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Case Report

Follicular Lymphoma Presenting with Skeletal Metastasis

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ABSTRACT

Follicular lymphoma is the most common low – grade lymphoma. Most patients of follicular lymphoma have widespread disease at diagnosis predominantly involving lymph nodes. Primary involvement of extranodal areas is very uncommon in follicular lymphoma. Skeletal involvement in follicular lymphoma is very rare. We present a case of follicular lymphoma that presented with bony pains and was diagnosed with follicular lymphoma with skeletal involvement.

Key Words: Follicular; extranodal; skeletal

INTRODUCTION

Follicular lymphoma is the second most common non Hodgkin's lymphoma (NHL) after diffuse large B cell lymphoma and it accounts for 70% cases of low-grade lymphomas making it the most common low – grade lymphoma.[1] As usual for low-grade lymphomas, most patients of follicular lymphoma have widespread disease at diagnosis, usually predominantly involving lymph nodes, but also spleen, bone marrow, and occasionally peripheral blood or extranodal sites. Primary involvement of extranodal areas is very uncommon in follicular lymphoma.[2] Extranodal sites that may be involved by nodal follicular lymphomas include the gastrointestinal tract,[3] skin,[4] ocular adnexa [5] testes.[6] Skeletal involvement in follicular lymphoma is very rare. We present a case of follicular lymphoma that presented with bony pains and was diagnosed with follicular lymphoma with skeletal involvement.

CASE REPORT

A 35 years old male gentleman presented to our hospital complaining of shoulder pain, hip joint pain, leg pain and back pain for 2 months. He also had low grade intermittent fever during this period. He was unable to perform active work due to extreme fatigue and also had lost weight over the past two months which he was unable to quantify. He himself did not notice swelling anywhere in body. He was a non smoker and non alcoholic with no significant past medical history. On examination we found a single 2×2 cm lymph node in left inguinal region with rest of the general and systemic examination revealing no abnormalities. His laboratory parameters showed Hb 7.9g/dl, LDH was high (527 U/L), alkaline phosphatase was

slightly raised (138 U/L), uric acid and calcium levels were within normal limits.HIV and HBsAg tests were negative. Inguinal lymph node biopsy showed that the neoplastic cells were positive for bcl6, CD20, CD10 and negative for bcl2, cyclin D1 and ALK. (figure1)The final histopathological impression was follicular lymphoma, grade 3 with Ki-67 proliferation index 60%. Bone scan done in view of bony pains showed increased tracer uptake in calvaria, multiple vertebrae, multiple ribs, bilateral scapulae, pelvic bones, upper end of bilateral femorii and humerii suggestive of skeletal involvement.(figure 2) Computed Tomography scan done after inguinal lymph node biopsy showed multiple mixed lytic sclerotic bone deposits with no other significant finding. His endoscopic evaluation ruled out possibility of gastrointestinal malignancy causing skeletal metastasis. Bone marrow biopsy showed no involvement by lymphoma. He was dignosed with follicular lymphoma, grade 3 with diffuse skeletal involvement (stage IVB, Ann Arbor staging). He belonged to high risk prognostic group as per Follicular Lymphoma International Prognostic Index-1 (FLIPI-1 score was 4). He was started on CHOP (cyclophosphamide, doxorubicin, vincristine and prednisolone) chemotherapy as he could not afford Rituximab. After first cycle of chemotherapy, his bone pain completely subsided and he is receiving further chemotherapy cycles.

DISCUSSION

Follicular lymphoma is the most common indolent NHL. As with other lymphomas the major etiologic factors include viruses; chemical such as pesticides and hair dyes; congenital immunodeficiencies and acquired immunodeficiencies (human immunodeficiency virus & use of immunosuppressant drugs after organ transplantation). It accounts for 15-20% of all NHLs and 70% of low-grade lymphomas.[7] The median age at diagnosis is well into the sixth decade of life, but up to 25% of patients are younger (40 years or less).[8] Our patient was diagnosed with follicular lymphoma at 35 years of age. Approximately 70% of patients have BM involvement, reflecting stage IV disease at presentation. Although our patient did not have bone marrow involvement, he had diffuse skeletal involvement which falls into stage IV as per Ann Arbor classification.

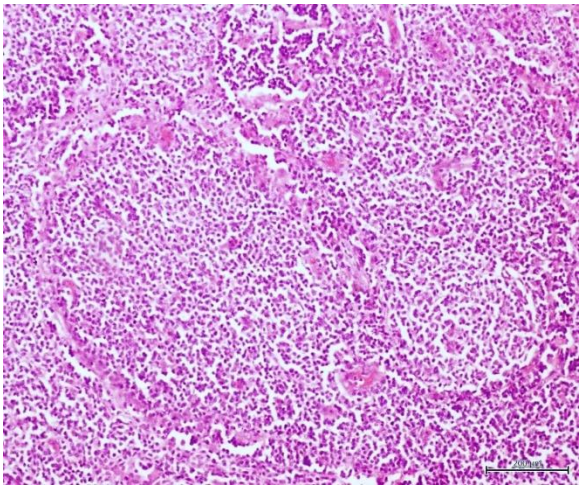

Figure 1- Inguinal lymph node biopsy showing characteristic histology of follicular lymphoma.

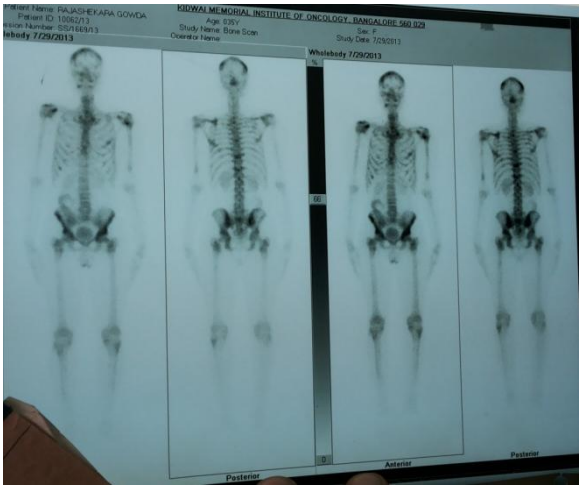

Figure 2. Bone scan showing increased tracer uptake in calvaria, multiple vertebrae, multiple ribs, bilateral scapulae, pelvic bones, upper end of bilateral femorii and hemerii.

The classical histological picture of follicular lymphoma includes the presence of closely associated follicles with obliteration of the normal nodal architecture and loss of interfollicular space.[9] The immunophenotype usually shows CD10,CD20,CD19 &CD22 positivity with cells expressing surface immunoglobulin. The hallmark diagnostic translocation in FL is t(14;18)(q32:q21). This translocation is present in 80% to 90% of cases. The median overall survival of most patients with follicular lymphoma is 12 to 15 years, however approximately 10% to 15% of patients have aggressive disease and short survival.[10] Genetic events associated with poor prognosis include *BCL6* rearrangements, *MYC* abnormalities,1p36 deletions, *TP53* mutations, *MLL2* and *EZH2* mutations.[11] Follicular lymphoma is further categorized into grades according to the number of centroblasts per high-power field (hpf), as grade 1 (0-5 centroblasts per hpf), grade 2 (6-15 centroblasts per hpf) and grade 3 (>15 centroblasts per hpf). Our patient had grade 3 FL. FL grade 3 is divided into FL3A, which retains centrocytes and FL3B, which consists of follicles composed of centroblasts. There is cumulative evidence that FL3B is a distinct entity, with frequent loss of t (14;18) and CD10 expression, increased p53 and MUM1/ IRF4 expression, and a prominent diffuse pattern. Both the pattern of biologic abnormalities and the clinical behavior suggest that FL3B is a distinct entity and is more closely aligned with DLBCL than with FL1-3A.

The decision to initiate treatment in FL patients is based on the assessment of tumor burden and associated symptoms. There are several definitions of high tumor-burden FL, including the Groupe d'Etude des Lymphomes Folliculaires (GELF), British National Lymphoma Investigation (BNLI), and National Comprehensive Cancer Network (NCCN) criteria which define high tumor burden with minor variations.Our patient had B symptoms of lymphoma, bone lesions and elevated LDH which put him into high tumor burden category. Standard options included R-CHOP (rituximab plus cyclophosphamide, doxorubicin, vincristine, prednisone/ prednisolone), rituximab plus bendamustine, or R-CVP (rituximab plus cyclophosphamide, vincristine, prednisone). Our patient could not afford and hence he was started on CHOP chemotherapy with bisphosphonates.

CONCLUSION

Although follicular lymphoma most commonly presents with nodal involvement, primary extranodal involvement at presentation has to be kept in mind. Here we have presented a case of follicular lymphoma that presented with bony pains and was diagnosed with follicular lymphoma with skeletal involvement.

REFERENCES

1. Armitage JO, Weisenburger DD. New approach to classifying non-Hodgkin's lymphomas: clinical features of the major histologic subtypes. Non-Hodgkin's Lymphoma Classification Project. J Clin Oncol 1998; 16:2780.
2. Goodlad JR, MacPherson S, Jackson R, Batstone P, White J. Extranodal follicular lymphoma: a clinicopathological and genetic analysis of 15 cases arising at non-cutaneous extranodal sites. Histopathology. 2004; 44:268-276.
3. Misdraji, J., N. Harris, and J. Ferry . Follicular lymphoma of the gastrointestinal tract. *Ann Oncol*. 2007; 18:109.
4. Pimpinelli, N. , E. Berti , and G. Burg . et al. Cutaneous follicle centre lymphoma. In: LeBoit P, Burg G, Weedon D, Sarasin A, eds. *Pathology and Genetics of Skin Tumours*. Lyon,

France: IARC Press; 2006:196–197. *World Health Organization Classification of Tumours*.
5. Ferry, J., C. Fung, and L. Zukerberg . et al. Lymphoma of the ocular adnexa: a study of 353 cases. Am J Surg Pathol 2007. 31:170–184.
6. Bacon, C., H. Ye , and T. Diss . et al. Primary follicular lymphoma of the testis and epididymis in adults. Am J Surg Pathol 2007. 31:1050–1058.
7. American Cancer Society. Cancer facts & figures, 2008. Available athttp://www.cancer.org/Research/CancerFactsFigures/cancer-facts-figures-2008. Accessed February 9, 2011.
8. Jaglowski SM, Linden E, Termuhlen AM, Flynn JM. Lymphoma in adolescents and young adults. *Semin Oncol*. 2009; 36: 381-418.
9. Swerdlow S, Campo E, Harris NL, eds; International Agency for Research on Cancer. *WHO Classification of Tumours of Haematopoietic and Lymphoid Tissue*. Geneva, Switzerland: World Health Organization; 2008.
10. Swenson WT, Wooldridge JE, Lynch CF, Forman-Hoffman VL, Chrischilles E, Link BK. Improved survival of follicular lymphoma patients in the United States. *J Clin Oncol*. 2005; 23: 5019-5026.
11. Kridel R, Sehn LH, Gascoyne RD. Pathogenesis of follicular lymphoma. *J Clin Invest*. 2012; 122:3424-3431.

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