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Introdução: A doença de Castleman (DC) é uma síndrome linfoproliferativa rara, com duas apresentações: unicêntrica e multicêntrica. A unicêntrica é benigna, geralmente assintomática, enquanto a multicêntrica está associada à infecção por herpesvírus humano 8 (HHV-8) em pacientes infectados pelo vírus da imunodeficiência humana (HIV), apresentando múltiplas linfadenopatias, hepatoesplenomegalia, sintomas B (febre, perda de peso ponderal e sudorese noturna), citopenias e falência de órgãos devido a excessiva atividade pró-inflamatória. Trata-se de uma doença cujo diagnóstico requer investigação por exames invasivos, sendo essencial relatar sua história clínica, alterações nos exames complementares e desfecho para melhor compreendê-la. **Apresentação do caso:** Paciente masculino, 45 anos, HIV positivo, em uso regular de tenofovir, lamivudina e dolutegravir, com carga viral indetectável, e diabetes mellitus de difícil controle, com uso de metformina e gliclazida. Apresentava queixa de febre vespertina intermitente, associada à sudorese há 4 meses, mais aparecimento de linfadenomegalias, sensação de enrijecimento abdominal e perda de 20 quilogramas. Evoluiu com fadiga, palidez e dispneia aos pequenos esforços. Foi atendido na emergência, com diagnóstico de anemia grave, com hemoglobina (Hb) de 4 g/dL, prescrita transfusão de concentrado de hemácias e transferido para hospital terciário para investigação. No exame físico apresentava linfonodos palpáveis em cadeias cervicais bilaterais, occipital, submandibular, e axilares, com consistência fibroelástica, sem sinais flogísticos, móveis e indolores. Hepatimetria de 18 cm, baço palpável à 5 cm do rebordo costal esquerdo e espaço de Traube maciço à percussão. Foram realizados exames laboratoriais, que apresentaram Hb 5,6 g/dL, 4500 leucócitos/mm^3, 45.000/mm^3 plaquetas, lactato desidrogenase (LDH) 799 U/L, e velocidade de hemossedimentação 150 mm/h, eletroforese de proteínas sérica sem pico monoclonal. A tomografia computadorizada (TC) de tórax e de abdômen total mostrou múltiplas linfonodomegalias acometendo diversas cadeias, hepatoesplenomegalia e múltiplas linfonodomegalias retroperitoneais, na raiz do mesentério, nas cadeias ilíacas e inguinais; com linfonodomegalias hipermetabólicas supra e infra diafragmáticas, e acometimento esplênico na tomografia por emissão de pósitrons (PET/TC) sugerindo doença linfoproliferativa. Foi submetido a duas biópsias, uma de linfonodo axilar direito e uma de medula óssea, com estudo imunohistoquímico (IHQ) inconclusivo. Nova biópsia de biópsia de linfonodo axilar direito mostrou IHQ com CD21, CD34 e HHV8 positivos e CD138 positivo em plasmócitos, compatível com DC multicêntrica, e biópsia excisional de linfonodo cervical direito, com IHQ com anticorpos κ e λ policlonais positivos, indicando DC forma mista hialino-vascular e de células plasmáticas. Realizou tratamento com rituximab e prednisona, obtendo resposta metabólica completa, evidenciado por PET/TC negativa. **Conclusão:** A DC multicêntrica é uma síndrome linfoproliferativa rara. Este caso destaca a importância de compreender a doença, para um diagnóstico e tratamento precoce, com melhor prognóstico para o paciente.

https://doi.org/10.1016/j.htct.2023.09.374

RAPID REDUCTION OF LYMPH NODE ENLARGEMENT IN A PATIENT WITH CHRONIC LYMPHOCYTIC LEUKEMIA TREATED WITH IBRUTINIB

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Introduction: Chronic lymphocytic leukemia (CLL) is the most prevalent leukemia in adults, with an estimated 18,740 new cases in 2023 in the United States and about 40,000 deaths worldwide per year. **Case report:** A 57-year-old woman diagnosed with CLL in 2020, Binet A, presented cervical lymphadenopathy without cytopenias. Referred to HSPE in July 2023 due to night sweats, weight loss, and progressive lymph node enlargement. Physical examination revealed a conglomerate in bilateral cervical region, occipital, retro and preauricular lymphadenopathy, submandibular, and supraclavicular lymph nodes. Complete blood count: Hemoglobin 8.8 g/dL, leukocytes 130,000/mm^3 (lymphocytes 127,850/mm^3) and platelets 77,000/mm^3. Peripheral blood immunophenotyping: CD5, CD19, CD20, CD23, and CD200 positivity; FISH revealed chromosome 13 deletion, unmutated IGHV and TP53. Hospitalized because of the risk of upper airway obstruction due to lymph nodes enlargement near to the rhino and oropharynx and to initiate ibrutinib therapy. The patient achieved rapid response, with significant lymphadenopathy reduction within 6 days of treatment and complete symptoms improvement. As an expected effect, lymphocytosis of 230,000/mm^3 was observed. **Discussion:** Regarding treatment, which until recently was limited to immunochemotherapy, there has been a significant change in the course of the disease since the introduction of oral Bruton's tyrosine kinase (BTK) inhibitors, offering greater safety, efficacy, and improved survival. Ibrutinib, a BTK inhibitor developed in 2009, has become a cornerstone of treatment for high-risk patients and is often recommended as a first-line therapy. BTK molecules regulate the migration and motility of B lymphocytes, and their inhibition results in impaired signaling through BCR, CXCR4, and integrins (responsible for pathway activation, cell growth, and reduced cell death). Inhibition of CXCR4 and integrins leads to loss of cellular adhesion to stromal cells and the extracellular matrix, causing in situ cell death (anoikis), resulting in a process called "redistribution lymphocytosis", in which a fraction of these cells migrates from lymphoid to bloodstream. Overall response rates typically exceed 80% in first-line therapy for naive-patients. Clinical evolution after starting Ibrutinib showed rapid reduction of lymph node mass in the initial days of medication use. A study demonstrated that lymph node burden significantly decreases after three cycles, with approximately 50% reduction in mass (this report showed significant reduction after 6 days). The choice of BTK inhibitor should be individualized, taking into account medication availability and patient comorbidities. Ibrutinib is generally not myelosuppressive; however, some adverse effects may be observed, such as tumor lysis syndrome,

cardiotoxicity, and opportunistic infections. **Conclusion:** BTK inhibitors are one of the options for CLL treatment; however, therapy choice should be individualized. Furthermore, potential long-term adverse effects of this drug require monitoring. In future, new combinations of BTK inhibitors with other targeted drugs may expand its role and reduce drug resistance.

https://doi.org/10.1016/j.htct.2023.09.375

CHYLOTHORAX AS A MANIFESTATION OF CHRONIC LYMPHOPROLIFERATIVE DISORDER (LPD)

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Objective: To report the case of a patient diagnosed with Chylothorax secondary to LPD. **Methodology:** Assessment of patient's information kept on HSPE computer-based patient records. Case report: 67-year-old-male with lymphocytosis in peripheral blood in Mar/2016. Complete blood counts:Hb 8.8 g/dL, WBC 38,850/mm^3, 92% of lymphocytes (Ly) and no other signs of active disease. Bone marrow flow Cytometry (FC) with 77% of anomalous B Ly (BLy) positive for CD19, CD20, CD22, CD38, CD200, FMC7, IgM and Lambda free light chain (FLC); negative for CD5, CD10, CD11c, CD28, CD103 and Kappa FLC. Matutes score 0. He was diagnosed with LPD and followed up closely. Six months later, he progressed with a history of low-grade fever, weight loss and nocturnal drenching sweats. He was started on Rituximab for 4 cycles in April/2017, followed by 12 cycles (maintenance), achieving disease control. In Feb/22, he got COVID-19 and presented with persistent respiratory symptoms, including dyspnea and dry cough. Thoracic CT scan revealed large right pleural effusion with no thrombosis. Analysis of pleural effusion showed a chylothorax pattern. Abdominal CT scan showed some lymph nodes enlargement (max. 2.3cm). He underwent thoracic drainage due to persistent dyspnea and low oxygen saturation. Pleural fluids built up quickly after drainage. He was submitted to lymphography and embolization of thoracic duct, building up pleural effusion once again a couple of days later. At that time, we considered he had active LPD after pleural effusion FC showed mature BLy positive for CD19, CD20, lambda FLC, CD79b, CD200, CD23, FMC7 and negative for CD5, CD10, CD11c. He was treated with Rituximab, Cyclophosphamide, Vincristine and Prednisone (R-CVP), after which he had complete resolution of the effusion and has been followed up regularly. Discussion: Chylothorax is a rare condition caused by the leak of chyle into the pleural cavity. Malignancies are the most common non-traumatic causes of chylothorax, as a result of infiltration of lymphomatous cells or compression by enlarged lymph nodes. It is defined by pleural fluid triglyceride levels >110 mg/dL, presence of chylomicrons, and low cholesterol level. Fifty percent of cases are due to traumas/surgeries while 39% are due to malignancies. Sarcoidosis and Tuberculosis are also possible causes. Lymphatic anomalies may be involved. As stated by Satriano et al. there are few reports on chylothorax related to COVID19 infection, along with thrombotic events. SARSCoV2 infection can cause cytokine storms with consequent hyperinflammation and arterial and venous vasculopathy associated with a prothrombotic state. Our patient didn't have any thrombotic event. Currently, there is no general standard therapy for such cases, so the correct approach (drainage, surgeries, drugs/chemotherapy) should be taken in regards to the causative injury. **Conclusion:** this case illustrates well how diverse LPD's manifestations can be. LPD needs to be considered every time a non-traumatic chylothorax appears, especially when there is already a history of malignancies, even though it's a rare condition. Despite his previous COVID-19 diagnosis, our patient didn't present any clear vascular injury which made us find it hard to explain his pleural effusion as secondary to that infection. After having been treated with R-CVP, he's still in disease remission up to this point.

https://doi.org/10.1016/j.htct.2023.09.376

PACIENTES COM LEUCEMIA LINFOCÍTICA CRÔNICA EXPOSTOS À COVID-19, EM USO DE RITUXIMAB E INIBIDORES DE TIROSINA QUINASE DE BRUTON

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Esta revisão apresenta uma visão geral de como a COVID-19 influencia o prognóstico de pacientes com leucemia linfocítica crônica (LLC) tratados com rituximab ou inibidores da tirosina quinase de Bruton (BTKi), com ou sem quimioterapia. A seleção do material foi baseada em estudos previos que examinaram as taxas de morbidade e mortalidade associadas à infecção por SARS-CoV-2 em pacientes com LLC submetidos a esses tratamentos. O objetivo deste texto é mostrar como a pandemia do COVID-19 afetou a evolução dos pacientes com LLC, os quais utilizam BTKi ou Rituximab. Sua metodologia empregou as bases de dados do PubMed e da Cochrane Library, com seleção criteriosa e estratégia de busca que abrangeu de forma adequada todos os artigos relevantes, em relação ao tema. As palavras chaves e estratégia utilizada são: ("Chronic lymphocytic leukemia" OR CLL) AND (SARS-CoV-2 OR COVID-19) AND (Rituximab OR Treatment OR "Anti-CD20 blocker" OR "BTK inhibitor"). Com os dados mais pertinentes dos estudos obtidos, foram montados os resultados e a discussão, assim reforçando a tese abaixo. Os indivíduos com LLC que usam rituximab apresentam um prognóstico pior por possuírem maior probabilidade de desenvolver uma forma mais grave da COVID-19. Por outro lado, os BTKi demonstraram apresentar uma possível redução na morbidade dos mesmos. Portanto, é necessário uma análise criteriosa na prescrição desses medicamentos aos pacientes com LLC.

https://doi.org/10.1016/j.htct.2023.09.377