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Megakaryoblastic Acute Myeloid Leukemia Associated with a Testicular Tumour in a Young Adult: a Case Report

Leucemia Mieloide Aguda Megacarioblástica Associada a Tumor de Testículo em Adulto Jovem: um Relato de Caso

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Abstract

Acute megakaryoblastic leukemia (M7 AML) is a rare subtype of acute myeloid leukemia in adults, the incidence of which is higher in children aged 1 to 3 years, especially in patients with Down Syndrome; and in the age group between 60 and 70 years old, with an adverse prognosis. We report the case of a 28-year-old male patient, with a history of non-seminoma germ cell tumour of the testis, diagnosed with M7 AML. Nine months after performing an orchiectomy to remove the testicular tumour, the patient developed dyspnea, dry cough and asthenia, associated with the presence of erythematous-purple lesions on the skin, ascites and pleural effusion. The myelogram demonstrated medullary hypocellularity, with the presence of 53% of blastic, pleomorphic and bulky cells, with positivity for the markers CD34, CD31 and CD117 in immature cells in immunohistochemistry. Despite undergoing cycles of chemotherapy with cisplatin and a BEP regimen (Bleomycin, Etoposide and Cisplatin), the patient presented with chest tomography with the presence of pulmonary nodules and magnetic resonance imaging of the skull and neuraxial with infiltration of the bone marrow in the spine and cranial vault, resulting in with neurological impairment and died. In view of the case presented, we observed agreement with previous reports of the adverse prognosis of M7 AML in young adults and we questioned its relationship with germ cell tumour.

Keywords: Leukemia. Hematology. Medical Oncology. Acute Megacarioblastic Leukemia.

Resumo

A leucemia megacarioblástica aguda (LMA M7) é um subtipo raro em adultos de leucemia mielóide aguda, cuja incidência é maior em crianças de 1 a 3 anos, especialmente em pacientes portadores de Síndrome de Down; e na faixa etária entre 60 e 70 anos, com um prognóstico adverso. Relatamos o caso de um paciente, do sexo masculino, 28 anos, com histórico de tumor germinativo não seminoma de testículo, diagnosticado com LMA M7. Nove meses após a realização de uma orquiectomia para a retirada do tumor testicular, o paciente apresentou quadro de dispneia, tosse seca e astenia, associado a presença de lesões eritemato-arroxeadas na pele, ascite e derrame pleural. O mielograma demonstrou hipocelularidade medular, com presença de 53% de células blásticas, pleomórficas e volumosas, com a positividade para os marcadores CD34, CD31 e CD117 em células imaturas na imunohistoquímica. Apesar da realização de ciclos de quimioterapia com cisplatina e esquema BEP (Bleomicina, Etoposídeo e Cisplatina), o paciente apresentou Tomografia de tórax com presença de nódulos pulmonares e ressonância magnética de crânio e neuroeixo com infiltração da medula óssea em coluna vertebral e calota craniana, intercorrendo com comprometimento neurológico e foi a óbito. Diante do caso apresentado observamos a concordância com relatos prévios do prognóstico adverso da LMA M7 em jovens adultos e indagamos a sua relação com o tumor de células germinativas.

Palavras-chave: *Leucemia. Hematologia. Oncologia. Leucemia Megacarioblástica Aguda.*

1 Introdução

Acute myeloid leukemias (AML) correspond to a heterogeneous group of hematologic malignancies characterized by a clonal proliferation of blast cells and the maturation arrest of hematopoietic cells with subsequent replacement of healthy bone tissue by neoplastic cells. They typically affect older age groups (average age of 65 years) and have a higher prevalence in males and the Caucasian population. Their incidence has varied between four and five cases per 100,000 inhabitants in the United States and Europe, depending on the population studied, and more than 20,000 new cases were estimated in the United States in 2023.[1,2] In Brazil, between 2009 and 2019, AML constituted the most prevalent bone marrow cancer with approximately 10,000 cases.[3,4]

Untreated AML leads to progressive hematopoietic failure, and the main symptoms at diagnosis are bleeding, petechiae, fever, asthenia, as well as secondary infections, due to an insufficient number of mature white cells.[4]

According to the French-American-British (FAB) classification, AMLs can be divided into eight subtypes: M0 or undifferentiated, M1 or with minimal maturation, M2 or with maturation, M3 or promyelocytic, M4 or myelomonocytic, M5 or monocytic, M6 or erythroid, and M7 or megakaryoblastic.

Acute megakaryoblastic leukemia (M7) is a rare subtype accounting for about 1 to 2% of AML cases, characterized by the presence of megakaryocytic antigens demonstrated by flow

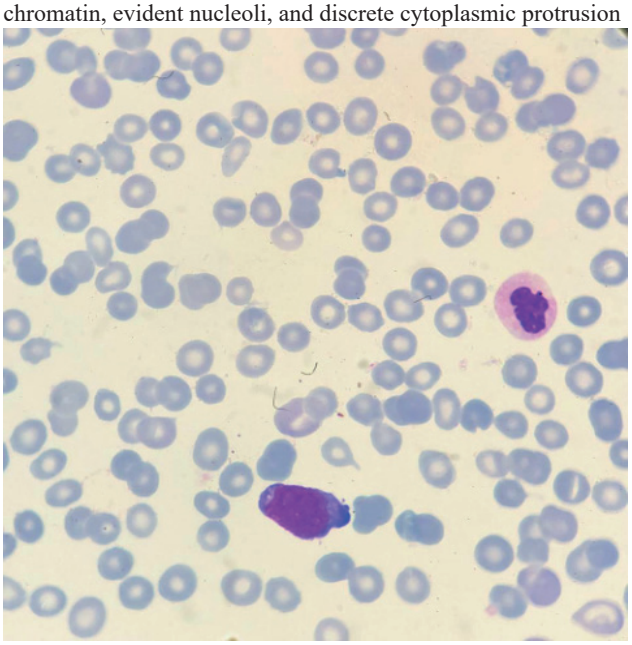
cytometry, immunohistochemistry, or the presence of platelet peroxidases.[5,6] Its prevalence, overall, is classified as bimodal, with the first peak in children aged 1 to 3 years, accounting for up to 10% of AML cases in the pediatric population, especially in patients with Down syndrome; and a second peak in the age range between 60 and 70 years with an adverse prognosis, being rare in adults and also having a bleak prognosis.[5-8] Due to the rare cases in adult individuals, we report here a case study of a 28-year-old patient diagnosed with AML of FAB type M7 associated with testicular carcinoma.

2 Case Report

The present study was approved by the ethics committee of the Hospital das Clínicas of the Federal University of Pernambuco under number 4579183.

Male patient, 28 years old, presented a history of non-seminomatous germ cell tumor of the testicle, consisting of 70% mature and immature teratoma, 20% yolk sac tumor, and 10% embryonal carcinoma, without invasion of adjacent structures. He underwent right orchiectomy in November 2021, with clear margins post-resection. Preoperatively, a total abdominal MRI was performed, showing a voluminous right testicular lesion measuring 11.2 x 9.4 x 7.8 cm, without signs of pelvic or retroperitoneal lymphadenopathy, associated with elevated levels of tumor markers alpha-fetoprotein (AFP = 1034 ng/mL), Beta-HCG (147 mIU/mL), and Ca 19.9 (69 U/mL). At the sixth month postoperatively, it was noted: LDH = 192 U/L; bHCG < 1.20 mIU/L; AFP = 2.03 ng/mL. However, nine months after the surgical procedure, the patient presented with exertional dyspnea, occasionally at rest, dry cough, and asthenia, without fever. On physical examination, the patient presented erythematous-purplish lesions on the skin, a distended, ascitic abdomen, painless, and bilateral pleural effusion evidenced by chest ultrasound. He was admitted to the oncology ward for diagnostic investigation. Furthermore, there were no alterations in the scrotal sac or contralateral testicle, with no palpable lymphadenopathy in the inguinal and crural chains. Laboratory tests revealed thrombocytopenia (12,000/mm^3), anemia with the presence of erythroblasts in peripheral blood, leukogram with left shift up to metamyelocyte, increased liver transaminases (AST = 417 U/L; ALT = 348 U/L), Urea = 115 mg/dL, and Ferritin = 2971 ng/mL. Review of peripheral blood smears showed the presence of immature mononuclear cells with delicate chromatin, evident nucleoli, and slight cytoplasmic protrusion (Figure 1).

Figure 1 - Presence of immature mononuclear cell with delicate chromatin, evident nucleoli, and discrete cytoplasmic protrusion



Source: the authors.

A bone marrow biopsy was performed to further investigate the cellularity of the bone marrow, which revealed marrow hypercellularity; erythroid sector: hypocellular (19%); granulocytic sector: hypocellular (21%), with 53% of pleomorphic and bulky blast cells; megakaryocytic sector: severe hypoplasia; lymphoplasmacytic sector: lymphocytes 7%, plasma cells <1%. The diagnostic hypothesis of acute leukemia was raised, with immunohistochemistry suggested for diagnostic complementation.

Meanwhile, while awaiting conclusive results from immunohistochemistry, the patient underwent two weekly cycles of isolated chemotherapy (CT) with Cisplatin (CDDP), without satisfactory medullary and clinical response. Therefore, the decision was made to initiate the BEP CT regimen (Bleomycin, Etoposide, and Cisplatin), and within 9 days, the patient progressed to severe leukopenia (Leukocytes = 320/mm3, Neutrophils = 48/mm3, Platelets = 17,000/mm^3). Prophylactic Levofloxacin and Filgrastim were immediately initiated, and a platelet concentrate transfusion (5 units) was requested, resulting in improvement of the laboratory parameters. During this period, a CT scan of the chest, abdomen, and pelvis revealed the presence of pulmonary nodules suspicious for secondary involvement, as well as right-sided pleural effusion, nearly complete atelectasis of the ipsilateral lower lobe, and the presence of a heterogeneous lytic lesion in the right iliac body measuring 1.1 x 0.5 cm not previously characterized. With the continuation of the BEP regimen and after approximately 30 days of hospitalization, the patient experienced an episode of candidiasis, unilateral crural paraparesis, paresthesias, and difficulty walking. Oral fluconazole was initiated, and an MRI of the skull and neuroaxis was performed, revealing signs of bone marrow infiltration throughout the spine and cranial vault with

extension to nerve roots and dural sac, without observable lesions in the brain parenchyma but with signs of brain volume reduction, which is unusual for the patient's age group. At the same time, the patient complained of disorientation, lack of appetite, and odynophagia, and the following day, due to a decrease in the level of consciousness, was admitted to the Intensive Care Unit (ICU), where he experienced dysglycemia without acidosis and required continuous intravenous insulin therapy, esophageal candidiasis, and delirium. Furthermore, cerebrospinal fluid did not show signs of infection or elevated protein levels. The electroencephalogram showed encephalopathy, defined by lower base rhythm involvement. Bone scintigraphy showed no abnormalities.

Despite the improvement in neurological symptoms and motor deficits, immunohistochemistry showed positivity for the markers CD34, CD31, and CD117 in predominantly intrasinusoidal immature cells, suggesting acute myeloid leukemia of the megakaryoblastic type. With the confirmed diagnosis, emergency chemotherapy with idarubicin was prescribed due to the severity of the case, and transfer to another specialized service, which had the medication available, was requested. Unfortunately, the patient passed away.

3 Discussion

We report the case of a 28-year-old male patient diagnosed with AML M7, which constitutes a rare subtype responsible for 1% to 2% of AML cases and predominates in the pediatric population, particularly individuals with Down syndrome, and in the elderly population aged 60 to 70 years. Thus, the patient in this case, a young adult, presented an unusual profile concerning the epidemiology of AML M7.[6-8]

No caso relatado, the patient underwent orchiectomy for the removal of a non-seminomatous germ cell tumor of the testicle and was subsequently diagnosed with AML M7. It is reported that patients with germ cell tumors suffer from hematologic malignancies (HM), including AML, with this association first discovered in 1985. Generally, germ cell tumors appear before HMs, as observed in the patient in the report; however, most cases associated with AML M7 are mediastinal.[9,10]

Nove meses after the surgical procedure, with clear margins post-resection and a decrease in tumor markers, the patient developed clinical, laboratory, and immunohistochemical features characteristic of acute leukemia. With the progression of the case, there was systemic deterioration of the patient, resulting in his demise. Thus, unfortunately, the bleak prognosis of AML M7 in adults was confirmed. A similar case was described in Japan with a 30-year-old male patient. However, the interval between the successful treatment of the germ cell testicular tumor and the development of AML was four years. Additionally, the approach to AML in this case involved chemotherapy and stem cell transplantation, with a positive response from the patient.[11]

4 Conclusion

In this regard, due to the rarity, scarcity of data, and adverse prognosis, we emphasize the need for the development and encouragement of further research to elucidate the natural history of AML M7 and its relationship with germ cell tumors, especially those of non-mediastinal origin.

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