Breaking the storm: Effective Rituximab Desensitization for severe cytokine release syndrome in Intravascular Large B-cell Lymphoma (IVLBCL)

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A. CONTEXT

1.Intravascular large B-cell lymphoma (IVLBCL):

- Aggressive and rare subtype of diffuse large B-cell lymphoma.
- Characterized by the proliferation of malignant B-cells within blood vessel lumina.

B. BACKGROUND

- Rituximab-based immunochemotherapy (R-CHOP) is the standard first-line treatment for IVLBCL.
- Patients with high tumor burden are at increased risk of severe cytokine release syndrome (CRS) during the first rituximab infusion.
- CRS manifests as hypotension, hypoxia, and systemic inflammation, potentially leading to treatment discontinuation.
- Desensitization protocols offer a strategy to safely reintroduce rituximab in such cases.

C. CASE PRESENTATION

1. Patient Presentation:

- 73-year-old female, 50 pack-year smoking history.
- **Symptoms**: Painful bilateral lower limb swelling (1 month), 10-pound weight loss, nighttime fevers, nausea, new thigh rash.
- **Exam:** Bilateral non-pitting edema (hips), waxy plaques, telangiectasias, peau d'orange appearance. [Figure 1]

2. Workup :

- **Initial Labs:** Normocytic normochromic anemia (Hb 10 g/dL), normal renal/liver function, ESR.
- **Skin biopsy:** Confirmed intravascular large B-cell lymphoma (IVLBCL). [Figure 2]
- **CT abdomen/pelvis:** Hepatosplenomegaly.
- **Further labs:** Elevated LDH (649 U/L), uric acid (9.4 mg/dL), ferritin (504 ng/mL), triglycerides (244 mg/dL).

3. Treatment & Complications:

- Started R-CHOP chemotherapy.
- **Severe reaction to rituximab:** Hypotension (72/38 mmHg), desaturation(SpO2 88%), CTCAE grade 3/5. (2)
- **Labs:** Hypoalbuminemia (1.9 g/dL), worsening anemia (Hb 6.6 g/dL).
- **Chest X-ray:** Bilateral pleural effusions.
- Managed with IV albumin, IV fluids, midodrine, and oxygen.

4. Outcome:

- Rituximab discontinued, desensitization (Brigham and Women's Hospital protocol) in 2nd cycle. [Table 1]
- Tolerated desensitization without adverse events.

Figure 1– Clinical Photography of skin lesions



Figure 2– Histopathology and IHC of the skin lesions

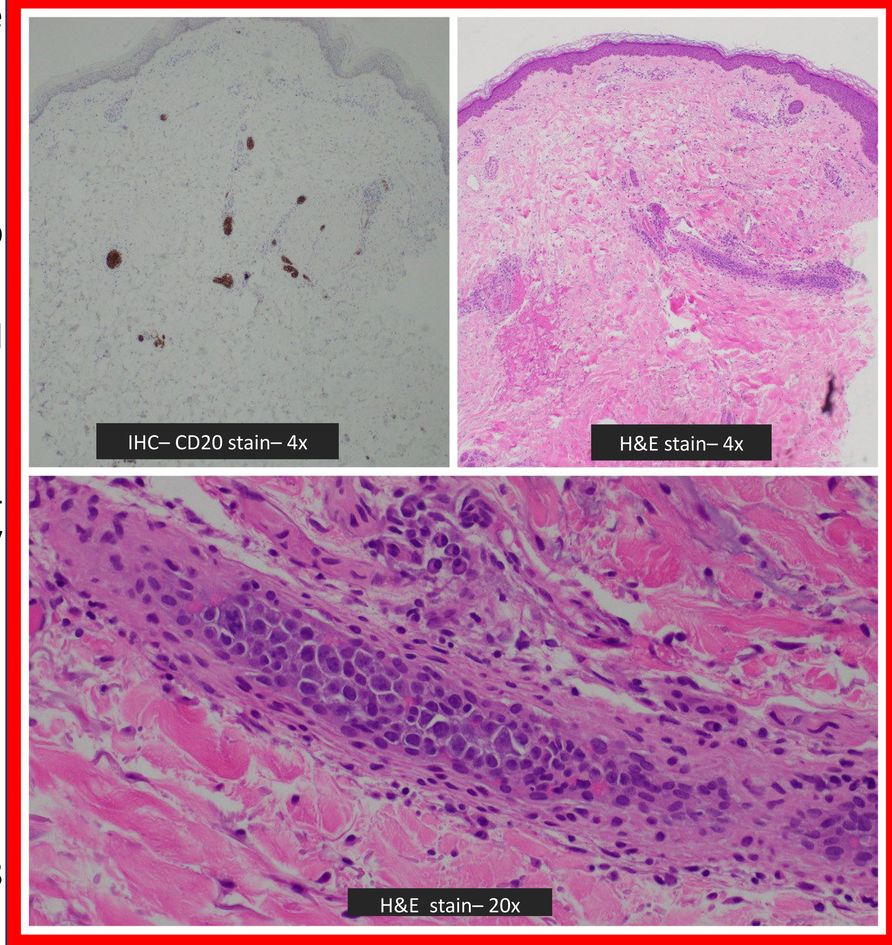


Figure 3– Timeline of the Patient

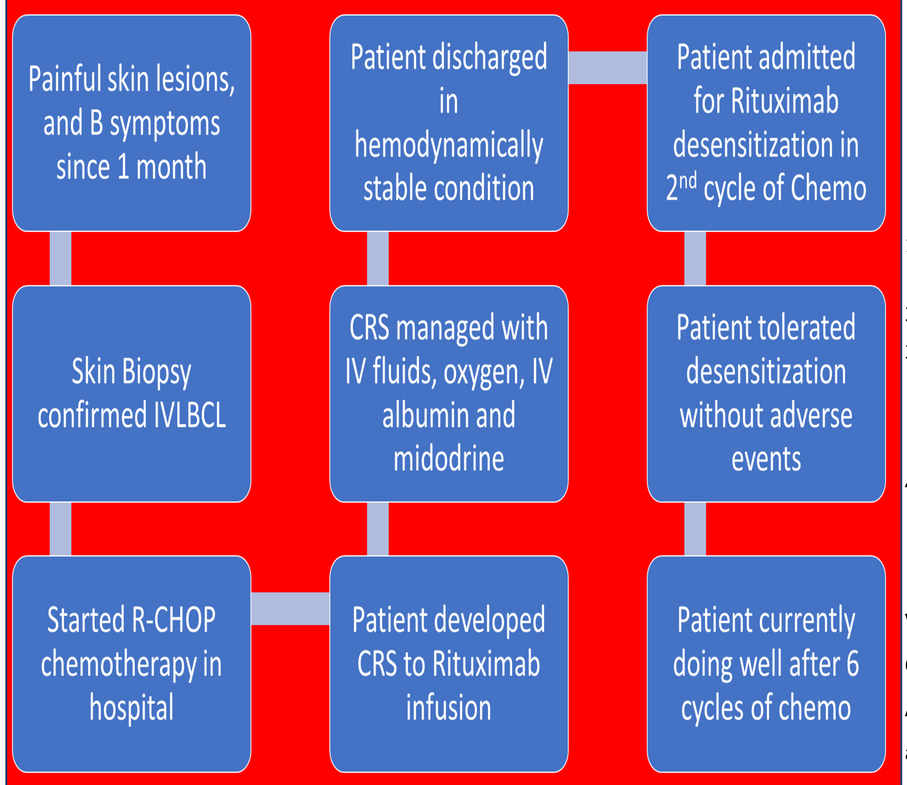


Table 1 -Rituximab infusion steps

Rituximab containing solution	Infusion titration step	Rate, (in mL/hr)	Infusion time, (in min)	Dose administered in this step (in mg)	Cumulative dose (in mg)
Solution 1 (10mg in 250mL NS)	1	2	15	0.02	0.02
	2	5	15	0.05	0.07
	3	10	15	0.1	0.17
	4	20	15	0.2	0.37
Solution 2 (90 mg in 250 mL NS)	5	5	15	0.45	0.82
	6	10	15	0.9	1.72
	7	20	15	1.8	3.52
	8	40	15	3.6	7.12
Solution 3 (600 mg in 250 mL NS)	9	10	15	6	13.12
	10	20	15	12	25.12
	11	40	15	24	49.12
	12	80	15	48	97.12

D. DISCUSSION

- Case underscores importance of monitoring for severe infusion reactions, especially with rituximab, in patients with IVLBCL who have a high tumor burden within the capillaries.
- Previous case reports highlighted shifting the rituximab administration to day 2 of the chemotherapy cycle may mitigate this serious adverse event in high-risk patients(3).
- Since rituximab is the cornerstone in the management of IVLBCL, desensitization should be attempted in every case, which, has a high success rate of 98.5-100% across various studies(1,4).

E. CONCLUSION

- Rituximab remains critical in IVLBCL treatment. Proactive desensitization can salvage therapy in CRS cases, improving outcomes.
- Future research should focus on predictive biomarkers and optimized premedication regimens to enhance safety in high-risk populations.

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