with what is available in the literature as a narrative review. **Methods:** We conducted a review of similar cases of MS published in the last 10 years by searching the PUBMED database. Our search identified 28 articles, 18 of which were included in this review. Results: (1) Case report: a 35-year-old male presented with lower abdominal pain associated with alternating episodes of diarrhea and constipation in January 2024. In April, he was hospitalized due to an intestinal obstruction, as the abdominal CT scan revealed a small intestine wall obstruction mass by the mesogastric region. He underwent emergency enterectomy with the resected material consistent with MS by immunohistochemistry (IHC): positive for MPO, CD71, CD34, c- KIT; negative for CD61. The patient was kept without any other intervention until his first consultation at our service in May 2024. His blood counts showed no alterations, and a bone marrow biopsy revealed no signs of infiltration. PET-CT demonstrated an area of abnormal uptake (SUV max of 7.3) in the pelvic region corresponding to a heterogeneous pre-sacral mass. He underwent a CT guided biopsy that confirmed the persistence of the MS. The patient started induction chemotherapy in May 2024 with daunorubicin and cytarabine (3+7), achieving a complete remission (CR) by the PET-CT performed in June 2024. The patient followed treatment with 4 cycles of consolidation with high dose cytarabine until October 2024 and additionally, he underwent RDT with 24 Gy in December 2024. A new PET-CT was performed in January 2025 still maintaining CR. (2) In our literature review, 18 cases of primary gastrointestinal MS were identified. The male-to-female ratio was 2:1, and the mean age was 45 years. The most affected site in the GI tract was the small intestine (50% of cases). IHC showed positivity for MPO, CD34, and CD117 in nearly all cases, along with high Ki-67 indices ranging from 30% to 95%. Most patients responded well to intensive chemotherapy regimens based on cytarabine and anthracyclines, with or without allo-SCT (only 3 paients underwent consolidation with all- SCT), whereas surgical treatment alone was insufficient for disease control. **Conclusion:** MS is a rare entity with a challenging diagnosis and no established standard of care. A transplant-free approach may be viable depending on patient-specific factors, with sustained complete responses achieved through chemotherapy and radiotherapy alone. Understanding the complex interplay of genetic, environmental, and immunological factors in the pathogenesis of isolated MS is essential to identifying effective treatment strategies and improving patient outcomes.

https://doi.org/10.1016/j.htct.2025.104558

ID - 959

INVESTIGAÇÃO TRANSLACIONAL DO TOLINAPANT (ASTX660) NA LEUCEMIA MIELOIDE AGUDA UTILIZANDO ABORDAGENS INTEGRADAS CLÍNICAS, BIOINFORMÁTICAS E FARMACOLÓGICAS

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Introdução: O tolinapant (ASTX660) é um antagonista das proteínas inibidoras da apoptose (IAPs) cIAP1 (BIRC2), cIAP2 (BIRC3) e XIAP. Essas IAPs atuam inibindo a atividade das caspases, suprimindo a apoptose. Recentemente, o tolinapant foi introduzido no tratamento de neoplasias hematológicas e demonstrou resultados promissores em modelos pré-clínicos de linfoma de células T (TCL), com efeitos imunomodulatórios benéficos confirmados em um pequeno grupo de pacientes com TCL. Na leucemia mieloide aguda (LMA), um estudo avaliando o tolinapant como agente único e em combinação com a cedazuridina (ASTX727) em pacientes com LMA recidivada/refratária foi encerrado precocemente (NCT04155580). **Objetivos:** Investigar a base farmacológica e molecular da atividade do tolinapant, bem como o papel de seus alvos, no contexto da LMA. **Material e métodos:** Investigamos os alvos do tolinapant (BIRC2, BIRC3, XIAP) quanto à expressão, impacto prognóstico e relevância funcional em LMA. Foram utilizados dados de pacientes da coorte TCGA (n = 121), dados ex vivo da coorte BeatAML (n = 570) e dados do DepMap com deleção de BIRC2, BIRC3 e XIAP em 25 linhagens celulares. Avaliamos a citotoxicidade do tolinapant (0–100 μM) em 14 linhagens de LMA por ensaio MTT. Testes combinatórios com venetoclax foram realizados em linhagens resistentes (Kasumi-1 e OCI-AML3), usando MTT (25 combinações), citometria de fluxo (Annexina V/PI) e Western blot (PARP1 clivado, γH2AX). Sobrevida foi analisada por Kaplan– Meier, e associações por testes estatísticos apropriados (ANOVA, Spearman, log-rank). Valores de IC50 foram obtidos por regressão não linear, e escores ZIP de sinergia foram gerados com SynergyFinder. **Resultados:** Alta expressão de BIRC2 (p = 0,04) foi associada à pior sobrevida global, enquanto BIRC3 e XIAP não mostraram essa associação. BIRC3 foi mais expresso em pacientes de risco intermediário. Citogeneticamente, BIRC2 esteve aumentado em del(5), t(9;11)+outros e del(7q); BIRC3 em del(7q)+outros e del(5q)+outros; XIAP foi reduzido em del(5). Em análises ex vivo, BIRC2 associou-se com resistência a 20 agentes, BIRC3 a 28 (e sensibilidade a 7), e XIAP a 12 (e sensibilidade a 20), todos com $p < 0,05$. No DepMap, observou-se dependência moderada de BIRC2 (−0,334) e mínima para BIRC3 e XIAP. O tolinapant isolado apresentou citotoxicidade modesta (IC50 mensurável em 5/14 linhagens; faixa: 29,8–77,2 μM; eficácia de 13,6% a 99,9%). Combinações com venetoclax mostraram sinergia em Kasumi-1 (ZIP = 13,8) e efeito aditivo em OCI-AML3 (ZIP = 8,4), com aumento de apoptose ($p < 0,05$). Análises moleculares revelaram maior clivagem de PARP1 e acúmulo de γH2AX com a combinação. **Discussão e conclusão:** Nosso estudo revela que a alta expressão de BIRC2 está associada a pior prognóstico e resistência a múltiplos agentes em LMA, sugerindo seu potencial como biomarcador e alvo terapêutico. Embora o tolinapant tenha eficácia

limitada como agente único, sua combinação com venetoclax apresentou efeitos sinérgicos ou aditivos em modelos resistentes. Esses achados sustentam o potencial de terapias combinadas baseadas em tolinapant em subgrupos específicos de LMA. **Financiamento:** FAPESP, CAPES e CNPq.

https://doi.org/10.1016/j.htct.2025.104559

ID - 3278

ISOLATED SPHENOIDAL HISTOPLASMOSIS IN A NEUTROPENIC PATIENT WITH ACUTE MYELOID LEUKEMIA: A DIAGNOSTIC AND THERAPEUTIC CHALLENGE

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Introduction: Invasive fungal infections (IFIs) are a major cause of morbidity and mortality in patients undergoing intensive chemotherapy for acute myeloid leukemia (AML). Histoplasma capsulatum, a dimorphic fungus, usually causes pulmonary disease after inhalation. Isolated sphenoidal involvement without pulmonary manifestations is exceedingly rare and diagnostically challenging. We report a case of sphenoidal histoplasmosis presenting as invasive fungal sinusitis during AML induction in a neutropenic patient. **Case report:** A 37-year-old woman was diagnosed with acute myeloid leukemia with monocytic differentiation (AML-M5) and started induction chemotherapy with the 7+3 regimen (cytarabine and daunorubicin) in April 2023. During medullary aplasia, she developed febrile neutropenia, managed with broad-spectrum antibiotics and amphotericin B due to high suspicion of invasive aspergillosis, with further clinical and radiologic improvement. Later during hospitalization, she developed a new febrile episode of unknown origin, along with progressive frontal headache, facial edema, and purulent rhinorrhea. Paranasal sinus CT revealed pansinusitis and sphenoidal bone erosion, suggestive of fungal sinusitis. Endoscopic sphenoidal biopsy was performed without complications. Histopathology revealed numerous intracellular yeast-like organisms staining positively with PAS and Grocott-Gomori methenamine silver, consistent with Histoplasma spp. No necrosis, granulomas, or leukemic infiltration were seen. Fungal cultures were negative. A diagnosis of localized sphenoidal histoplasmosis was established, and oral itraconazole was initiated, with progressive clinical improvement. The patient remained under close infectious surveillance, with full resolution of symptoms. She later received reinduction chemotherapy with the MITO-FLAG protocol (mitoxantrone, fludarabine, high-dose cytarabine) without recurrence of fungal disease. She ultimately progressed to refractory leukemia and died of multiorgan failure, unrelated to the resolved infection. **Conclusion:** Localized histoplasmosis of the paranasal sinuses is exceptionally rare, particularly in immunocompromised patients with hematologic malignancies. Sphenoidal involvement with bone erosion typically raises suspicion for Aspergillus spp. or Mucorales, more common causes of invasive fungal sinusitis. In contrast, H. capsulatum rarely causes isolated sinonasal disease, and sphenoidal presentation without lung involvement (as in this case) is highly atypical. Diagnosis is challenging due to nonspecific symptoms, overlapping radiologic features, and frequent negative cultures. Histopathology with fungal-specific stains was essential for definitive diagnosis in this case. This report underscores the need for clinical vigilance regarding uncommon fungal presentations in AML, especially when empiric antifungal therapy fails. Although fungal culture is the standard reference, tissue histopathology may be the only reliable diagnostic method in localized histoplasmosis. Therefore, isolated sphenoidal histoplasmosis, though rare, should be considered in neutropenic patients with refractory sinonasal symptoms, particularly in endemic areas. Given the low sensitivity of cultures and nonspecific imaging, histopathologic confirmation remains critical. This case highlights the diagnostic value of early endoscopic evaluation and broad differential consideration in immunosuppressed hosts.

https://doi.org/10.1016/j.htct.2025.104560

ID - 3225

LEISHMANIOSE VISCERAL EM PACIENTE COM LEUCEMIA AGUDA DE FENÓTIPO MISTO: RELATO DE CASO

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Introdução: A Leishmaniose visceral é doença potencialmente fatal com prevalência no norte e nordeste do Brasil com transmissão causada pela picada de flebotomíneos, enquanto que a Leucemia aguda de fenótipo misto é um subtipo raro de leucemia aguda com coexistência de marcadores celulares mieloides e linfoides, de causa não muito bem esclarecida, mas que envolve fatores genéticos e ambientais. Esta última é subdividida em bifenotípica, quando uma mesma população de blastos expressa marcadores de mais de uma linhagem, e em bilinear, quando dois grupos de blastos preenchem os critérios de diferentes linhagens. A ocorrência das duas doenças é rara e este caso clínico serve de alerta para o diagnóstico diferencial em áreas endêmicas desta associação, uma vez que a leishmaniose também apresenta alterações hematológicas importantes. **Descrição do caso:** Mulher, 68a, leucemia aguda bilinear diagnosticada em maio de 2024 (mielograma 75% de blastos mieloides),