Case Report

Promyelocytic Sarcoma of the Spine: A Case Report and Review of the Literature

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Myeloid sarcoma (MS, previously named granulocytic sarcoma or chloroma) is a rare extramedullary tumour of immature myeloid cells. It can be present before, concurrently with, or after the diagnosis of acute myeloid leukemia. MS is extremely uncommon in acute promyelocytic leukemia (APL). In the case described here, MS was the sole site of APL relapse and the cause of spinal cord compression. The patient presented with neurologic symptoms due to a paravertebral mass of MS after 7 years of complete remission. He was treated with excision of the mass followed by local radiotherapy. Systemic treatment was also given with combined arsenic trioxide and all-trans retinoic acid and the patient was able to achieve a second prolonged clinical and molecular remission.

1. Introduction

Myeloid sarcoma (MS, previously named granulocytic sarcoma or chloroma) is a rare extramedullary tumour of immature myeloid cells [1]. It can occur in association with myelogenous leukemia, myeloproliferative disorders, and myelodysplasia. MS has different modalities of presentation and can affect any organ. It may occur otherwise in healthy individuals who subsequently develop an overt typical myelogenous leukemia [1, 2]. MS can also develop in leukemia patients concurrently with or after diagnosis, or as a manifestation of disease relapse [3, 4]. The WHO recognizes three major variants of MS based on the predominant cell type and the degree of maturation, namely respectively, a myeloblast variant, with a mix of myeloblasts and promyelocytes variant, and more differentiated variant with promyelocytes and more mature granulocytes [5]. Acute promyelocytic leukemia (APL) accounts for approximately 10% of acute myeloid leukemia (AML) and cases of MS due to APL have been only occasionally reported [1–4]. We report the case of a patient with APL who presented right paraparesis after 7 years of complete remission. The patient had a MS with paravertebral localization as the only site of APL relapse.

2. Case Report

In November 1999, a 38-year-old male presented with a history of recurrent episodes of gum bleeding. Physical examination was unremarkable, but a complete blood count showed Hb 6.1 g/dL, WBC 1 × 10^9/L, and platelets 2 × 10^9/L. Microscopic examination of a blood smear showed 8% hypergranular promyelocytes, with Auer rods. At examination of bone marrow aspirate a diffuse infiltration by atypical promyelocytes was apparent. The immunophenotype profile of leukemic cells was consistent with APL (CD33+ve, CD45+ve, HLA-DR-ve, CD34-ve, CD16-ve, and CD56-ve). Cytogenetics revealed the characteristic t(15;17) (q22;q21-q22) and the RT-PCR assay showed the typical PML/RARα fusion gene thereby confirming the diagnosis of APL [6]. The patient was treated with all-trans retinoic
3. Discussion

Extramedullary disease (EMD) at diagnosis or at relapse develops in 3%–8% of patients with acute myelogenous leukemia, more frequently in those with myelomonocytic and monocytic morphology [9–11] (M4 and M5 French-American-British subtypes). Its occurrence in APL is relatively rare but after the advent of ATRA it is increasingly reported at time of relapse [11–29]. The case reported here, is a rare case of CNS isolated relapse [13]. The patient presented with neurologic symptoms due to a paravertebral mass after 7 years of complete remission. He entered a second prolonged clinical and molecular remission after local radiotherapy followed by a combination of ATRA and ATO. This case represents the second report of MS resulting in spinal cord compression due to APL extramedullary relapse. The other case, reported by Tsimeridou et al. [30], was a man who remained in complete remission for 3 years after treatment of APL. This patient later developed paraplegia due to a paravertebral mass at the level of T7–T8. Following decompression laminectomy, an isolated extramedullary promyelocytic relapse was diagnosed. The bone marrow was not involved. The patient was treated with local radiotherapy followed by ATRA and idarubicin, achieving a short second remission. He subsequently developed a second relapse with marrow and skin involvement.

The occurrence of EMD has long been considered a rare event in APL patients treated with chemotherapy alone, whereas this phenomenon has increasingly been reported in the ATRA era [5, 9, 38]. The question arises as to whether treatment of APL with ATRA predisposes patients to the development of EMD [38, 51]. This question is still open, as various trials have shown contrasting results. Wiernik et al. [3] suggested that extramedullary APL occurs more frequently after ATRA than other therapies. Ko et al. [23] demonstrated that patients receiving ATRA induction had a 2.1 increased relative risk of EMD compared with those with chemotherapy alone. In a literature review by Bae et al. [51], only three of 21 cases with CNS relapse received systemic chemotherapy without ATRA. Among 172 patients with APL treated at MDACC between 1980 and 2003, a total of three patients relapsed with isolated EMD and it occurred exclusively in patients who had received ATRA-containing induction regimens [51]. Ohno et al. [52] noted that EM relapse was absent from all 37 patients with relapsing APL in the Japanese chemotherapy only studies, while it was seen in 8% of 121 patients in the chemotherapy plus ATRA protocols and this raised the possibility that the doses of chemotherapy given with ATRA-based regimens are less intensive than those previously used and thus may not reach therapeutic levels in the EM tissues. This could be particularly relevant to protocols without cytarabine. A relationship between EMD and ATRA treatment has been suggested. Two possible explanations are considered. The first suggests a direct effect of ATRA on adhesion molecules resulting in increased infiltration capability of APL leukemia blasts [23]. The second postulates the occurrence of MS in relapsed patients as a consequence of the prolonged survival [38]. In a study of the GIMEMA [38], the authors found...
Table 1: Clinical features of patients with MS in APL.

<table>
<thead>
<tr>
<th>References</th>
<th>No. cases</th>
<th>disease status</th>
<th>Time since diagnosis/EMD relapse (months)</th>
<th>Site of involvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fukushima et al. [31]</td>
<td>1</td>
<td>onset</td>
<td></td>
<td>cerebellum + hematological</td>
</tr>
<tr>
<td>Worch et al. [32]</td>
<td>1</td>
<td>onset</td>
<td></td>
<td>lytic lesions of humerus, tibia, femur + molecular hematological</td>
</tr>
<tr>
<td>Ajarim et al. [33]</td>
<td>1</td>
<td>onset</td>
<td></td>
<td>thymus + hematological</td>
</tr>
<tr>
<td>Savranlar et al. [34]</td>
<td>1</td>
<td>onset</td>
<td></td>
<td>thoracic-epidural</td>
</tr>
<tr>
<td>Brown et al. [35]</td>
<td>1</td>
<td>onset</td>
<td></td>
<td>optic nerve + hematological</td>
</tr>
<tr>
<td>Agarwal et al. [36]</td>
<td>1</td>
<td>relapse</td>
<td>31</td>
<td>hip + hematological</td>
</tr>
<tr>
<td>Disel et al. [37]</td>
<td>1</td>
<td>relapse</td>
<td>9</td>
<td>pleura</td>
</tr>
<tr>
<td>Tsimberodou et al. [30]</td>
<td>1</td>
<td>relapse</td>
<td>36</td>
<td>thoracic spine</td>
</tr>
<tr>
<td>Specchia et al. [38]</td>
<td>1</td>
<td>relapse</td>
<td>NA</td>
<td>lung + hematological</td>
</tr>
<tr>
<td>Latagliata et al. [39]</td>
<td>3</td>
<td>relapse</td>
<td>7</td>
<td>mastoid + mol hematological</td>
</tr>
<tr>
<td>Sanz et al. [40]</td>
<td>6</td>
<td>relapse</td>
<td>7</td>
<td>mastoid, subcutaneous nodules at sternal manubrium + wrist at level of the radial artery pulse + site of intravenous catheter scar + mol hematological</td>
</tr>
<tr>
<td>Magliulo et al. [41]</td>
<td>1</td>
<td>relapse</td>
<td>24</td>
<td>external auditory canal + mol hematological</td>
</tr>
<tr>
<td>Nasilowska-Adamska et al. [42]</td>
<td>1</td>
<td>relapse</td>
<td>21</td>
<td>pleura, heart and pericardium</td>
</tr>
<tr>
<td>Slavecheva et al. [43]</td>
<td>1</td>
<td>relapse</td>
<td>120</td>
<td>lymph node</td>
</tr>
<tr>
<td>Kai et al. [44]</td>
<td>1</td>
<td>relapses</td>
<td>NA</td>
<td>4 time at different sites</td>
</tr>
<tr>
<td>Tobita et al. [45]</td>
<td>1</td>
<td>relapses</td>
<td>NA</td>
<td>1st and 2nd external auditory canal</td>
</tr>
<tr>
<td>Forrest et al. [46]</td>
<td>1</td>
<td>relapse</td>
<td>1st 48-2nd 24</td>
<td>1st testicular -2nd retroperitoneal nodes, psoas muscle and skin</td>
</tr>
<tr>
<td>Skarin et al. [47]</td>
<td>1</td>
<td>relapse</td>
<td>8</td>
<td>CNS + hematologic</td>
</tr>
<tr>
<td>Leoni et al. [48]</td>
<td>2</td>
<td>relapse</td>
<td>NA</td>
<td>(1) central nervous system + middle ear + lymph nodes.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(2) skin + lymph nodes</td>
</tr>
<tr>
<td>Ammatuna et al. [49]</td>
<td>1</td>
<td>relapse</td>
<td>NA</td>
<td>1st and 2nd -scalp + mol hematological 3rd mol hematological + breast</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(1) left auricular canal + mastoid + mol hematological</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(2) left mastoid + mol hematological</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(3) left mastoid</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(4) left mastoid + hematologic</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(5) left mastoid + hematologic</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(6) right auricular canal</td>
</tr>
<tr>
<td>Breccia et al. [50]</td>
<td>7</td>
<td>relapse</td>
<td>6 from 2nd CR</td>
<td>(7) right mastoid + CNS + mol hematological</td>
</tr>
</tbody>
</table>

NA: not available; mol: molecular; CR: complete remission;
that elevated WBC count (39). Breccia et al. [50] described three adult patients with frequent among the AIDA treated patients (8% versus 1%) involved other extramedullary sites (the skin in 3, the middle ear in 2, and the lung in 1). Thus CNS disease at relapse seems frequent among the AIDA treated patients (8% versus 1%) [39]. Breccia et al. [50] described three adult patients with middle ear localizations at relapse. They had been previously treated with ATRA and CT. Their characteristics are shown in Table 1.

Similarly, C. Samanez et al. [53] reported 7 cases of EMD relapse in APL patients receiving chemotherapy (CT) alone (102 patients) or combined with ATRA (155 patients). EMD relapse rate was 4.4% in the CT group and 8.7% in the group CT plus ATRA, with no statistical differences. EMD localizations were in soft tissues (3 patients), the CNS (2 patients), the tonsils (1 patient), liver (1 patient), and the testis (1 patient). De Botton et al. [54] analyzed EMD relapse occurring in patients with APL treated with ATRA and CT. Of 740 patients included in three multicenter trials (APL91, APL93 trials, and PETHHEMA 96) 10 patients developed EMD relapse. Of these, 9 were in the CNS and one in the skin. Only two patients had isolated EMD relapses. A significant correlation could be found between high WBC count and the risk of CNS relapse. More recently, Casanova et al. [55] reported a similar pattern of increased CNS EMD relapse in APL patients treated with ATRA and CT. EMD relapse was found in 8 of 74 (15%) APL patients (CNS: 5, external ear: 3). Together, these studies confirm that the CNS is the preferential site of extramedullary involvement in APL, raising an issue of whether or not to consider CNS prophylaxis in APL treatment protocols especially in patients presenting with hyperleukocytosis, as suggested by the expert panel of the European Leukemia Net. However, the benefit of this policy has not been established. For patients without hyperleukocytosis, in whom the risk of CNS relapse is extremely low, there is a general consensus to avoid CNS prophylaxis.

CNS prophylaxis for patients in this particular high-risk setting. For such patients, it is advisable to postpone CNS prophylaxis until after the achievement of CR because lumbar puncture at presentation and during induction is extremely hazardous. However, the benefit of this policy has not been established. For patients without hyperleukocytosis, in whom the risk of CNS relapse is extremely low, there is a general consensus to avoid CNS prophylaxis.

In conclusion, the increasing number and special pattern of EMD involvement in relapsing APL patients emphasize its importance in the differential diagnosis of EMD localization in patients with history of APL. They also highlight the need for understanding the underlying pathogenesis and predisposing factors, as well as for selecting the optimal treatment approach.

References


