Journal of Cancer Therapy, 2013, 4, 1049-1051
http://dx.doi.org/10.4236/jct.2013.46118 Published Online August 2013 (http://www.scirp.org/journal/jct)

Simultaneous Diagnosis of Myeloid Sarcoma of the Jaw and *Mycobacterium tuberculosis* Infection

Luís Arthur Flores Pelloso[1,2], Sandra Serson Rohr[1], Mihoko Yamamoto[1], Maria de Lourdes L. F. Chauffaille[1]

[1]Section of Hematology and Blood Transfusion, Department of Clinical and Experimental Oncology, Federal University of São Paulo (UNIFESP-EPM), São Paulo, Brazil; [2]PPD, Pharmaceutical Product Development, Inc., Pharmacovigilance, São Paulo, Brazil. Email: chauffaille@unifesp.br

Received May 15th, 2013; revised June 17th, 2013; accepted June 24th, 2013

ABSTRACT

Granulocytic or myeloid sarcoma (MS) is a rare neoplastic condition consisting of a tumor mass of myeloid blasts with or without maturation occurring at an anatomical site other than the bone marrow the association between tuberculosis and MS is extremely rare. A 21-year-old female patient presented cough, sore throat and a suppurative swollen gum for 10 days prior to hospital admission. Physical examination revealed moderate pallor and swollen inferior gum. CBC revealed Hb 6.5 g/dL, hematocrit 18.4% MCV 97 fL MCH 34 pg, WBC 18.5 × 10^9/μL (1 My/3 Bt/69 Sg/1 Eo/0 Ba/20 Ly/6 Mo), Platelets 43 × 10^9/μL. The peripheral blood smear presented with 3% blast cells (type 1) and granulocytic dysplasia. Bone marrow biopsy showed 100% cellularity. 50% of cells were from granulocytic precursors, diagnosis of granulocytic sarcoma. The diagnosis of AML was established: granulocytic sarcoma with massive gum infiltration (immature granulocytic cells) and 10% of blasts in bone marrow. The patient received induction chemotherapy (3 + 7 daunorubicin 90 mg/m^2), and gum tissue culture was positive for *Mycobacterium tuberculosis*. Simultaneously, a qRT-PCR test confirmed the same bacteria in the gum tissue. Patient treated with isoniazid, rifampicin, pyrazinamide and ethambutol ciprofloxacin and amikacin). Remission was achieved and the patient was submitted for consolidation/ intensification (HiDAC x3) schema and referred to allogeneic HSCT. After induction and full hematological recovery there was no further evidence or recurrence of fever and lytic lesions. Currently patient is under CR and ling follow up (48 months) did not show recurrence of either AML or tuberculosis.

Keywords: Myeloid Sarcoma; *Mycobacterium tuberculosis*; Granulocytic Sarcoma

1. Introduction

Granulocytic or myeloid sarcoma (MS) is a rare neoplastic condition consisting of a tumor mass of myeloid blasts with or without maturation occurring at an anatomical site other than the bone marrow [1]. MS may develop as *de novo* or simultaneously to acute myeloid leukemia (AML), myeloproliferative neoplasm (MPN) or myelodysplastic syndrome (MDS) [1]. Hence, MS may be the first manifestation of AML and precede it by months or years, or equally represent the initial relapse manifestation in a previously treated AML. The occurrence of MS is quite rare. The male:female ratio is 1.2:1 and the median age is 56 years (range 1 month - 89 years) [1].

The association between tuberculosis and hematological neoplasms has been recognized for many years because of the T-cell immunodeficiency caused by the underlying disease and/or its treatment. However, the diagnosis of tuberculosis may be problematic because the immunodeficiency may attenuate or mitigate its symptoms and also symptoms and signs can be overlapped by those from the hematologic malignancy [2].

The reported prevalence of tuberculosis in patients with hematologic malignancies is between 0.72% and 2.6% [2]. Conversely, the diagnosis of a simultaneous occurrence of a rare hematological neoplasm such as MS and bone tuberculosis at initial presentation and from the same involved site seemed quite unusual and due to its rarity and interest, we aimed to report this case [3-9].

2. Case Report

A 21-year-old female patient presented cough, sore throat and a suppurative swollen gum for 10 days prior to

hospital admission. Physical examination revealed moderate pallor and swollen inferior gum. Past medical history included weight loss, fatigue, hypermenorrhea, previous use of iron salt for anemia and this subject denied previous exposure to chemical agents or pesticides. CBC revealed Hb 6.5 g/dL, hematocrit 18.4% MCV 97 fL MCH 34 pg, WBC 18.5 × 10^9/μL (1 My/3 Bt/69 Sg/ 1 Eo/0 Ba/20 Ly/6 Mo), Platelets 43 × 10^9/μL. The peripheral blood smear presented with 3% blast cells (type 1) and granulocytic dysplasia (hypogranular cells and abnormal nuclei condensation). Bone marrow aspiration, although hemodiluted, was normocellular, G:E ratio 2.4:1 and there were 6.3% type 1 myeloid blast cells (no Auer rods). Immunophenotyping from bone marrow revealed 10% blast cells positive for CD34, HLA-DR, CD-117, $CD65^{dim}$, $CD64^{dim}$ and CD7. Bone marrow biopsy showed 100% cellularity, 50% of cells were from granulocytic precursors, there was evident dysplastic megakaryocytes and fibrosis grade 2. Immuhistochemistry studies were positive for lysozyme, MPO in granuloncytic cells and LCA and CD34 in immature cells. Bone marrow karyotype was unsuccessful due to absence of metaphases.

Imaging studies revealed lytic jaw lesions not other bone was involved (CT scans). Abdominal and thorax CT scans were unremarkable. Bone scan showed increased uptake in jaw. Gum biopsy showed increased number of immature cells positive for LCA and MPO favoring the diagnosis of granulocytic sarcoma.

Given the clinical picture and histological findings thee diagnosis of AML was established: granulocytic sarcoma with massive gum infiltration (immature granulocytic cells) and 10% of blasts in bone marrow. The patient was assigned to receive intent of treatment therapy: induction chemotherapy (3 + 7 cytarabine 100 mg/m^2 D1-D7 and daunorubicin 90mg/m^2 D1-D3), and gum tissue culture was positive for *Mycobacterium tuberculosis*. No other pathogens were found in tissue culture. Simultaneously, a qRT-PCR test confirmed the same bacteria in the gum tissue. Within two concomitant diagnosis tuberculosis and myeloid sarcoma in the same topography the gum biopsy and bone marrow slides were reviewed by hematology and pathology team both attempts in order to look up and review for any evidence of tuberculosis granuloma and granuloma-associated necrosis but neither slides and tissue samples did not demonstrate any of latter. Since jaw tuberculosis was established she was treated with isoniazid, rifampicin, pyrazinamide and ethambutol ciprofloxacin and amikacin). Curiously, when tuberculosis reports were available patient was in nadir after induction. We were concerned that patient could develop milliary or disseminated tuberculosis but did not occur.

Complete remission was achieved and the patient was submitted for consolidation/intensification (HiDAC x3) schema and referred to allogeneic HSCT. After induction and full hematological recovery there was no further evidence or recurrence of fever and lytic lesions. Currently patient is under CR and ling follow up (48 months) did not show recurrence of either AML or tuberculosis.

3. Discussion

According to the 4th edition of the WHO classification (2008), myeloid sarcoma is categorized into AML and related precursor neoplasms as a distinct pathologic entity [1]. Differential histological diagnosis at conventional light microscopy are lymphoblastic lymphoma, Burkitt's or diffuse large B-cell lymphoma or tissue infiltration by a non-hematopoietic tumor. As this implies a wrong treatment, the application of immunophenotyping, immunohistochemistry is of paramount importance for the lineage definition, differential diagnosis and specific treatment.

This case presented several medical challenges. Despite the certainty of current MS in the jaw, bone marrow was not massively infiltrated by abnormal blast cells. In the present case dysplastic features were evident in bone marrow and there were no other medical conditions that could be related to such morphological abnormalities. Moreover, MS usually occurs in patients with AML, MDS, or MPN, but it may present as *de novo* or rarely precede peripheral blood or bone marrow involvement, posing a diagnostic challenge. Plus, the gingival/gum/jaw anatomical site of MS was quite unusual and in addition patient presented suppurative gum lesion on the same anatomical site of the MS. This suppurative gum lesion which was initially managed with large spectrum antibiotics and was found to be caused by tuberculosis. After induction chemotherapy and proper tuberculostatic treatment there were no clinical or radiological recurrence of suppurative gum or other lesions elsewhere nor disseminated tuberculosis. Quite often patients who present tuberculosis may suffer from other medical conditions that are associated with poor health status, immunodeficiency, chronic conditions including but not limited to chronic alcohol exposure, malnutrition, drug abuse or other acquired immunodeficiency diseases which were not found in this case. Systematic tuberculosis screening was made after jaw culture was positive for *M. tuberculosis* and no other site was involved with mycobacterium infection. Tuberculosis diagnosis was performed during nadir and medical attention was given to assess and treat any other additional infectious disease which did not occur. To date the course of disseminated tuberculosis is usually fatal in immunocompromised patients and the current present case patient presented successful bone marrow recovery, achieved complete remission and did

not present any further infectious disease complications throughout AML chemotherapy treatment [2-9].

In a previous survey, tuberculosis was detected in 2.6% (n = 24 in 129) in all hematological neoplasms in a 10-year period [1]. In this published series no tuberculosis was diagnosed in AML or MS only MDS (n = 2). The univariate analysis of that study identified several factors associated with a high risk of tuberculosis: chronic lymphocytic leukemia, malnutrition (OR 38.78, 95% CI 2.35 - 639, $p = 0.05$), previous corticosteroid use and use of fludarabine. In the case presented we could only envision poor dental care but not any of the conditions associated with a high risk tuberculosis.

According to a study published on Leukemia (2007) [1], with 92 MSs so far evaluated there were no significant differences in survivor incidence between the group with *de novo* tumor and the one with concomitant or those ones with a previous hematological disorder. Interestingly, all survivors achieved complete remission following the first line of therapy. By contrast, only eight out of sixty patients who deceased obtained complete remission following the initial therapeutic approach. Six out of seven survivors underwent allogeneic bone marrow transplant, the remaining one having received several courses of conventional chemotherapy. Notably, according to that study, the patients who died of disease within the group of transplanted patients (two following Autologous HSCT used as initial therapy and two who received allogeneic HSCT as salvage therapy) experienced prolonged survival (from 8 months to six years; mean 41 months). By contrast, the mean survival of the patients who underwent chemotherapy, imatinibmesylate, surgery and radiotherapy were as follows: 7.1 months, 5.6 months, 36 days and 1 week respectively. The survival rates at 48 months of the patients who did and did not undergo auto/allogeneic HSCT are 76% vs 0%; $p = 0.0000$. The clinical behavior and response to therapy were not influenced by age, sex, anatomic site(s) involved, clinical presentation, previous clinical history, histology type, phenotype and cytogenetic findings. These data support the indication of bone marrow transplant as a consolidation therapy. We concluded this patient had a synchronous diagnosis of myeloid sarcoma and jaw tuberculosis.

REFERENCES

[1] S. A. Pileri, S. Ascani and M. C. Cox, "Myeloid Sarcoma: Clinico-Pathologic, Phenotypic and Cytogenetic Analysis of 92 Adult Patients," *Leukemia*, Vol. 21, 2007, pp. 340-350. doi:10.1038/sj.leu.2404491

[2] F. A. Silva, J. O. Matos, Q. M. F. C. de and M. Nucci, "Risk Factors for and Attributable Mortality from Tuberculosis in Patients with Hematologic Malignances," *Haematologica*, Vol. 90, No. 8, 2005, pp. 1110-1115.

[3] A. Klossek, C. Dannenberg, M. R. Feuerhahn and D. Körholz, "Pulmonary Tuberculosis in a Child Receiving Intensive Chemotherapy for Acute *Myeloblastic leukemia*," *Journal of Pediatric Hematology/Oncology*, Vol. 26, No. 1, 2004, pp. 64-67. doi:10.1097/00043426-200401000-00019

[4] I. K. Neonakis, M. G. Alexandrakis, Z. Gitti, G. Tsirakis, E. Krambovitis and D. A. Spandidos, "Miliary Tuberculosis with No Pulmonary Involvement in Myelodysplastic Syndromes: A Curable, yet Rarely Diagnosed, Disease: Case Report and Review of the Literature," *Annals of Clinical Microbiology and Antimicrobials*, Vol. 7, 2008, p. 8. doi:10.1186/1476-0711-7-8

[5] Y. C. Chen, J. M. Sheen, L. T. Huang, K. S. Wu and C. C. Hsiao, "Disseminated Tuberculous Myositis in a Child with Acute Myelogenous Leukemia," *Pediatrics & Neonatology*, Vol. 50, No. 2, 2009, pp. 74-77. doi:10.1016/S1875-9572(09)60037-1

[6] J. S. Ahn, D. H. Yang, Y. K. Kim, S. H. Cho, I. Y. Kim, J. J. Lee, I. J. Chung and H. J. Kim, "Multiple Intracranial Tuberculomas Mimicking Granulocytic Sarcomas in Acute Myeloid Leukemia," *Journal of Korean Medical Science*, Vol. 22, 2007, pp. S171-S173. doi:10.3346/jkms.2007.22.S.S171

[7] P. C. Jutte, R. Van Altena, E. Pras and C. J. Thijn, "Causes of Misdiagnosis and Mistreatment of Spinal Tuberculosis with Radiotherapy in Nonendemic Areas: A Pitfall in Diagnosis and Treatment: Hazards of Radiotherapy on the Tuberculous Lesion," *Spine*, Vol. 30, No. 11, 2005, pp. E 300-E304.

[8] M. Gesse, G. Mall, D. Fritze and M. Gartenschläger, "Granulocytic Sarcoma of the Tonsils Associated with Myelodysplastic Syndrome," *Deutsche Medizinische Wochenschrift*, Vol. 127, No. 50, 2002, pp. 2673-2676.

[9] S. H. Swerdlow, E. Campo, N. L. Harris, E. S. Jaffe, S. A. Pileri, H. Stein, J. Thiele and J. W. Vardiman, "WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues," 2008.

