (20 mg/m^2), 6-Mercaptopurine (6MP) (50 mg/m^2), and folic acid. Despite this regimen, the patient experienced a relapse in October 2020 and was treated with ATO at 0.15 mg/kg. Following remission, he underwent an autologous HSCT, a procedure rarely performed in APL patients. Subsequent follow-ups showed that PML/RARα was negative, and the patient achieved molecular complete remission (mCR).

Discussion

The optimal approach for post-remission treatment in patients with late recurrence is still not well established. A study conducted by the European Leukemia Network registry on 155 patients with relapsed APL demonstrated that autologous and allogeneic HSCT are effective consolidation therapies for those who did not achieve mCR and experienced both early and late relapses. According to the present research, autologous HSCT should be the first option for qualified patients who achieve second molecular remission. Nevertheless, the latest National Cancer Research Institute report emphasized the critical role of transplantation, particularly for patients who have undergone a full course of consolidation with ATO, have achieved molecular remission with ATO and ATRA, and are free of neurological complications at the time of relapse (14,15). However, the necessity of a transplant strategy may be questioned for patients who relapse after a prolonged first CR, as maintaining ATRA-ATO therapy could be curative.

There is limited information on patients who experienced an initial relapse and underwent extended ATRA/ATO therapy without final consolidation through stem cell transplant (16,17). A recent study performed on 22 patients revealed that only two received transplants, while the others continued with additional cycles of ATRA/ATO (18). This approach resulted in a disease-free survival rate of 74% and an overall survival rate of 85% over four years, suggesting that ongoing ATO treatment may have a curative effect, especially on patients with a long initial mCR (19). Moreover, a cohort study found that the 5-year overall survival rates were similar between patients who underwent transplantation and those who did not. Given the small sample size, selection biases, and treatment heterogeneity, these findings contrast with the literature that generally indicates poorer outcomes for patients who do not receive transplantation (20,21).

In conclusion, this case report presented a 31-year-old male initially diagnosed with Ankylosing Spondylitis, who later developed cervical lymphadenopathy. The persistence and progression of lymphadenopathy despite discontinuation of MTX therapy led to further investigations, ultimately revealing a diagnosis of AML M3. This case highlighted the importance of considering hematologic malignancies in patients with atypical presentations and underscored the role of genetic testing in confirming diagnoses and guiding treatment.

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