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Dose Adjusted Epoch - Rituximab Used in Primary Mediastinal B Cell Lymphoma Associated Superior Vena Cava Syndrome with the Right IJV Thrombosis - A Case Report

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Abstract

Primary mediastinal large B-cell lymphoma (PMLBCL) is a unique type of B-cell lymphoma probably arising from a putative thymic medulla B-cell. PMLBCL is characterized by a locally invasive anterior mediastinal mass, often producing cough, chest pain, dyspnea, and superior vena cava syndrome. We present with a 17-year-old boy with primary mediastinal B cell lymphoma associated with superior vena cava syndrome and right IJV thrombosis. DA-EPOCH- R regimen [etoposide phosphate, prednisone, vincristine sulfate (Oncovin), cyclophosphamide, doxorubicin hydrochloride (hydroxydaunorubicin), and rituximab] were used over 6 cycles.

Keywords

Primary Mediastinal B Cell Lymphoma, Superior Vena Cava Syndrome, Da-Epoch-R

Introduction

Primary mediastinal large B-cell lymphoma (PMBCL) represents approximately 2% to 4% of all non-Hodgkin lymphomas and 6–10% of all diffuse large B cell lymphoma (DLBCL), occurring more often in young females. PMBCL is considered as a fully identified disease entity in the World Health Organization (WHO) classification of lymphoid neoplasms. Previously, in the revised European-American classification of lymphoid neoplasms, PMBCL was considered a subtype of diffuse large B-

cell lymphoma (DLBCL), arising in the mediastinum. WHO classification listed PMBCL as a separate entity in 2001.[1] Most PMBCL patients have stage I–II, bulky disease, with pleural or pericardialeffusions in a third of cases. With the progression of the lymphoma, infiltration of surrounding thoracic regions leads to compression of the airways and blood vessels may occur, resulting in superior vena cava syndrome.[2] The diagnosis of this syndrome is made on the clinical signs and symptoms such as dyspnea, hoarseness, headache, chest pain, and dysphagia. On physical examination, it was noted that many patients presented with facial swelling, upper limb edema, venous distention in the neck and on the chest wall. Systemic symptoms such as fever and weight loss are observed in <20% of cases. Also, increased (lactate dehydrogenase test) LDH levels are observed in 70–80% of the patients. Treatments that included (cyclophosphamide, hydroxydaunomycin, oncovin, prednsone)CHOP regimen and radiation therapy were associated with 5-year survival.The superior vena cava syndrome is considered a medical emergency resulting from superior vena cava compression and accounts for about 2%-4% of non-Hodgkin lymphomas(NHL). Primary mediastinal (thymic) large B-cell lymphoma is an unusual and aggressive non-Hodgkin lymphoma that can present with superior vena cava syndrome(SVCS).[3] We report a case of a 17-year-old male with this condition and the associated management.

Case Presentation

A 17-year-old boy presented to the oncology department with complaints of breathlessness which aggravates in a supine position. Hoarse voice, dry cough, and intermittent profuse sweating had been noted at night for 2 weeks. He was admitted to the hospital with complaints of fever, throat pain, and difficulty in swallowing associated with mouth ulcers along with diffuse swelling over the right side of the neck. His CT thorax showed a soft-tissue attenuating mass (11.4x 7.7x 6.8 cm) with ill-defined borders involving the prevascular compartment of the mediastinum with extension into the visceral compartment showing few tiny hyperdense foci, necrotic areas, and discrete cardiophrenic lymph nodes (largest measuring 11x 10 mm), the lesion is causing mass effect as evidenced by compression of the trachea, bilateral brachiocephalic veins, and SVC - possibility of Lymphoma

A thrombus in the confluence of the left brachiocephalic vein was observed with SVC and mild pericardial effusion. Also, an enlarged right supraclavicular lymph node measuring 3.2x 2.2 cm in size was noted. He underwent a CT-guided biopsy of the mediastinal mass which showed Poorly differentiated Neoplasm. The IHC report showed evidence of Non-Hodgkin Lymphoma- B type. His blood investigation showed a raised LDH(958) and CRP(10.3) values.

His tumor markers Beta-HCG, AFP were normal and serologic markers for human immunodeficiency virus, hepatitis B, and C virus came negative. His Bone marrow Aspiration and Biopsy showed apoptotic cells and lymphocytosis and occasional foamy histiocytes. His CECT (abdomen, pelvis, thorax, and neck) showed large ill-defined enhancing soft tissue density lesions involving superior mediastinum, with extension into anterior, middle mediastinum, and lower neck. Lesion encasing the mediastinal vessels – arch of aorta and branches, pulmonary trunk with narrowing of the left main pulmonary artery and compressing SVC and brachiocephalic veins with the collateral flow. Lesion involving the pericardium with moderate pericardial effusion and compressing the lower trachea. Bilateral carotid and jugular vessels encased by the

lesion, with thrombus in the right (internal jugular vein) IJV.

Because of Right IJV thrombosis, Low Molecular weight Heparin was given for 2 days. Hence, the features were suggestive of SVC syndrome, he was started on steroids and pre-phase chemotherapy with a CVP regimen. He was initiated with DA-EPOCH- R regimen chemotherapy after obtaining informed consent from the parent group.

After completing 4 cycles of the DA-EPOCH- R regimen, his lab report showed features of pancytopenia and ANC was below 500/cumm. Blood cultures were sent and he was empirically started on broad-spectrum IV antibiotics (Inj. Meropenem and Inj. Teicoplanin) and growth factors along with adequate hydration. He was also given symptomatic care for mouth ulcers which improved gradually. CT Chest after5 cycles of chemotherapy showed a significant decrease in the size of the soft tissue density lesion involving superior mediastinum than the primary report. Doses of the further chemotherapy cycles were adjusted accordingly because of neutropenia history.

Discussion

PMBCL is a rare type of NHL, comprising 2% to 4% of all NHL and 6% of diffuse large B-cell lymphomas. It affects mainly young adult females (median age of 35) and presents as a large, proliferating invasive tumor in the mediastinum. On the other hand, the main causes of SVCS include malignant conditions (60%–85%).[4]

DA-EPOCH- R regimen includes the drugs etoposide phosphate, prednisone, vincristine sulfate (Oncovin), cyclophosphamide, doxorubicin hydrochloride (hydroxydaunorubicin), and rituximab. Dunleavy K et al stated that the use of DA-EPOCH-R eliminated the need for radiotherapy in all except 2 of 51 patients (4%) with PMBCL in a prospective cohort.

In this case, a 17-year-old school-going football aspirant was admitted with swelling in the right side of the neck. He noticed shortness of breath while playing sports and it aggravated in the following months. He complained about breathlessness while lying down. Under evaluation, a small attenuating mass was spotted at the right side of the neck. The thrombus was treated with low molecular weight heparin. This mass induced compression of the trachea, bilateral brachiocephalic veins, and SVC. The biopsy conducted showed poorly differentiated neoplasm

Because of the features of SVC syndrome, he was started on steroids and pre-phase with CVP in the initial phase. Later he has switched to DA-EPOCH- R regimen because of stage II bulky disease and Pericardial effusion. CT chest taken after the 4th cycle of his chemotherapy showed a significant decrease in the size of the previously described soft tissue density lesion involving superior mediastinum compared to CT Chest taken before initiating DA-EPOCH-R regimen. After 6 cycles of the DA-EPOCH-R regimen he was stable and there was a significant reduction in the tumor mass. The dose of each chemotherapy was calculated based on the ANC nadir of his previous cycle.

Similar to our case, it was also observed by Kieron D. et al that no patients had recurring disease over a median follow-up of more than 5 years. Moreover, in an independent retrospective cohort, treatment with DA-EPOCH-R in patients with PMBCL showed an event-free survival rate of 100%.[4]. Rieger M et al observed that the benefit of survival in PMBCL occurs when rituximab was added to CHOP-like regimens.[5]]

In this case, 4th and 6th cycles were associated with neutropenia and he was managed with i.v antibiotics and G CSF similar to this in a study conducted by Wilson et al showed the targeted neutropenia level was achieved in 49% of cycles, whereas hospital admissions for fever and neutropenia occurred in only 8% of cycles by analyzing 49 patients with large B cell lymphoma.[7]

Conclusion

This case provides an insight into the DA-EPOCH-R regimen usage with constant monitoring of vitals and adverse events especially, the occurrence of neutropenia. We intended to highlight the efficacy of dose-adjusted rituximab used for the treatment of PMBCL than the usually preferred CHOP regimen. This regimen used in our patient has shown significant tumor size reduction throughout the treatment period and has completed 6 cycles successfully, except for incidences of neutropenia which was carefully handled. However, further studies are required on a large scale to fully understand the survival benefit of DA- EPOCH-R over CHOP regimen in PMBCL.

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