

Objective: To describe a child with neutropenia and carrying inborn error of metabolism (IEM). **Results:** A 10 months-old boy, first child of non-consanguineous parents, presented severe neutropenia ($0.02 \times 10^9/L$) with fever, feeding problems, hypertonia and seizures. The frequency of fever and oscillating neutropenia is raised beyond use of antibiotics and granulocyte colony-stimulating factors. Some facial features present during physical examinations (hypertelorism, coarse face and skin dyspigmentation). He has failure to thrive and neuropsychomotor developmental delay. Viral diseases, organic acid in urine and mass spectrometry in tandem was normal. Abdominal ultrasound showed right hydronephrosis. Other image exams not detected alterations. The bone marrow aspirate analysis with karyotype resulted normal, with mild maturation arrest of granulocytic series. He did not have monocytosis or other hematologic disorders. Serum immunoglobulins were normal for the age group. Viral chronic diseases were negative, and she had no other autoimmune disorders. His mother had a first trimester spontaneous abortion, his father has no illnesses, and he has no siblings. A whole exome NGS sequencing showed compound heterozygous: one missense pathogenic CLPB variant (p. Arg408Gly) and other VUS c.1770+2T>A, splicing site. Hospitalizations is still frequent, and neutropenia did not remit to date. **Discussion:** This patient presents neutropenia and neurologic involvement, characteristics of caseinolytic peptidase B (CLPB) deficiency, which can range from severe to mild. In this reported case, a severe CLPB deficiency, death usually occurs at a few months of age due to neonatal neurologic involvement (hypotonia or hypertonia, respiratory insufficiency, swallowing problems, absence of voluntary movements, and epilepsy) and severe neutropenia associated with life-threatening infections. A multidisciplinary team is necessary, and no specific dietary or metabolic treatment is available. Hematopoietic stem cell transplant is not indicated in this case. Granulocyte-colony stimulating factor to increase neutrophil counts to reduce the frequency of infections should be used. Neutropenia associated with CLPB disease is present from birth and may be chronic or intermittent with absolute neutrophil counts ranging from severe (< 0.5 per mm^3) to mild (< 1.5 per mm^3). Elevated urinary excretion of 3-methylglutaconic acid (3-MGA) (typically 2x-10x higher than the reference range) has been observed in most of affected individuals to date. **Conclusion:** This case may be useful to understand the neutropenia in inborn error of metabolism and clinical signs and symptoms of the disease. The molecular evaluation is fundamental to elucidate diagnostic of neutropenia in newborns.

<https://doi.org/10.1016/j.htct.2022.09.136>

LINFOMA DE HODGKIN

O PAPEL DA IMUNOTERAPIA NO LINFOMA DE HODGKIN

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O linfoma de Hodgkin clássico é derivado de uma complexa e imunomediada transformação maligna de linfócitos B originando células neoplásicas conhecidas como Reed-Sternberg (RS). Este tipo de célula sofre ativação dos fatores de transcrição NFκB promovendo o desenvolvimento e sobrevivência celular. Devido à recombinação e hipermutação genética das células RS, observa-se no cromossomo 9p24.1 a super-expressão dos ligantes de morte celular programada PDL-1 e PDL-2. Esses ligantes limitam as respostas imunológicas mediadas por células T ao desencadear sua exaustão e perda progressiva de função. Dessa forma, as células tumorais que expressam ligantes PD-1 em sua superfície evitam uma resposta imune antitumoral eficaz. Atualmente de 20 a 30% dos pacientes com linfoma de Hodgkin clássico são refratários ou sofrem recaídas após tratamento envolvendo quimioterapia e ou radioterapia. A incorporação de novas terapias, incluindo inibidores de check point e conjugados de anticorpo-droga, no cenário da linha de frente, abordagens sequenciais e intensidades de tratamento individualizadas adicionais podem atender a essas necessidades. Por isso, essa pesquisa tem como objetivo reforçar a importância da incorporação de anticorpos monoclonais no tratamento do Linfoma de Hodgkin. Foram pesquisados nas plataformas de dados virtuais Scielo, PubMed e Google Acadêmico os artigos da literatura nacional e estrangeira e selecionados quinze de maior relevância sobre o tema. A quimioterapia de alta dose (HDCT) seguida por um transplante autólogo de células-tronco (ASCT) é o tratamento padrão para a maioria dos pacientes que apresentam recidiva após a terapia inicial. Para pacientes que falham HDCT com ASCT, brentuximabe vedotin, bloqueio PD-1, transplante alogênico não mieloablativo ou participação em um ensaio clínico poder ser considerados. Conclui-se que o bloqueio de PD-1 com pembrolizumabe tem demonstrado altas taxas de resposta e sem eventos adversos graves. Observa-se taxa de resposta objetiva em torno de 65% para os pacientes refratários ou recidivados pós-transplante medula óssea autóloga ou naqueles inelutáveis ao transplante.

<https://doi.org/10.1016/j.htct.2022.09.137>

TREATMENT OUTCOMES IN CLASSICAL HODGKIN LYMPHOMA (HL): 5-YEAR UPDATE REPORT FROM THE BRAZILIAN PROSPECTIVE REGISTRY

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Introduction: Data about HL in developing countries are scarce. In 2009, a HL prospective registry was launched in Brazil. **Methods:** The first analysis was presented with patients (pts) diagnosed from 2009 to 2014. Here we present an updated analysis with pts diagnosed until 2018 and a median follow-up of 5 years. **Results:** A total of 1357 pts with HIV negative classical HL were registered from January 2009 to December, 2018. 28 pts were excluded for various reasons, leaving 1329 pts for this analysis. Median age was 30 y/o (13-90). Females comprised 50%. The median time from onset of symptoms to diagnosis was 6 (0-60) months. 862 (65%) had advanced disease. Stage IVB was present in 28%, and a high-risk IPS score in 40%. Comparing pts included from 2009-2014 and 2015-2018, there was an increase in the use of PET for staging (11% vs 36%, $p < .0001$) and for end-of-treatment (40% vs 79%, $p < .0001$). ABVD was the first-line treatment in 94% of pts. 34 pts (2.6%) died during the first treatment. Radiotherapy (RT) was used in 72% of pts with limited, 59% with intermediate, and 28% with advanced disease. There was a reduction in the use of RT (44% vs 35%, $p = .002$) from 2009-2014 to 2015-2018. This reduction was higher in advanced disease (32% vs

24%, $p = 0.01$). The 5-year progression-free survival (PFS) and 5-year overall survival (OS) were 70% and 86%, respectively. The 5-year PFS in limited, intermediate, and advanced disease were 97%, 82%, and 62% ($p < .0001$), respectively. The 5-year OS for limited, intermediate and advanced disease were 100%, 94%, and 80% ($p < .0001$), respectively. The impact of socioeconomic status (SES) on outcomes was analyzed in pts treated with ABVD. The 5-year PFS in higher and lower SES were 75% and 60% ($p < .0001$). The 5-year OS in higher and lower SES were 90% and 77% ($p < 0.0001$). The fatality ratio during treatment was 5.0% and 1.1% for lower and higher SES ($p < 0.0001$). After adjustments for potential confounders, lower SES remained independently associated with poorer survival (HR 2.10 [1.52-2.90] for OS and HR 1.58 [1.26-1.99] for PFS). **Conclusions:** This analysis confirmed the predominance of advanced disease and high-risk profile pts. There was an increase in the use of PET and a reduction in RT in recent years. We confirmed that the outcomes are 10-15% lower in Brazil than reported in the literature. SES was an independent factor associated with shorter survival.

<https://doi.org/10.1016/j.htct.2022.09.138>

TREATMENT PATTERNS AND OUTCOMES FOR HODGKIN'S LYMPHOMA (HL) PATIENTS (PTS) AGED 60 AND OLDER: A REPORT FROM THE BRAZILIAN PROSPECTIVE HODGKIN'S LYMPHOMA REGISTRY

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