doi: 10.5262/tndt.2018.1001.11

Rapidly Progressive Renal Failure and Multiple Primary Extranodal Involvement in a Patient with CD5 Positive Diffuse Large B Cell Lymphoma

CD 5 Pozitif Diffüz Büyük B Hücreli Lenfomalı Hastada Multiple Primer Ekstranodal Tutulum ve Hızlı İlerleyen Renal Yetmezlik

ABSTRACT

CD5 positive diffuse large B cell lymphoma is a very rare subtype of diffuse large B cell lymphoma with an aggressive lymphoid neoplasm. Extranodal involvement of lymphoma usually appears secondarily in the setting of disseminated disease, but the disease may originate from various extralymphatic organs. We present a case of primary extranodal lymphoma with coexistence of skin and renal involvement with rapidly progressive renal failure due to lymhpomatous infiltration. Renal biopsy revealed diffuse infiltration of the renal parenchyma by CD20+ atypical lymphoid cells. The patient was treated with rituximab, cyclophosphamide, doxorubicin, vincristine and prednisolone. After the chemotherapy regimen, a dramatic improvement in the clinical picture was noticed.

KEY WORDS: CD5 positive diffuse large B cell lymphoma, Primary extranodal lymphoma, Rapidly progressive renal failure, Renal biopsy

ÖZ

CD5 pozitif diffüz büyük B hücreli lenfoma, diffüz büyük B hücreli lenfomanın agresif seyreden nadir bir subtipidir. Lenfomada ekstranodal tutulum genellikle hastalığın yayılımı sırasında sekonder olarak ortaya çıkar, fakat hastalık birçok ekstralenfatik organdan gelişebilir. Biz burada cilt ve böbrek tutulumunun eş zamanlı gözlendiği ve lenfomatöz infiltrasyona bağlı hızlı ilerleyen renal yetmezlikli primer ekstranodal lenfoma olgusunu sunmayı amaçladık. Renal biyopside CD20+ atipik lenfoid hücrelerin diffüz infiltrasyonu görüldü. Hasta rituksimab, siklofosfamid, doksorubisin, vinkristin ve prednizolon ile tedavi edildi. Kemoterapi sonrası, klinik tabloda anlamlı iyileşme gözlendi.

ANAHTAR SÖZCÜKLER: CD5 pozitif diffüz büyük B hücreli lenfoma, Hızlı ilerleyen renal yetmezlik, Primer ekstranodal lenfoma, Renal biyopsi

Şiyar ERDOĞMUŞ[1]
Seçil SARAL[2]
Pelin ERTOP[2]
Tolga AYDIN[1]
Gizem KUMRU[1]
Gülşah KAYGUSUZ[3]
Kenan KEVEN[1]
Neval DUMAN[1]
Şule ŞENGÜL[1]

1 Ankara University Faculty of Medicine, Department of Nephrology, Ankara, Turkey
2 Ankara University Faculty of Medicine, Department of Dermatology, Ankara, Turkey
3 Ankara University Faculty of Medicine, Department of Pathology, Ankara, Turkey

INTRODUCTION

Extranodal involvement of lymphoma is most often seen along with dissemination of systemic disease. About one-third of patients with non-Hodgkin's lymphoma (NHL) present with disease originating in diverse extralymphatic organs and are referred to as primary extranodal lymphoma. Primary extranodal lymphoma can occur in almost every organ. Most common presentation of primary extranodal lymphoma is gastrointestinal involvement followed by skin. Genitourinary tract (e.g., kidney, testis, ovary) is less common manifestation of the disease (1-4). Herein, we describe a 61-year-old male patient with skin involvement of primary extranodal lymphoma, who developed rapidly progressive renal failure requiring hemodialysis due to lymphomatous infiltration.

CASE PRESENTATION

A 61-year-old male was admitted to our hospital with one year history of growing red-purple skin lesions. The patient's medical history had no comorbidities. He denied use of alcohol, tobacco, and drugs. Upon physical examination, there were numerous erythematous macular, plaque, and nodular type of lesions on the anterior trunk (Figure 1A). There was no lymphadenopathy, hepatosplenomegaly, and edema. His blood pressure was 110/60 mm Hg.

Received : 28.02.2017
Accepted : 21.04.2017

Correspondence Address:
Şiyar ERDOĞMUŞ
Ankara Üniversitesi Tıp Fakültesi,
Nefroloji Bilim Dalı,
Ankara, Turkey
Phone : +90 312 508 21 68
E-mail : si.yar21@hotmail.com

Laboratory workup showed a white blood cell count of 9000 cells/μL, a hemoglobin level of 9.7 g/dL, a hematocrit of 31%, and a platelet count of 458,000 cells/ μL. His serum creatinine level was 2.7 mg/dL (corresponding to estimated glomerular filtration rate of 24 ml/min/1.73 m^2 as calculated by the CKD-EPI [Chronic Kidney Disease Epidemiology Collaboration] equation). Other blood work included calcium level of 9.8 mg/dL, phosphate level of 4.2 mg/dL, uric acid level of 6.9 mg/dL, and lactate dehydrogenase level of 142 U/L. On a spot urine sample, protein level was 30 mg/dL, with no hematuria, and no red blood cell or white blood cell casts. Skin biopsy was done. Then, he was referred to the nephrologist for evaluation of elevated creatinine, and proteinuria.

Further laboratory tests showed antinuclear antibody, antineutrophil cytoplasmic antibody, human immunodeficiency virus, and hepatitis B and C serologic test results negative. Serum complement levels were within the reference ranges. Serum protein electrophoresis, and immunofixation showed no monoclonal proteins. 24-hour urine protein level was 1.2 g/day. Renal ultrasonography demonstrated the right kidney as 13 cm and the left kidney 16 cm with no evidence of hydronephrosis, and bilateral slightly increased parenchymal echogenicity. Chest X-ray was unremarkable. Noncontrast computed tomography (CT) scan of the neck-thorax-abdomen was performed but no pathologic finding was found, except bilateral kidney enlargement.

At follow-up, renal function continued to deteriorate. Serum creatinine was increased at 6.9 mg/dL from a baseline creatinine of 1 mg/dL obtained one month prior. As the patient's urinary output was gradually decreased, and serum creatinine levels rapidly increased with metabolic acidosis, hemodialysis was started. Subsequently, we performed percutaneous tru-cut renal biopsy for rapidly progressive renal failure.

Skin biopsy from the nodular lesion was characterized by the infiltration of atypical large lymphoid cells in a diffuse manner (Figure 2A). Immunohistochemically, the tumor cells were positive for CD20, CD5, and BCL6 (Figure 2C,D), whereas CD10, BCL2, and MUM1 were negative. Ki-67 proliferation index was 90% (Figure 2E). EBV encoded RNA (EBER) by chromogenic in situ hybridization was negative. t(11;14) by FISH was not seen. The rearrangement of BCL2, BCL6 or MYC genes could not studied. Microscopic examination showed extensive infiltration of the renal parenchyma by atypical lymphoid cells (Figure 2B). Immunohistochemically, positive staining with CD20 on the neoplastic cells was determined (Figure 2F). In addition, immunofluorescence microscopy was negative for immunoglobulins and complement components on the glomeruli. In according to these findings, the diagnosis of CD5 positive diffuse large B cell lymphoma (CD5+ DLBCL) with germinal centre B-cell phenotype was made. Bone marrow biopsy was also performed and no infiltration with lymphomatous cells was found.

Chemotherapy regimen including rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisolone (R-CHOP) was commenced. After a cycle of chemotherapy, the clinical course improved. His serum creatinine levels dropped and the need for hemodialysis was disappeared. At discharge, patient's serum creatinine level was 2.1 mg/dL.

After five cycles of R-CHOP regimen, patient's CT imaging finding completely regressed, creatinine level returned to normal limits, and skin lesions disappeared (Figure 1B). The patient is still followed and treated by the hematology clinic.

DISCUSSION

NHL, may also arise from sites other than lymph nodes and even from sites which are normally without lymphoid tissue. The gastrointestinal tract, in particular the stomach is the most

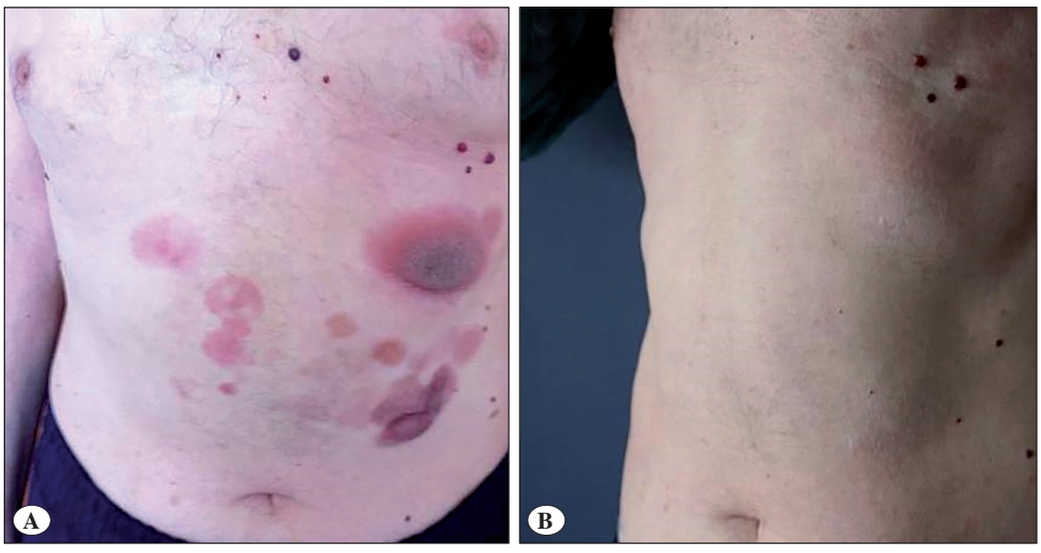

Figure 1: *Skin lesions in the patient before and after initiation of treatment.* ***A)*** *Skin involvement of CD5-positive diffuse large B cell lymphoma, erythematous macular, plaque and nodular lesions on the anterior trunk,*
B) *After chemotherapy skin lesions completely disappeared.*

often primary extranodal site, followed by skin and bone (1). The disease may also involve two or more extranodal sites (5). Although lymphomatous involvement of the kidney is more commonly seen secondarily to spread of systemic disease, primary renal lymphoma is not a common clinical entity (6). Kidney involvement in a lymphoma patient usually presents as either direct invasion of retroperitoneal mass, single and multiple renal mass, perirenal mass or with enlargement of kidney (7). The clinical presentation of the disease is associated with the type of lymphoma and the sites of involvement. DLBCL, which is an aggressive form and accounts for the majority of cases, is the most common histologic subtype of NHL (4).

CD5+ DLBCL, which is a subtype of DLBCL, is one of the immunohistochemical subgroups in 2008 WHO classification. Clinical features of patients with CD5+ DLBCL are associated with an aggressive clinical course, female preponderance, older age, advanced stage at diagnosis, and frequent extranodal

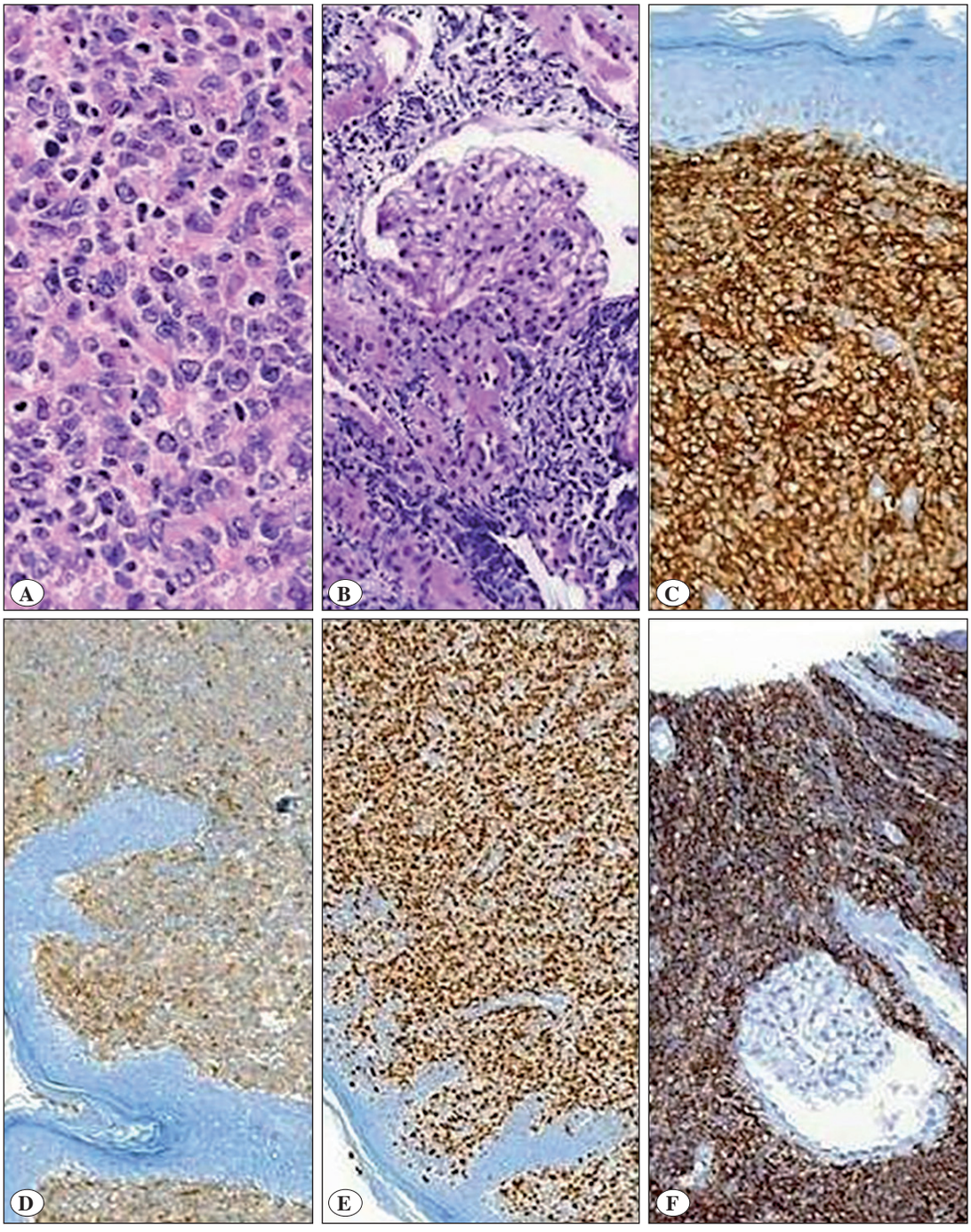

Figure 2: *Skin and renal involvement with biopsy.* ***A)*** *Atypical large lymphoid cells infiltrating the dermis (H&E 1010 x), and* ***B)*** *The renal interstitium (H&E 513 x).* ***C)*** *Immunohistochemically, the neoplastic cells infiltrating the dermis showed CD20 (443 x), and* ***D)*** *CD5 positivity (247 x), and* ***E)*** *Ki67 proliferation index was high (186 x).* ***F)*** *The tumor cells involving the renal parenchyma were also positive for CD20 (382x).*

involvement (8). The prognosis of CD5+ DLBCL is extremely poor and it is usually fatal without treatment. A prompt tissue diagnosis and treatment can increase survival and remission (9). Retrospective studies have shown that addition of rituximab to an anthracycline based chemotherapy regimen improves the outcomes of patients with CD5+ DLBCL (10).

Our patient presented with skin lesions, renal failure, and enlargement of kidneys. There were no causes of renal failure such as obstructive uropathy, hypercalcemia, uric acid nephropathy, volume depletion, and nephrotoxic drugs. Lymphomatous infiltration of the kidneys was diagnosed by tru-cut renal biopsy. Clinical course of disease and radiologic findings were consistent with primary extranodal lymphoma. In addition, following R-CHOP regimen, patient's clinical and laboratory findings improved.

In conclusion, in cases with primary extranodal lymphoma, it should be kept in mind that the disease can occur in many organs concurrently. Renal involvement of lymphoma should be considered in patients with bilateral kidney enlargement and unexplained renal failure.

CONFLICTS of INTEREST

The authors declare that they have no conflict of interest. The informed consent is obtained from the patient.

REFERENCES

1. Freeman C, Berg JW, Cutler SJ: Occurrence and prognosis of extranodal lymphomas. Cancer 1972;29:252-260
2. Zucca E, Roggero E, Bertoni F, Cavalli F: Primary extranodal non-Hodgkin's lymphomas. Part 1: Gastrointestinal, cutaneous and genitourinary lymphomas. Ann Oncol 1997;8:727-737
3. Zucca E, Roggero E, Bertoni F, Conconi A, Cavalli F: Primary extranodal non-Hodgkin's lymphomas. Part 2: Head and neck, central nervous system and other less common sites. Ann Oncol 1999;10:1023-1033
4. Vannata B, Zucca E: Primary extranodal B-cell lymphoma: Current concepts and treatment strategies. Chin Clin Oncol 2015;4:10
5. Economopoulos T, Papageorgiou S, Rontogianni D, Kaloutsi V, Fountzilas G, Tsatalas C, Pavlidis N, Pectasides D, Papageorgiou E, Dimopoulos M; Hellenic Cooperative Oncology Group: Multifocal extranodal non-hodgkin lymphoma: A clinicopathologic study of 37 cases in Greece, a Hellenic Cooperative Oncology Group study. Oncologist 2005;10:734-738
6. Stallone G, Infante B, Manno C, Campobasso N, Pannarale G, Schenna FP: Primary renal lymphoma does exist: Case report and review of the literature. J Nephrol 2000;13:367-372
7. Urban BA, Fishman EK: Renal lymphoma: CT patterns with emphasis on helical CT. Radiographics 2000;20:197-212
8. Miyazaki K: CD5-positive DLBCL: Molecular basis and treatment strategies. Rinsho Ketsueki 2015;56:1038-1044
9. Úbeda Romero A, Santonja C, Blanco García A, Requena L, Rodríguez Pinilla SM: De Novo CD5-positive diffuse large B-cell lymphoma: Report of a case presenting with cutaneous involvement and featuring extensive intravascular dissemination on postmortem examination. Int J Surg Pathol 2016;24:763-768
10. Jain P, Fayad LE, Rosenwald A, Young KH, O'Brien S: Recent advances in de novo CD5+ diffuse large B cell lymphoma. Am J Hematol 2016;88:798-802