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Case Report

A rare entity: Richter transformation presented with spontaneous tibia fracture

Nadir Bir Vaka: Spontan Tibia Kırığı ile Presente Olan Richter Transformasyonu

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ABSTRACT

Richter syndrome (RS) is defined as the transformation of chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma into an aggressive lymphoid malignancy. The incidence of RS varies from 1% to 9% and it is generally characterized by an aggressive clinical course. The case is here reported of CLL patient with RS and its unique presentation with bone involvement. RS is a heterogeneus condition that is characterised by an aggressive presentation, with low treatment response rates and and very poor survival. Lymph none and Bone marrow are mainly involved but extra-nodal involvement is also observed. Our patient is the first case of RS with bone involvement.

Keywords: Bone lesion, Chronic lymphocytic leukaemia, lymphoma, Ritchter syndrome,

ÖZ

Richter sendromu (RS), kronik lenfositik lösemi/küçük lenfositik lenfomanın agresif lenfoid maligniteye dönüşmesi olarak tanımlanır. RS insidansı %1 ile %9 arasında değişir ve genellikle agresif bir klinik seyir gösterir. Sunulan olgu, KLL tanısı ile izlenen ve kemik tutulumu ile atipik şekilde presente olan RS vakasıdır. RS, düşük tedavi yanıt oranları ve kötü sağkalım ile karakterizedir. Esas olarak lenf nodu ve kemik iliği tutulur ancak vakamızdaki gibi ekstra nodal tutulumlar da görülebilir. Hastamız kemik tutulumu olan ilk RS olgusudur.

Anahtar kelimeler: Kemik lezyonu, Kronik lenfositik lösemi, lenfoma, Ritchter sendromu,

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Introduction

The most common type of leukaemia in adults is chronic lymphocytic leukaemia (CLL) [1]. Richter syndrome (RS) is the transformation of chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) into an aggressive lymphoid malignancy [2]. The incidence of RS has been reported to vary from 1% to 9% in large series [3]. CLL most commonly transforms into diffuse large B-cell lymphoma (DLBCL) in 90–95% of cases [4].

RS is generally characterized by an aggressive clinical course that presents with fever without infection, weight loss, night sweats, massive splenomegaly and rapidly enlarging lymph nodes. Lactate dehydrogenase (LDH) and beta-2 microglobulin levels are dramatically increased [5].

Richter's syndrome most frequently affects lymph nodes (LN) and bone marrow (BM) but extra-nodal localizations such as the gastrointestinal tract, skin, liver, or tonsils may also be involved [6, 7]. The gold standard for establishing diagnosis is a biopsy of an enlarging LN or the involved tissues.

Herein, we reported our unique RS case who presented with bone involvement. To our knowledge, bone involvement in RS has not been previously reported in the literature.

Case Report

A 66-year-old female patient was diagnosed with stage 2 CLL, 2 years ago, was followed up for 18 months without treatment. At 18 months after the diagnosis, spontaneous bone fracture developed in the right tibia. On radiographic examination, bone lesion was also detected in the fracture line (figure 1-2). Morever the patient had complained of B symptoms such as fatigue, night sweating and weight loss. In blood examinations; white blood count (WBC) was 13300 µL, hemoglobin was 8.8 gr/dl, and platelet count was 145000 µL. Renal and liver function tests were normal and the lactate dehydrogenase (LDH) level (540 U/L) and beta-2 microglobulin (4,2 mg/L) were detected elevated. Patient operated and the lesion was totaly excised by department of orthopedics and traumatology. Biopsy from the bone lesion showed DLBCL (non germinal centre type; c-myc, bcl-2, bcl-6, MUM1: positive; ki-67 proliferation index:%90). Mutation analysis of 17p deletion was negative. A PET-CT scan revealed multiple LAP with abnormal FDG uptake in the neck and thorax, in addition to the lesion in the tibia. The patient was diagnosed as ritchter sydrome; stage-4 DLBCL and R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone) chemotherapy was planned. After 6 cycles of chemotherapy, the lymph nodes and tibial lesion regressed completely. Also, B symptoms was disappeared. The patient achieved complete remission (CR) according to PET-CT imaging. At 20 months after diagnosis, the patient is still being followed up without treatment in CR.

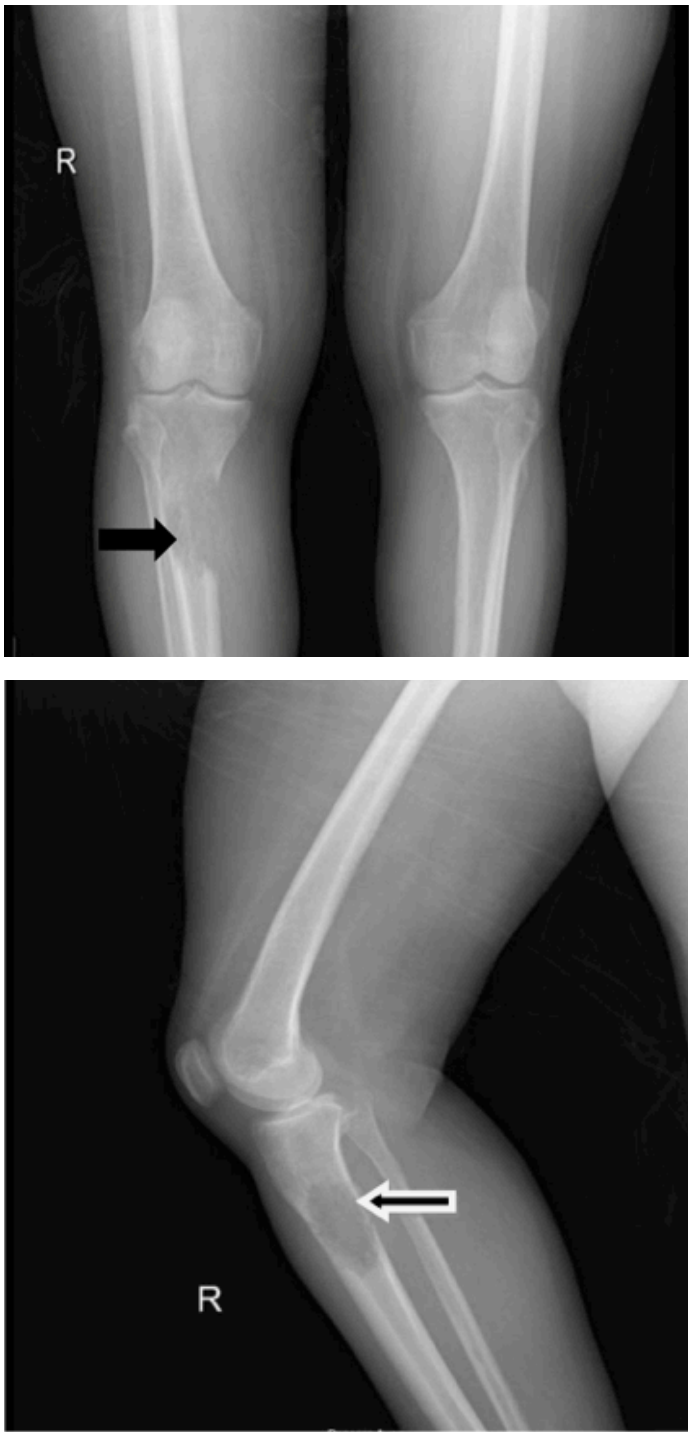

Figure 1-2 : Bone lesion on radiography

Discussion

In approximately 2%–10% of CLL patients, aggressive lymphoma transformation, known as RS, can develop [8]. RS independent from the CLL duration, stage, treatment or response to treatment [7]. In the past, RS was generally believed to be a late complication of CLL. However recent studies have demonstrated the median time to transformation of 1.8–1.9 years [7, 9]. In accordance with the literature, in the current case, the time to Richter transformation was 18 months after CLL diagnosis.

Risk factors for transformation to RS that have been identified in previous studies include clinical, biological and genetic characteristics. Germline (over-expression of CD38 and ZAP70, unmutated immunoglobulin heavy chain variable gene [IGHV]) and somatic (TP53 and NOTCH1 disruption, c-myc activation, CDKN2A loss) genetic mutations are associated with an increased risk of RS. Cytogenetic factors such as del(13q), del(11q) and del(17 p) are also thought to contribute to the development of RS. In the current patient, conventional cytogenetic examinations were performed and neither 17p deletion nor 11q deletion was detected. It has been shown that advanced Rai stage and adenopathy >3 cm are major clinical risk factors related to the development of RS [7].

An 18F-FDG PET/CT scan is important to identfy the optimal site of the biopsy, and to determine the extent of the disease [10].

Although lymph nodes and BM are mainly involved in RS, extra-nodal involvement such as in the gastrointestinal system, eyes, testicles, central nervous system, lung, kidneys or skin has also been reported [6]. Extranodal bone involvement has not been reported in the literature as in our patient.

RS has a poor prognosis and is resistant to chemotherapy. The median overall survival (OS) rate has been reported to be less than 1 year [11]. The most common first-line chemotherapy is RCHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone) [12]. Recent studies showed the effectiveness of novel treatments such as idelalisib, ibrutinib and venetoclax [13]. Stem cell transplantation (SCT) may be an option in only selected patients due to older age, poor performance status, and comorbidities [14]. The current patient received R-CHOP CT regimen and fully responded the treatment. Patient who has been diagnosed RS 24 months ago, is still alive and has being followed in remission.

In summary, RS is a heterogeneus condition that is characterised by an aggressive presentation, with low treatment response rates and and very poor survival. LN and BM are mainly involved but extra-nodal involvement is also observed. Our patient is the first case of RS with bone involvement. In this context, it is important not to ignore the multisystemic approach in hematological diseases.

Compliance With Ethical Standards

Conflict of interest: The Authors declare that there is no conflict of interest.

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Ethical approval: This article does not contain any studies with human participants or animals performed by any of the authors.

References

1. Hallek, M., Chronic lymphocytic leukemia: 2017 update on diagnosis, risk stratification, and treatment. American journal of hematology, 2017. 92(9): p. 946-965.
2. Richter, M.N., Generalized reticular cell sarcoma of lymph nodes associated with lymphatic leukemia. The American journal of pathology, 1928. 4(4): p. 285.
3. Molica, S., A systematic review on Richter syndrome: what is the published evidence? Leukemia & lymphoma, 2010. 51(3): p. 415-421.
4. Rossi, D. and G. Gaidano, Richter syndrome. Adv Exp Med Biol, 2013. 792: p. 173-91.
5. Seymour, J. and J. Campbell, Richter's syndrome. BASIC AND CLINICAL ONCOLOGY, 2001. 26: p. 459-484.
6. Omoti, C.E. and A.E. Omoti, Richter syndrome: a review of clinical, ocular, neurological and other manifestations. British journal of haematology, 2008. 142(5): p. 709-716.
7. Rossi, D., et al., Biological and clinical risk factors of chronic lymphocytic leukaemia transformation to Richter syndrome. British journal of haematology, 2008. 142(2): p. 202-215.
8. Parikh, S.A. and T.D. Shanafelt, Risk factors for Richter syndrome in chronic lymphocytic leukemia. Current hematologic malignancy reports, 2014. 9(3): p. 294-299.
9. Parikh, S.A., et al., Diffuse large B-cell lymphoma (R ichter syndrome) in patients with chronic lymphocytic leukaemia (CLL): a cohort study of newly diagnosed patients. British journal of haematology, 2013. 162(6): p. 774-782.
10. Falchi, L., et al., Correlation between FDG/PET, histology, characteristics, and survival in 332 patients with chronic lymphoid leukemia. Blood, 2014. 123(18): p. 2783-2790.
11. Tadmor, T., et al., Richter's transformation to diffuse large B-cell lymphoma: A retrospective study reporting clinical data, outcome, and the benefit of adding rituximab to chemotherapy, from the I sraeli CLL S tudy G roup. American journal of hematology, 2014. 89(11): p. E218-E222.
12. Jenke, P., et al., Cyclophosphamide, adriamycin, vincristine and prednisone plus rituximab (CHOP-R) in fludarabine (F) refractory chronic lymphocytic leukemia (CLL) or CLL with autoimmune cytopenia (AIC) or Richter's transformation (RT): final analysis of a phase II study of the German CLL Study Group. 2011, Am Soc Hematology.
13. Eyre, T.A. and A. Schuh, An update for Richter syndrome–new directions and developments. British journal of haematology, 2017. 178(4): p. 508-520.
14. Rossi, D., et al., The genetics of Richter syndrome reveals disease heterogeneity and predicts survival after transformation. Blood, 2011. 117(12): p. 3391-3401.