Successful desensitization to Rituximab in a case of Intravascular Large B-cell Lymphoma (IVLBCL) with severe cytokine release syndrome.

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Abstract:

Intravascular large B-cell lymphoma (IVLBCL) is a form of Non-Hodgkin lymphoma, and is a rare, aggressive subtype of diffuse large B-cell lymphoma. Treatment with rituximab, cyclophosphamide, vincristine, doxorubicin, and prednisone (R-CHOP) chemotherapy is used as a first-line therapy to improve patient prognosis and survival, but, adverse reactions to rituximab, especially during the first-dose is quite common in patients with high tumor burden.

We present the case of a 72-year-old female with IVLBCL, which was confirmed by skin biopsy for histopathological examination (HPE) and immunohistochemistry demonstrating CD45, CD20, and MUM1 expression in the tumor cells, who developed a severe reaction to rituximab, in the form of hypotension and desaturation, graded as common terminology criteria for adverse events (CTCAE) grade 3/5. Her vital signs at the time of reaction revealed BP-72/38 mmHg, which was treated with IV albumin, IV fluid bolus of 1L of normal saline (NS), and oral midodrine, which improved her BP to 104/50mmHg and desaturation to 88% SpO2 on room air, which required 3L via nasal cannula for improving her oxygen saturation to 95% SpO2, which was her baseline.

Laboratory investigations, showed acute drop in her albumin levels to 1.9g from 3.3g, drop in her hemoglobin/hematocrit to 6.6/21 from 9.1/28, and imaging showed new areas of patchy opacity on the right mid-zone of the lung and bilateral pleural effusions on the X-ray AP view, consistent with new-onset hydrostatic edema in the patient, both the lab and imaging findings were thought to be related to the cytokine release syndrome (CRS) associated with rituximab use.

Further rituximab administration in cycle 1 of chemotherapy was suspended for the patient, with an aim to desensitize the patient to rituximab in the 2nd cycle of the R-CHOP chemotherapy after 21 days. Successful desensitization was carried out in the second cycle of chemotherapy by using the 12-step, 3-bag protocol, originally devised by Brigham and Women's Hospital (BWH), along with pre-medications with acetaminophen, cetirizine, ondansetron, montelukast, and zileuton. The patient tolerated the desensitization to rituximab, and the 2nd cycle of chemotherapy, with no breakthrough reactions, or adverse events.

This case underscores the importance of watching out for severe infusion reactions, especially with rituximab, in patients with IVLBCL, who are thought to have a high tumor burden, especially within the capillaries. Previous case reports have highlighted that shifting the rituximab administration to day 2 of the chemotherapy cycle may mitigate this serious adverse event, especially in high-risk patients. Since rituximab is the cornerstone in management of IVLBCL, desensitization should be attempted in every case, and it has a high success rate of 98.5-100% across various studies. Further research is needed into developing preventive strategies for predicting and managing the infusion reactions.