A RARE CASE OF COEXISTENT DISSEMINATED VARICELLA ZOSTER AND ERPES SIMPLEX IN A NON-HODGKIN'S LYMPHOMA PATIENT.

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Abstract: A 65 years old male, a known case of Non-Hodgkin’s lymphoma patient on treatment, was admitted with fever, painful swallowing, swelling of face and lips and multiple blisters all over the body in our hospital. On investigating further, he was diagnosed with both Herpes Simplex and Varicella Zoster infection in a disseminated pattern. He was treated with antibiotics, antiviral drugs and he responded well with complete resolution of skin lesions and became asymptomatic and was discharged in a reasonably good health and now he is on regular follow up.


Introduction:
Diffuse Large B Cell Lymphoma constitutes 30-40% of Non-Hodgkin’s Lymphoma cases. There are five morphologic variants in Diffuse Large B Cell Lymphoma like centroblastic, immunoblastic, b plasmablastic, anaplastic, T cell/histiocyte rich, among which T cell variety constitutes 1-3% . These immunocompromised patients are more prone for disseminated infections and our patient got affected by both Herpes Simplex and Varicella Zoster virus in a disseminated pattern.

Case report:
A 65 years old male, a known case of Non-Hodgkin’s lymphoma- Large B cell type (T cell rich) on chemotherapy, got admitted with history of fever, painful swallowing, swelling of face and lips and multiple blisters, itching and pain all over the body for two weeks duration. He had one episode of chicken pox infection 1 year back. He was not a known diabetic or HIV patient.

On examination, he was moderately built and nourished, conscious, oriented, afebrile. There was no cyanosis, clubbing, pedal edema. Pallor, bilateral submandibular, cervical, axillary, inguinal lymphadenopathy were noted. He also had facial puffiness, swelling of lips, oral mucositis, multiple vesicular and bullous eruptions all over the body on an erythematous base in a disseminated pattern sparing palms and soles. His ophthalmological and ENT examination were normal. Pulse rate was 106/min, regular, BP was 130/80 mmHg in supine position, RR-16/min, regular. His respiratory, central nervous system and other systemic examination were within normal limits.
His renal, liver function tests, electrolytes, urine routine examination, ECG, Echocardiography were within normal limits. Ultrasound of the abdomen and pelvis did not reveal any significant abnormality. Chest x ray: mediastinal widening present due to enlarged lymph nodes.

CT-Neck: Multiple enlarged lymph nodes in submandibular, submental, both jugular chain and posterior cervical group and in right parotid region suggestive of lymphoma.

CT-THORAX showing enlarged aortopulmonary group of lymph nodes

CT-THORAX showing enlarged right axillary group of lymph nodes

CT-Neck showing enlarged bilateral jugular group of lymph nodes

CT-THORAX showing mediastinal widening due to enlarged lymph nodes

CT-Abdomen: Perirectal lymphadenopathy present. Bone marrow smear: Normal study. Lymph node – FNAC smear: showed lymphoid cells and few clumps of large pleomorphic cells with hyperchromatic nuclei. Submental lymph node excision biopsy: showed Non-Hodgkin's lymphoma- Large B cell type (T cell rich) on histopathological examination. On immunohistochemistry, large CD 20 positive cells seen with pericapsular infiltration interspersed with CD 20 negative pale histiocytes and CD 3 positive small lymphocytes. No CD 15 or CD 30 positive cells seen.

Above is UNIPLEX PCR positive for HSV 1 and VZV

Below is NESTED PCR positive for HSV 1 and VZV
POLYMERASE CHAIN REACTION (UNIPLEX, NESTED TYPE):
Done with fluid from skin lesions, positive for Herpes Simplex virus and Varicella Zoster virus. Patient was treated with iv fluids, antibiotics, iv acyclovir and steroid for 10 days for which he responded well with resolution of skin lesions without any fresh lesions and started taking oral diet normally and he is on follow up.

Patient after treatment with healed skin lesions

Discussion:
As per WHO classification, Diffuse large B cell lymphoma has 5 morphologic variants and 3 subtypes like mediastinal, intravascular, effusion lymphoma. It is a high grade aggressive tumour but with modern therapy, it is potentially curable. It has bimodal age distribution with high incidence among AIDS patients and has male predominance. In more than half of cases, tumour is limited to one side of diaphragm. In T cell variety, large lymphoma cells are 10% or less and the vast majority of cells are non neoplastic T cells and or histiocytes. The characteristic morphologic feature shows host inflammatory response and is just as aggressive as diffuse large B cell lymphoma and should be treated similarly. It should be distinguished from Hodgkin’s lymphoma of either classic or nodular lymphocyte predominant type.

Although both humoral and cell mediated immunity plays a role against herpes infection, patients with defective cell mediated immunity experience more severe and extensive lesions than those with defective humoral immunity. Oropharyngeal herpes simplex infection in immunocompromised patients can present with widespread involvement of skin, mucosa, extremely painful friable, hemorrhagic and necrotic lesions similar to the mucositis caused by cytotoxic agents. The lesions can spread locally causing esophagitis presenting as odynophagia, dysphagia, substernal pain and multiple ulcerative lesions, but can occur directly by reactivation of herpes simplex virus and its spread to esophagus via the vagus nerve and dissemination to internal organs can occur. Histologically, two types of degenerative changes like ballooning degeneration leading to acantholytic or Tzanck cells and reticular degeneration leading to vesicular formation occurs in herpes infections. Recurrent varicella infection can occur in immunocompromised patients. Disseminated herpes zoster particularly affects patients with HIV or NHL with an incidence of 25-50% and it manifests as generalised vesicles, papulovesicles or erosions and may involve internal organs with an incidence of 10% of patients with cutaneous dissemination. Relapsing chicken pox can occur in patients with Non Hodgkin’s lymphoma. Herpes infections can be identified by Tzanck smear which shows multinucleated giant cells. Culture and Polymerase chain reaction techniques are used to identify herpes simplex virus and varicella zoster virus separately among which PCR is the most sensitive. Iv acyclovir is reserved for those with disseminated varicella zoster virus infection, ophthalmic involvement, severe immunosuppression. Antiviral prophylaxis is 90% effective during chemotherapy. Glucocorticoids as anti inflammatory used during acute phase of herpes zoster to further decrease acute pain and prevent post herpetic neuralgia.

Conclusion: Our immunocompromised patient, has a rare type of Non Hodgkin’s Lymphoma, who also had both herpes simplex and varicella zoster lesions in a disseminated pattern, a rare occurrence and he responded well with treatment and he is on follow up.

Reference:
3. Fitzpatrick’s Dermatology in General Medicine, seventh edition.
5. Rosai and Ackerman’s Surgical Pathology, ninth edition.