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QUITE INDOLENT FOLLICULAR LYMPHOMA SINCE 20 YEARS IN 40 YEARS OLD MALE - A CASE REPORT

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ABSTRACT

Follicular lymphoma comprises about 20 - 25% of cases of non-Hodgkin lymphomas. Patients with follicular lymphoma typically present withsuperficial lymphadenopathy as well as rarely extra nodal involvement. We are presenting a case of 40 years old male patient with generalized lymphadenopathy and massive splenomegaly. Patient was also having leukocytosis with lymphocytosis and bone marrow infiltration by lymphoma cells. As follicular lymphoma is rare to find in a 40 year old as well as here we are able to find and document the typical features of follicular lymphoma.

INTRODUCTION

Follicular lymphoma is a B-cell neoplasm that recapitulates the architectural and cytologic features of the normal secondary lymphoid follicle. This tumor comprises up to 40% of all adult non-Hodgkin lymphomas in the United States, but in other countries like Asia the relative incidence is much lower. Most cases occur in elderly individuals. It is very unusual under 20 years of age and relatively uncommon in blacks. Grossly and at low-power examination, the most distinctive feature of these tumors is the nodular pattern of growth. The cytologic composition of the neoplastic nodules is characterized by a mixture in different proportions of small and large lymphoid cells. Primary involvement of extra nodal areas is very rare [1] and bone marrow involvement is seen in 50 - 60% of the cases. There are evidences that approximately 20% of patients with Follicular lymphoma [2] having symptoms of fever, unexplained weight loss, and profuse night sweats. As there is vagueness of symptoms or the lack of symptoms altogether, the variation in patients' presentation is considerable. Here the patient was having complaint of heaviness ofabdomen as well as multiple cervical and inguinal swellings which highlights the variability of this disease.

CASE REPORT

A 40 years old male patient came to the Medicine OPD with multiple swellings in the neck and inguinal region since 20 years. (Photo - 1) Patient was also having complained of heaviness of abdomen since 1 month. All swellings were initially smaller in size and progressively increasing in size over a period of 20 years. Findings of per abdominal examination of patient were massive splenomegaly up to umbilicus, moderate hepatomegaly and palpable para-aortic lymph nodes. Hematological investigation of the patient showed raised leukocyte count (15,000/cmm) with lymphocytosis (70%). Peripheral smear showed atypical lymphocytes with few smudge cells and microcytic hypo chromic anemia. (Photo – 2)Biochemical analysis showed raised LDH level 601 IU/L (50-285 IU/L) and serological examination showed negative HIV

(ELISA) and HbsAg (ELISA). Ultrasonography of hepatomegaly, multiple paracaval and para aortic lymph nodes having largest size of 64x45 mm. Multiple lymph nodes also noted in iliac region with largest size of 41x31 mm. Patient had underwent surgery and inguinal lymph nodes wereexcised. Gross pathology of excised lymph nodes showed nodular pattern of growth. (Photo – 3)Histopathological examination showed lymphocytes arranged in follicular pattern with folded nucleus giving cleaved cell appearance. The size is similar to or slightly larger than that of normal lymphocytes, the chromatin is coarse, and the nucleolus is inconspicuous. (Photo - 4, Photo – 5) Immunohistochemistry (IHC) showed CD 20 positive which was expressed by B lymphocytes (Photo – 6), bcl 2 positive by B lymphocytes in follicular pattern (Photo – 7), CD 5 positive which was expressed by naïve B cells, Ki 67 (proliferative index) < 30% which was showing indolent lymphoma. (Photo – 8) Overall findings suggested of follicular lymphoma. Patient's bone marrow biopsy showed para trabecular arrangement of the lymphoma cells. (Photo – 9)

abdomen showed massive splenomegaly, moderate

Photo 1. Patient with multiple cervical swellings

Photo 2. Smear shows atypical lymphocytes. (Leishman stain, 100 X)

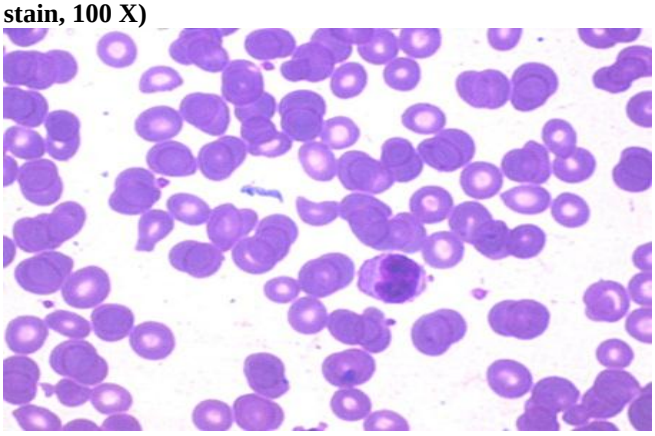

Photo 3. Gross pathology of excised lymph nodes with nodular pattern of growth

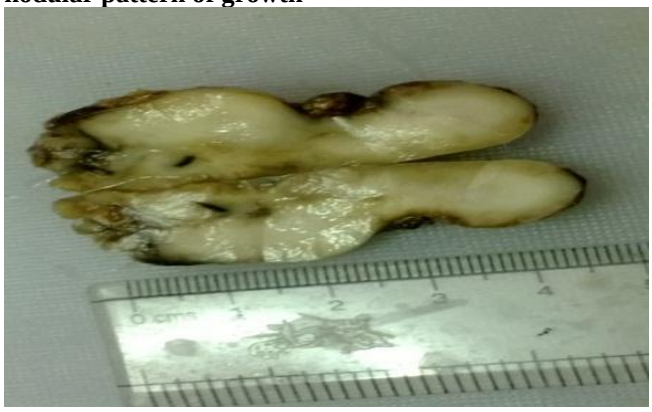

Photo 4. Lymphocytes arranged in follicular pattern. (H & E, 4 X)

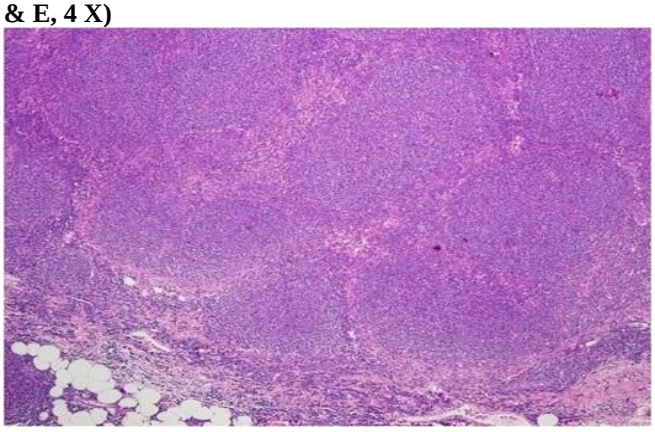

Photo 5. Homogeneous population of small cleaved cells. (H & E, 40 X)

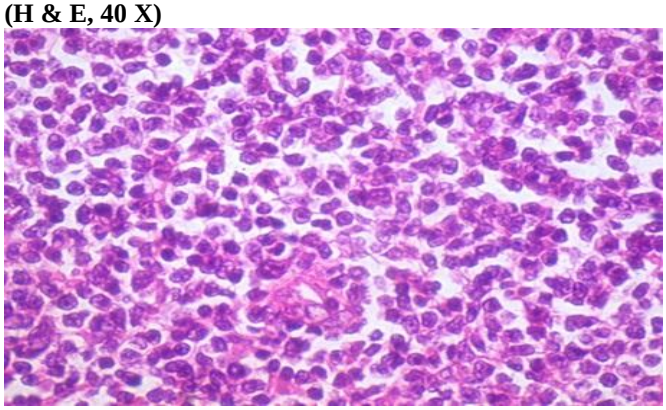

Photo 6. Positive expression of CD 20. (IHC, 40 X)

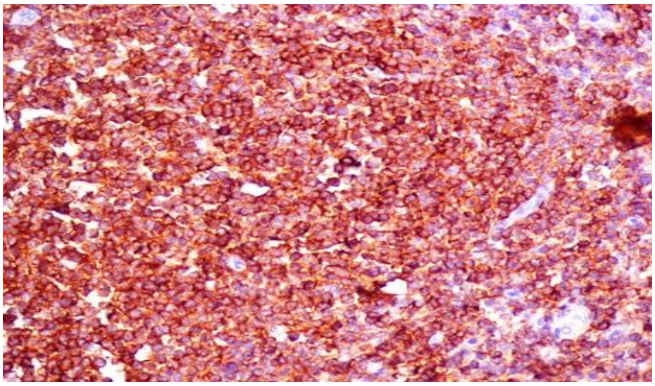

Photo 7. Positive expression of BCL 2 by follicular cells. (IHC, 10 X)

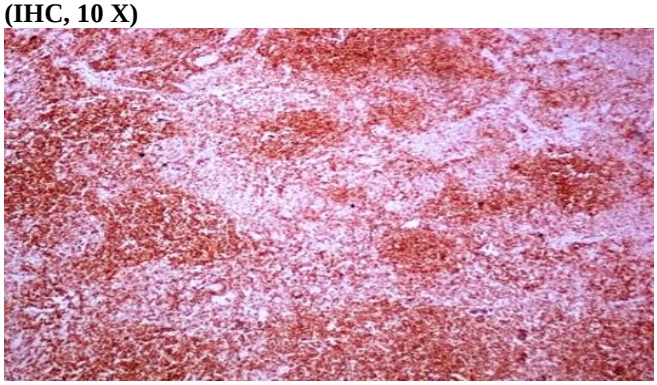

Photo 8. <30% positive expression of Ki 67 / MIB 1. (IHC, 4 X)

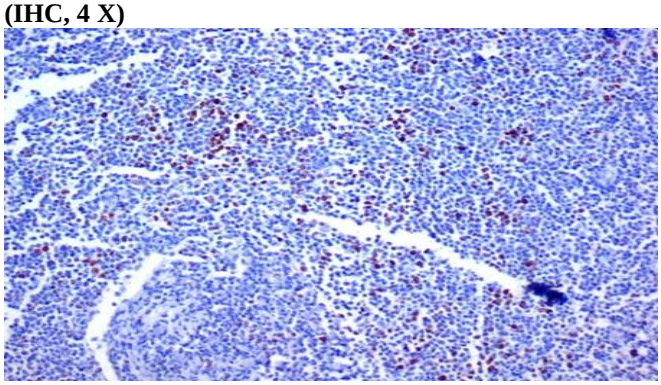

Photo 9. Paratrabecular involvement bone marrow by lymphoma cells. (H & E, 4 X)

DISCUSSION

Two general categories of lymphomas are Hodgkin lymphoma and non-Hodgkin lymphoma (NHL). As compared to Hodgkin lymphoma, NHL is relatively more common. [3] Out of all subtypes of lymphoma, follicular lymphoma is the second most common and represents about 20% to 25% of cases of all cases of non-Hodgkin lymphomas in the U.S. and Europe [4]. Clinical presentation of the patients with follicular lymphoma is typical. Most of them present with enlarged superficial lymph nodes of small to medium size over a long period of time. Few patients present with slow growth of lymph node in deeper areas e.g. mesenteric, iliac, retroperitoneal or infra diaphragmatic. Patient's general health is always preserved. Primary involvement of mediastinal and extra noal areas are uncommon, as well as isolated splenic enlargement [1]. The bone marrow is involved in 50% to 60% of the cases.

Around 20% of patients with follicular lymphoma have systemic complaints, or B symptoms [2] which consist of fever, unexplained weight loss, and profuse night sweats. In view of the vagueness of symptoms or the lack of symptoms altogether, the variation in patients' presentation is considerable.

About pathogenesis of follicular lymphoma, up to 90% of cases having breakpoint regions in chromosome 18 and reshuffled aspects of BCL-2 [5,6]. A resulting translocation, t(14;18), leads to an increased expression of BCL-2, an oncogene that hastens apoptosis and leads to increased cell survival time [7]. Origin of follicular lymphoma is from follicle B cells which comprise of both centrocytes (smaller) and centroblasts (larger) types of cells [8]. Obtaining a tissue sample for histologic analysis is paramount for the diagnosis because histopathological examination is the gold standard diagnostic tool.

Histopathologically, follicular lymphoma is characterized by a mixture in different proportions of small and large lymphoid cells, both of which resemble their normal follicular counterparts. The small cells have scanty cytoplasm and an irregular, elongated cleaved nucleus with prominent indentations and infoldings; the size is similar to or slightly larger than that of normal lymphocytes, the chromatin is coarse, and the nucleolus is inconspicuous. These cells have been variously referred to as germinocytes, centrocytes, poorly differentiated lymphocytes, and small cleaved follicular center cells. The large cells are two or three times the size of normal lymphocytes; they have a distinct rim of cytoplasm and a vesicular nucleus with one or three nucleoli often adjacent to the nuclear membrane. These cells, which have a rapid turnover rate and probably represent the proliferating component of the tumor, have been designated over the years as germinoblasts, centroblasts, histiocytes, large (cleaved or non cleaved) follicular center cells, large lymphoid cells, and lymphoblasts. Some may be binucleated and simulate Reed–Sternberg cells. The tumor

cells express pan–B-antigens, such as CD19, CD20, CD22, and CD79a, bcl 2 in addition to HLA-DR. CD5 and CD43 are usually negative [9].

The Follicular Lymphoma International Prognostic Index (FLIPI), which can be helpful when considering prognosis in follicular lymphoma. Based on five simple independent risk factors (hemoglobin < 12 g/dL, serum LDH > upper normal value, Ann Arbor stage III–IV, number of nodal sites > 4, and age > 60 years), the FLIPI enabled the separation of patients into 3 groups (equilibrated in term of size) with distinct survival probabilities [10]. Higher value of FLIPI score indicates higher risk of death. FLIPI score of 3 to 5 is dangerous, 2 is moderate and 0 to 1 indicates minimal risk of death. In present case, 1 point is for stage and 1 point is for number of lymph nodes involved, which led to FLIPI score of 2. Follicular lymphoma staging depends upon the number of lymph nodes involved and anatomical extent of the disease. Usually there is wide variation in the course of follicular lymphoma. Sometimes obstruction and discomfort occurs in patient due to organs and lymph nodes enlargement as a result of fast tumor growth and spread.

Few patients with follicular lymphoma may show transformation in diffuse large B cell lymphoma (DLBCL) which is associated with poor outcome [11,12]. This disease is incurable so far only watchful waiting is acceptable in asymptomatic patients and may live free of symptoms for years. Median survival of the patient is around 8-10 years from the diagnosis [13]. Spontaneous regression of follicular lymphoma has also been observed [14]. Therapy is required for disease related symptoms and patients will respond to "gentle chemotherapy" but will relapse. Nowadays, recent advances in understanding the biology underlying follicular lymphoma prognosis have been enabled by genome-wide analyses of nucleic acids.

CONCLUSION

The average age of patients at diagnosis of follicular lymphoma is 63.5 years. The case described here involves a 40 years old man. This disparity highlights one aspect of the variable presentation of follicular lymphoma. We can also conclude that lymphocytosis in elderly patients almost always a lymphoproliferative disorder. Cure is not possible so that wait and watch should be the strategy of the treatment for patients without any symptoms.

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