Double-hit primary unilateral adrenal lymphoma with good outcome

**CASE REPORT**

Double-hit primarni limfom nadbubrežne žlezde sa povoljnim ishodom

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**Abstract**

**Introduction.** Primary adrenal non-Hodgkin’s lymphoma (NHL) is a rare neoplasm with poor prognosis. On the other side, double-hit lymphomas with BCL2 and MYC translocation are characterized by advanced disease stage, extranodal and central nervous system involvements at presentation or disease progression.

**Case report.** We reported a 73-year-old male patient with double-hit primary adrenal lymphoma and preserved adrenal function, showing a favorable clinical course. Computed tomography of abdomen showed a 9 × 7 cm mass of the left adrenal gland. Laparotomy with left adrenalectomy was done and histological examination revealed diagnosis of a diffuse large B-cell NHL (DLBCL), non-GCB subtype. The patient was treated with 6 cycles of R-CHOP chemotherapy with reduced doses of doxorubicin because of the decreased left ventricle ejection fraction. The patient was followed up regularly for 20 months with no evidence of tumor recurrence despite the inherently poor prognostic profile and double-hit phenotype of the disease.

**Conclusion.** R-CHOP chemotherapy in combination with adrenalectomy can be an effective first-line regimen for primary adrenal DLBCL, despite the inherently poor prognostic profile (non-GCB subtype, bulky disease, elevated lactate dehydrogenase and double-hit phenotype of the disease).

**Key words:**

lymphoma, non-hodkin; adrenal gland neoplasms; drug therapy; surgical procedures, operative; prognosis.

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Introduction

The adrenal gland is a rare site of primary extranodal non-Hodgkin lymphoma (NHL), accounting for less than 1% of all NHL cases and only 3% of primary extranodal lymphomas. Compared with nodal diffuse large B-cell NHL (DLBCL), primary adrenal DLBCL is frequently accompanied with many adverse features such as bulky disease, elevated lactate dehydrogenase (LDH), advanced clinical stage and adrenal insufficiency. Prognosis is poor and most patients die due to the progressive disease or its complications within one year after the diagnosis. Double-hit lymphomas with MYC and BCL-2 translocation are rare types of lymphoma (around 2% of NHL) with frequent extranodal disease and extremely poor prognosis. We presented the patient with double-hit primary unilateral adrenal lymphoma, with preserved adrenal function and good outcome.

Case report

A 73-year-old man, with complaints of abdominal pain, fatigue and weight loss for 4 months was admitted to the Hematology Department of the Clinical Hospital Center “Bežanijska kosa”, Belgrade, Serbia. The patient had acute myocardial infarction in 2007 and underwent gastrectomy due to bleeding of gastric ulcer 12 years ago. His past medical history was also significant for alcohol abuse (20 years) and cigarette smoking (55 years). Hematological analysis showed mild anemia (hemoglobin level of 103 g/L). Blood biochemistry showed elevated LDH (920 U/L). Ultrasonography and computed tomography (CT) of abdomen demonstrated a 9 × 7 cm mass of the left adrenal gland, without splenomegaly or abdominal lymphadenopathy. The patient was referred to the Endocrine Surgery Clinic where left adrenalectomy was done in May 2011.

Histological examination of adrenal tumor revealed diagnosis of DLBCL, non-germinal center B-cell (non-GCB) subtype with following immunophenotype: EMA-, LCA+, PAX5+, inhibin-, synaptophysin-, CD79+, CD20+, CD5-, CD3-, CD10-, CD30-, CD38-, Mum-1+, BCL2+, BCL6-, ALK-1-, Ki-67 (positive in 60% of lymphoma cells). Fluorescence in situ hybridization (FISH) showed MYC(q24) and BCL2(q21) rearrangement. In June 2011 the patient was referred back to the Hematology Department. The clinical examination showed pale skin without superficial lymphadenopathy or organomegaly. A serum biochemistry profile showed elevated LDH (506 IU/L) and β2 microglobulin of 4.3 mg/L. Serum sodium, potassium and calcium levels were normal. Endocrinology assessment proved that the patient was euthyroid and eucortisolemic. Mineralocorticoid function and the function of adrenal medulla were also intact. Thoracic CT scan did not show any lymph node enlargement. CT of brain revealed only a few old ischemic lesions. Cerebrospinal fluid sediment did not show any lymphoid cells. Bone marrow trephine biopsy showed no lymphoid infiltration. Echocardiography showed reduced ejection fraction (40%) and aneurysmatic dilatation of the inferior left ventricular wall. Therefore, the patient received immunochemotherapy regimen rituximab–cyclophosphamide/doxorubicin (hydroxydaunomycin)/vincristine (Oncovin®)/prednisolone (R-CHOP) with reduced doses of an anthracycline (doxorubicin 25 mg/m2 i.v. every 3 weeks). After 6 cycles of R-CHOP chemotherapy the patient was in good condition with no evidence of tumor on fludeoxyglucose – positron emission tomography (FDG-PET) scans. The patient was followed regularly in our Outpatient Hematology Clinic. On the
last follow-up (January, 2013), the patient was in good clinical condition, with no evidence of lymphoma recurrence.

**Discussion**

Primary adrenal non-Hodgkin’s lymphoma (PAL) is a rare neoplasm with approximately 120 cases reported worldwide. The disease most frequently affects older men with the mean age of 68 years at diagnosis. The symptoms of the disease and response to treatment vary depending on the type of lymphoma, tumor size, and the presence of adrenal failure. Literature data based mostly on case reports, revealed a high rate of bilateral involvement (60–79% of cases) and adrenal failure (67–69% of cases). Nodal and extranodal disease in PAL is rare at diagnosis. However, involvement of unusual extranodal organs is often reported at the disease relapse. The most frequent histological subtype of PAL is a diffuse large non-GCB subtype. The presented patient had typical age, histology and symptoms for PAL, but he presented without bilateral involvement and consecutive adrenal failure.

The pathogenesis of PAL is not clear. Immune deregulation may predispose to PAL as well as to certain other lymphomas in some patients. Proposed hypothesis for the occurrence of PAL includes preexisting autoimmune adrenalitis with lymphocyte infiltration, although not conclusively proven due to the rarity of both autoimmune adrenalitis and lymphomas. It is supported by frequent development of adrenal failure in patients with lymphoma than in patients with bilateral adrenal metastases. Namely, adrenal failure occurs in 1% of patients with adrenal metastasis and only when more than 90% of the adrenal tissue is destroyed. In contrast, a very high frequency of primary adrenal failure (60–70%) has been reported in patients with PAL, including patients with mildly enlarged adrenal glands.

Given the rarity of PAL, the optimal therapeutic modality is poorly defined. Available data on outcomes of patients treated by chemotherapy, unilateral or bilateral adrenalectomy, and/or adjuvant radiotherapy gave inconclusive results. In earlier trials of CHOP or CHOP-like therapy, the results of PAL treatment have been disappointing; a review of the literature data has shown that most patients died due to the disease or its complications within one year after diagnosis. In contrast, Kim et al. have recently reported that treatment outcomes with R-CHOP for primary adrenal DLBCL were not inferior to those of nodal DLBCL.

**Conclusion**

This first published case of double-hit primary adrenal lymphoma in Serbia suggests that R-CHOP chemotherapy in combination with adrenalectomy can be an effective first-line regimen for primary adrenal diffuse large B-cell lymphoma, despite the inherently poor prognostic profile and double-hit phenotype of the disease.

**REFERENCES**


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