ISSN: 2584-0355
DOI: doi.org/10.51219/MCCRJ/Dulce-Marta-Schimieguel/107

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Medical & Clinical Case Reports Journal

https://urfpublishers.com/journal/case-reports

Vol: 2 & Iss: 3

Case Report

Involvement of the Central Nervous System in Plasma Cell Leukemia: Case Report

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Citation: Schimieguel DM, Sousa RDS, Silva NDL, et al. Involvement of the Central Nervous System in Plasma Cell Leukemia: Case Report. *Medi Clin Case Rep J* 2024;2(3):397-399. DOI: doi.org/10.51219/MCCRJ/Dulce-Marta-Schimieguel/107

Received: 18 July, 2024; **Accepted:** 20 July, 2024; **Published:** 23 July, 2024

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ABSTRACT

Plasma cell leukemia (PCL) is a rare malignant hematologic disease with an aggressive and poor prognosis characterized by the uncontrolled proliferation of plasma cells in the bone marrow and peripheral blood. Some clinical and laboratory manifestations resemble multiple myeloma (MM), so the treatment of PCL is based on therapies similar to those for MM. We present a case of a 47-year-old male patient diagnosed primary plasma cell leukemia. The treatment was initiated with VDT-PACE, despite the occurrence of complications and relapses, the patient showed a good response to the proposed treatment, however after some symptoms, the involvement of the disease in the central nervous system was confirmed. Despite adequate monitoring and treatment, this type of complication in patients with neurological symptoms still requires further investigation to support therapeutic decisions.

Keywords: Plasma cell leukemia; Central nervous system

Introduction

Plasma cell leukemia (PCL) is a rare and highly aggressive hematological disease that is characterized by uncontrolled proliferation of plasma cells in the bone marrow and peripheral blood. PCL can be categorized as primary in most cases, or it can arise as a progression from pre-existing multiple myeloma (MM), designated as secondary plasma cell leukemia. Some clinical and laboratory manifestations resemble MM, such as genetic profile, proportion of cytogenetic abnormalities, appearance of tumor mass, impaired renal function, anemia, increased lactate dehydrogenase, and β2-microglobulin[1-3]. Worldwide, the annual incidence of PCL is around 0.04 cases per 100,000 individuals. Among patients with acute leukemia, the incidence of PCL reaches rates of approximately 0.9% and between 2-4% among patients with MM. According to the World Health Organization (WHO), among the plasma cell neoplasms, primary PCL represents 3-5% worldwide[2,4]. Recently, a significant increase in the number of cases of secondary PCL has been observed, which may be related to better survival of MM cases, as the longer the disease progresses, the greater the probability of developing PCL, for example, in the late and advanced stages of the initial disease[5,6]. PCL treatment has

been adapted from MM, and it is based on bortezomib-like therapies, such as VDT-PACE (bortezomib, dexamethasone, thalidomide, cisplatin, adriamycin, cyclophosphamide and etoposide), VDT (bortezomib, thalidomide and dexamethasone), VRD (bortezomib, lenalidomide and dexamethasone), VCD (bortezomib, cyclophosphamide and dexamethasone), VAD (bortezomib, doxorubicin and dexamethasone) or VMP (bortezomib, melphalan and prednisone)[6-8].

Case Report

A 47-year-old male patient was admitted at the Oncology Center Oswaldo Leite at the Emergency Hospital of Sergipe, on October 19th, 2021, presenting tachycardia, eupnea and evident bruises on the upper and lower limbs. Patient was also found to have palpable liver, weight loss of 10 kg in 2 months, bone pain, nausea, vomiting, fever and sweating. On admission, the blood count demonstrated a hemoglobin of 11.5 g/dL and leukocytosis of 98,000/uL. Additionally, peripheral blood and bone marrow smears revealed plasma cell morphology compatible with PCL, as seen in **(Figure 1)**.

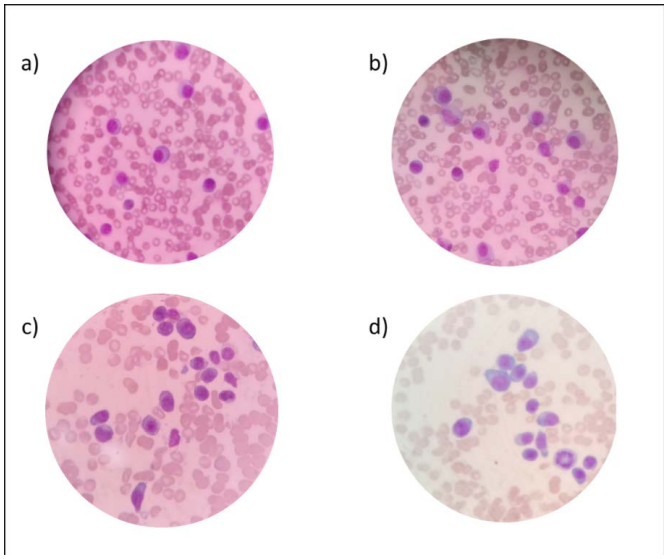

Figure 1: Morphological analyzes of peripheral blood (a, b, c) and bone marrow smears (d) of the patient showing malignant plasma cells. Photomicrograph of peripheral blood and bone marrow cells on slides stained with May-Grünwald-Giemsa. Common optical microscope. (100X magnification).

Immunophenotypic flow cytometrics studies revealed 78.1% of monoclonal plasma cells with CD45-/partial CD38/partial CD138/CD13+/CD28+/CD81+/partial CD117 phenotype, with Lambda light chain expression being observed in 89.3% of the plasma cells, as seen in **(Figure 2)**.

The patient underwent a bone screening, which revealed no evidence of lytic lesions, but cervical spine radiography showed signs of bone rarefaction. An echocardiogram was performed, indicating preserved systolic function in the right ventricle, mild diastolic dysfunction and increased left atrium volume. Serological tests for hepatitis B and C, HIV and VDRL were all negative.

The patient underwent the first of three cycles of the DV-PACE (dexamethasone, bortezomib, cisplatin, cyclophosphamide, doxorubicin and etoposide) on October 26th, 2021. Febrile neutropenia was corrected with cefepime and G-CSF. On March 16th, 2022, 2% of plasma cells were observed in the bone marrow, indicating complete remission. Two months later, a new bone marrow examination confirmed recurrence of the disease with the presence of 39% of plasma cells. Treatment was followed with three cycles of CED-TAL (cyclophosphamide, etoposide, dexamethasone and thalidomide), achieving complete remission again. In September 2022, the patient was referred to collect peripheral stem cells for autologous transplantation at the Real Hospital Português de Beneficência in Pernambuco state, Brazil.

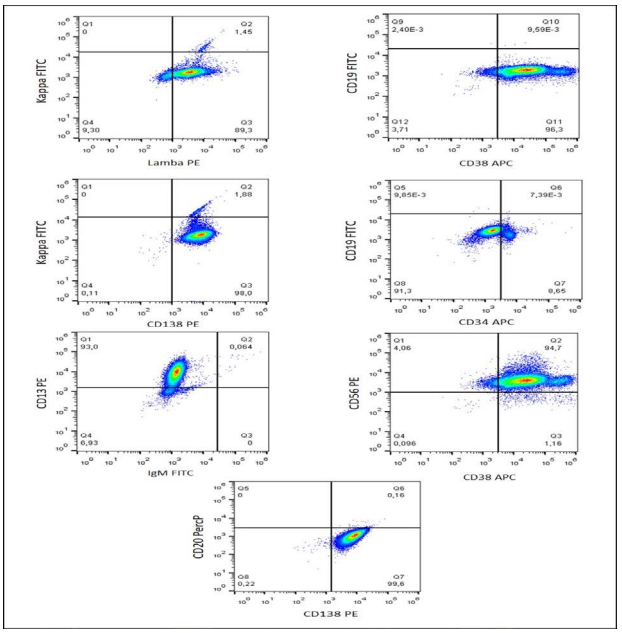

Figure 2: PCL with monoclonal plasma cells. Immunophenotyping by flow cytometry demonstrates plasma cells with CD45-/partial CD38/partial CD138/CD13+/CD28+/CD81+/partial CD117 phenotype and clonality observed through lambda chain positivity in 89.3% of plasma cells.

After the collection of the cells, a new recurrence of the disease was detected, with 18% of plasma cells in the peripheral blood and suspected infiltration in the central nervous system (CNS), manifesting through peripheral facial paralysis, deviation of the labial commissure to the right, and eyelid flaccidity. The patient's siblings were invited to be evaluated as donors for allogeneic bone marrow transplantation. On September 29th, 2022, the patient began treatment with cyclophosphamide 300 mg/m2 and dexamethasone 20 mg/IV for cytoreduction. On October 4th, 2022, CNS infiltration was confirmed, with cerebrospinal fluid (CSF) showing 426 atypical plasma cells. On October 6th, 2022, the patient underwent cycle 1 (28/28 days) of DRD treatment (daratumumab, lenalidomide and dexamethasone), followed by cycle 2 in November, cycle 3 in December, cycle 4 in January, with concomitant administration of cytarabine, dexamethasone and methotrexate, in four sessions of intrathecal chemotherapy. After 16 months of overall survival, the patient died in February 2023.

Discussion

The case described in this paper refers to primary plasma cell leukemia, a rare malignant hematologic disease with an aggressive and poor prognosis. Despite new treatments implemented in recent decades, there has still been no improvement in survival rates when compared to other plasma cell neoplasms, such as multiple myeloma[9,10]. In addition to the classic features of PCL diagnosis, patients commonly present anemia, leukocytosis and thrombocytopenia, as well specific morphology of plasma cells, with a high nucleus/cytoplasm ratio, basophilic cytoplasm, eccentric nucleus and cytoplasmic projections[8,11].

Similar to the case cited by Tuazon and collaborators (2021), the morphology of this case indicated similar conditions in the peripheral blood (78.1% of clonal plasma cells), emphasizing the need and importance of morphological evaluation of peripheral blood and bone marrow as the initial laboratory assessment approach[12]. In addition to the characteristic morphology, the immunophenotypic profile of B cell neoplasms definitely contributes to the characterization of the cell lineage and maturation stage, showing the expression of CD38 and CD138, and clonality of light chains, such as the lambda chain in this case.

PCL has a very poor prognosis, with an average overall survival of 4 months, and average rates of 28%, 14%, and 6% at four months, one year, two years and five years, respectively[9]. In this case, despite the occurrence of complications and relapses, the patient showed a good response to the proposed treatment, with an overall survival of 16 months. Regardless of the therapeutic advances, there is still no specific treatment protocol for PCL, and therapeutic protocols used in the treatment of MM have been adapted, with the aim of eradicating neoplastic plasma cells and reversing organ damage. In this case, the patient's treatment was initiated with 4 cycles of VDT-PACE due to the severe state of the disease, resulting in the patient's first complete remission. Subsequently, there was the first relapse of the disease, with 38% of plasma cells in the bone marrow, followed by a change to the CED-TAL protocol. Finally, after proving the involvement of the disease in the central nervous system, the patient began the DRD protocol with satisfactory initial prospects for a therapeutic response.

Conclusion

Although the literature describes few cases of CNS involvement in PCL, this case report demonstrated that, despite adequate monitoring and rapid modification of the treatment regimen, this type of complication in patients with neurological symptoms and rapid progression of the disease still requires further investigation to support therapeutic decisions. However, limited data to guide the treatment of relapsed or refractory PCL demonstrate the need for prospective multicenter clinical trials exploring more aggressive regimens. This may include chemotherapy combination, immunomodulatory drugs, proteasome inhibitors, and other novel compounds.

Acknowledgements: The authors would like to thank the professionals at the Hospital de Urgências de Sergipe, involved in this study.

Conflicts of Interests: This manuscript has not been published, is not being considered for publication elsewhere, and we have no conflicts of interest to disclose.

Funding: This study was supported by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior- Brasil (CAPES).

Ethical Approval: The Human Ethics Committee of the Federal University of Sergipe study approved protocol: 3.225.938.

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