International Journal of Scientific Research and Management (IJSRM)
||Volume||11||Issue||01||Pages||MP-2023-801-808||2023||
Website: www.ijsrm.in ISSN (e): 2321-3418
DOI: 10.18535/ijsrm/v11i01.mp04

An Unusual Lupus like Malar Rash Pattern with Hepatosplenomegaly as a Presentation of Gamma Delta T Cell Lymphoma

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Abstract

About 12% of all lymphoid tumors worldwide are peripheral t cell lymphomas, which are uncommon subtypes of non-hodgkin lymphoma. they have a poor prognosis and are more common in populations and countries in asia. T cell lymphomas with gamma delta t cell receptors expressed in them are very rare (less than 1% of lymphoid neoplasms) and extremely aggressive; they originate from gamma delta t cells; a small subset of peripheral t cells with direct antigen recognition capability acting at the interface between innate and adaptive immunity .

Lymphoid tissue, skin, gastrointestinal tract, and the red pulp of the spleen are where gamma delta t lymphocytes tend to cocentrate, representing only 1-5% of the total circulating lymphocytes, but accounting for up to 30% of the entire t cell population.

In contrast to alpha beta t cells, gamma delta t lymphocytes develop from cd4/cd8 thymic precursors in the bone marrow and usually lack the major histocompatibility complex restriction.

These lymphocytes conduct as cytotoxic cells similar to natural killer cells in their activity as early effectors of innate, non-specific immune response and are capable of t cell receptor rearrangement as well as phagocytosis.

Hepatosplenic t cell lymphoma and primary cutanous gamma delta cell lymphoma are recognized as two different gamma delta t cell lymphoma entities.

A well characterized extranodal lymphoma, hepatosplenic t cell lymphoma has a disguised onset, secondary to intrasinusoidal infiltrationn of the spleen, liver, and bone marrow, has a rapidly progressive course, is poorly responsive to chemotherapy.

A panniculitis-like clinical picture with prominent epidermal involvement can be a presentation of primary cutaneous gamma delta t cell lymphoma.

In this case study , the authors will discuss a case of 19 year old male patient present with a lupus like malar rash and hepatosplenomegaly and who had been diagnosed with gamma delta t cell lymphoma.

Keywords : Gamma Delta T Cell Lymphoma ,Hepatosplenic T Cell Lymphoma , Primary Cutanous Gamma Delta T Cell Lymphoma ,Non Hodgkin Lymphoma

Introduction

Peripheral t cell lymphomas are a rare and heterogenous group of disorders with optimal treatment is uncertain (2) **.** T cell lymphomas with expression of gamma delta t cell receptors are very rare and very aggressive. They are gamma delta lymphocytes in origin. these cells, which naturally perform a role in the innate, non-specific immune response, develop from thymic precursor in the bone marrow, lack the major histocompatibility complex restrictions. (3).

Hepatosplenic t cell lymphoma and primary cutaneous gamma delta t cell lymphoma are two different gamma delta t cell entities that are recognized. (1).

Hepatosplenic gamma delta t cell lymphoma predominates in young adult with a male female ratio of 10:1 and a median age of 20–25 years. Chronically immunosuppressed subjects, such as patients with solid organ transplanation or those under long-term antigenic stimulation, are very popular. Gamma delta t cell lymphomas represent the majority of post transplant t cell lymphoproliferative disorder with a higher median age at presentation, specifically in solid organ transplanted patients (39 year) (4).

The clinical benchmarks of this disease are systemic b symptoms, marked hepatosplenomegaly, and lack of lymphadenopathies. Fever, abdominal pain, and weakness are the most common presenting symptoms. Hepatomegaly is seen in between 75 and 90 percent of cases, while splenomegaly is a constant. (5).

In half of the cases, abnormalities in liver function tests are present. almost inevariably involved is bone marrow. Anemia is present in 75% of cases, while thrombocytopenia is seen in 85% of cases and appears to be related to clinical behavior as it is linked to easy bruising and purpura (6).

The exact mechanism that causes pancytopenia in these patients is yet unknown, while cytokine release, which may be the cause of the hemophagocytic syndrome, may in fact suppress hemopoiesis. However, the severity of pancytopenia does not appear to be directly correlated with the percentage of bone marrow infiltration; instead, other factors that have not yet been clearly identified, such as autoimmunity-mediated mechanisms, likely play a significant causal role in the development of cytopenia. In 50–80% of cases, peripheral blood samples contain neoplastic lymphocytes. (7,8).

Autoimmune hemolytic anemia has been reported in anecdotal cases, but skin and mediastinal involvement are exceptional events. (9).

A rapidly progressive behavior and marked primary resistance to most chemotheraputic agents are often seen in hepatosplenic gamma delta t cell lymphoma. After conventional chemotherapeutic regimens, complete remission is very rare.

Most patients with lymphoma pass away within two years of their diagnosis, with a median overall survival time of less than one year following anthracycline-containing chemotherapy. (10). A blast like terminal transformation can occasionally be observed (11).

The second entity of gamma delta t cell lymphoma which can present with prominent epidermal involvement or with a panniculitis like clinical picture that can be complicatted by a concurrent hemophagocytic syndrome , the disease exhibits phenotypic and biological overlap with other extranodal gamma delta t cell lymphomas that involve the respiratory or gastrointestinal tract mucosa. (1).

In this case, a 19-year-old male patient was diagnosed with gamma delta t cell lymphoma after presenting with a rash that resembled that of lupus. He also had hepatosplenomegaly.

Case report

A 19-year-old male patient was referred to our hospital for a second opinion and diagnosis of his condition. He is a nonsmoker with no known prior medical conditions.

The patient sought medical advice after complaining of fatigue and anorexia for a month. Prior to the onset of his complaint, which was preceded by an upper respiratory tract infection that lasted for two weeks, the patient was rather healthy.

After his infection cleared up, he began to complain of anorexia and a progressive feeling of fatigability. During the course of a month, he lost 20 kilograms of weight. He also experienced night sweats and abdominal pain.

His abdominal pain was dull, diffused, without radiation, provocation, or alleviation, and he did not experience any changes in his bowl movements, nausea, or vomiting..

The patient started to develop a non itchy rash on his cheeks two weeks after the above-mentioned symptoms, saving the nasal arch and nasolabial folds (figure 1). The rash involved also his upper back, neck, and upper limbs and progressed slowly (figure 2,3). Other areas of his body were not involved.

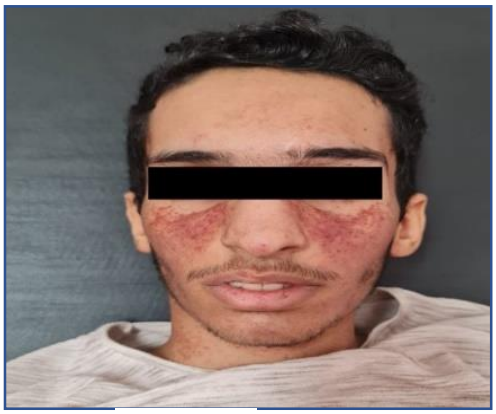

Figure 1

Figure 2

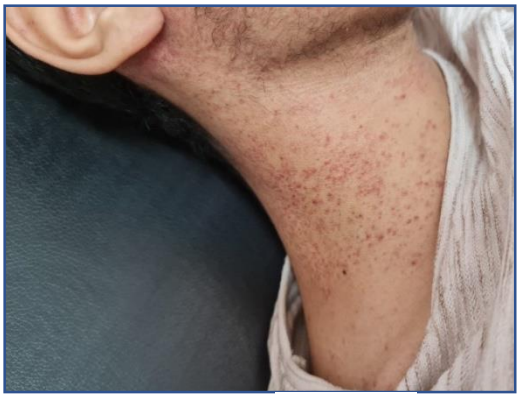

Figure 3

The patient described the feeling of early satiety and he denied any previous similar symptoms.

He also experienced pain in the small joints of his hands. He made no mention of any prior bleeding incidents or bruising easily. Other systemic review components of other symptoms were not significant.

The patient has no known drug allergies and doesn't take any drugs.

His family didn't have any hereditary conditions or chronic ailments.

The physical examination yielded the following positive results:

Petechial non blanchable rash on his cheek , neck and upper limbs

Hepatosplenomegaly , no palbable lymphadenopathy .

The patient was referred by his general practitioner to rheumatology team for review , anti nuclear antibody , anti double stranded antibody , c3 level , c4 level , antineutrophil cytoplasmic antibodies all were negative .

His initial complete blood count showed anemia and thrombocytopenia and his blood film was as the following :

Red blood cells : macrocytic normochromic anemia with anisocytosis .

White blood cells : normal count and hypersegmented neutrophils .

Platelets : thrombocytopenia with giant thrombocytes.

Prothrombin time , partial thromboplastine time , international normalized ratio , kidney function test , liver function test , ferritin level ,thyroid stimulating hormone , thyroxine level all were within normal range .

His folate level and vitamin b 12 level were low , he was treated as a combined anemia with no improvement so he was referred to hematology oncology team .

We reviewed the patient , labs were repeated and were as the following :

Creatinine 59 umol/l (normal range 53-97)

Urea 4.1 mmol/l (normal range 1.7-8.3)

Calcium level 2.24 mmol/l (normal range 2-2.6)

Potassium level 4.23 mmol/l (normal range 3.5-5.3)

Sodium level 138 mmol/liter (normal range 135-148)

Glucose 5.4 mmol/liter (normal range 4.2-6.4)

White blood cell count 6.9 *10^3/ul (normal range 4.5-13)

Red blood cell count 2.19 *10^6/ul 9normal range 4.3-5.7)

Hemoglobin 8.1 g/dl (normal range 13.2-17.3)

Hematocrit 22.7%(normal range 39-49)

Mean corpuscular volume 103 fl (normal range 80-99)

Mean corpuscular hemoglobin 37 pg (normal range 27-34)

Mean corpuscular hemoglobin concentration 35 g/dl (normal range 32-37)

Platelet 25*10^9/ul (normal range 150-450 *10^9)

Red blood cell distribution width 22% 9normal range 11.-14.5)

Neutrophils 69%

Monocytes 2%

Lymphocytes 23%

C reactive protein 1.9 mg/dl (normal range 0-0.5)

Brucella screen negative

Prothrombin time 18 seconds (normal range 11-15 seconds)

Partial thromboplastin time 36 seconds (normal range 22-40 seconds)

International normalized ratio 1.4 (normal range 0.9-1.1)

Rheumatoid factor 9.4 iu/ml (normal range 0-14)

C3 0.8 g/l (normal range 0.9-1.8)

C4 0.27 g/l (normal range 0.1-0.4)

ANA negative

Blood film :

Macrocytosis , anisocytosis,leukocytopenia with presence of blasts ,atypical lymphocytes and nucleated red blood cells , thrombocytopenia .

Hepatitis B surface antigen negative

Hepatitis c virus antibodies negative

HIV antibodies and antigens negative

Folate level 34nmol/liter (normal range 7-39)

B12 level 328 pmol/l (normal range 141-490)

His liver function test was unremarkable .

Blood culture and urine culture were negative .

Pan ct scan was reported as the following :

Clear both lungs , no sizable nodules .

No pleural effusion .

No mediastinal mass.

Normal cardiothoracic ratio.

Intact chest cage with no destructive bony lesion.

Liver appears enlarged measuring 17.8 cm in span with a smooth margins , without evidence of focal lesions .

The spleen appears grossly enlarged measuring 19.7*9.7 cm with homogeneous texture without evidence of focal lesions.

The pancreas and both kidneys are unremarkable..

No definite lymphadenopathy in the abdomen.

Free fluid noted in the pelvis.

Urinary bladder and rectum are unremarkable .appearance are suggestive of lymphoma.

Bone marrow aspiration (figure 4) :

The following markers were performed :

CD2 ,CD3, CD4, CD5, CD7, CD8, CD10, CD19, CD99, TCR ALPHA/BETA , TCR GAMMA/DELTA , CD 16, CD56, KAPPA AND LAMBDA LIGHT CHAINS .

Approximately 64 % of marrow cells are abnormal t cells , expressing CD2,CD3,CD16,TCR GAMMA/DELTA,CD57,CD99,CD7,CD8,NEGATIVE FOR CD4,cd8,CD56 AND ALPHA BETA T CELL RECEPTORS.

Bone marrow biopsy :

Erythroid line shows megaloblastic changes.

Myeloid line seen with shift to left .

Aggregation of plasma cells and abnormal t cell .

According to the patient's clinical findings, test results, bone marrow aspiration, and biopsy, gamma delta t cell lymphoma, an exceptionally rare and aggressive lymphoma, was identified as the disease.

To complete his therapy, the patient was transferred to a specialized cancer facility.

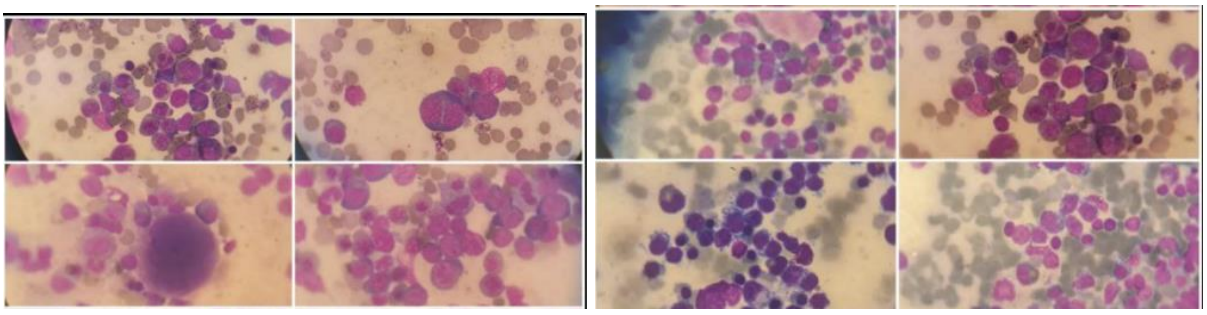

Figure 4

Discussion

Peripheral t cell lymphomas, a subset of t cell non-Hodgkin lymphomas, are a variety of illnesses with generally poor prognoses. In the United States, there is less than 1 instance of peripheral t cell lymphoma for every 100,000 persons. (12).

Gamma delta cells give rise to gamma delta t cell lymphomas. Hepatosplenic t cell lymphoma and primary cutaneous gamma delta t cell lymphoma are the two different forms of gamma delta t cell lymphomas.

An uncommon and aggressive extranodal lymphoma is hepatosplenic gamma delta t cell lymphoma. Males are more likely to experience the peak occurrence, which occurs in adolescence and young adults. up to 20% of hepatosplenic t cell lymphoma arise in the setting of chronic immune suppression , most commonly solid organ transplantation (13).

A neoplastic infiltration of medium-sized lymphocytes with a modest quantity of cytoplasm and ill-defined cellular boundaries characterizes hepatosplenic gamma delta t cell lymphoma. (14,15).

Double negative T cells (CD4 NEGATIVE AND CD8 NEGATIVE), coupled with CD2 POSITIVE, CD3 POSITIVE, CD5 NEGATIVE, and CD 7 POSITIVE, are often defined by immunophenotyping. (16,17,18)

The clinical criteria of this disease are substantial hepatosplenomegaly, a lack of lymphadenopathies, and systemic b symptoms, which include an unknown-cause fever, night sweats, and weight loss of more than 10% of body weight. Our patient had all of these signs and symptoms.

Gamma delta t cell lymphoma has been treated with splenectomy, corticosteroids, alkylating drugs, purine analogues, anthracycline-containing regimens (such as CHOP LIKE, HYPER CVAD), and cytrabine-cisplatinium combinations . Anthracycline based chemotherapy (CHOP regimen or derivatives) is the most commonly used strategy. However, long-term outcomes are poor, with a median time to recurrence of 4 months, even in patients with initially responsive disease. In general, response rates attained with this treatment are satisfactory (between 30% and 45% full remission rate). (19,20,21).

Most patient die of lymphoma within 2 years from diagnosis , with a median overall survival after anthracycline containing chemotherapy shorter than one year (22).

Our patient first displayed an uncommon and unusual lupus-like malar rash, but when the disease spread to other organ systems, he developed hepatosplenomegaly, anemia, and thrombocytopenia without lymphadenopathy.

This emphasizes how crucial it is to maintain a high clinical suspicion for the diagnosis of gamma delta t cell lymphoma in any young male adult presenting with systemic symptoms, hepatosplenomegaly, and thrombocytopenia.

The authors are grateful to the patient for allowing them to publish and discuss his story.

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