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Double-Hit Lymphoma Presenting with Aggressive Progression: A Case Report

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Abstract

Double-Hit lymphoma is an aggressive B-cell malignancy with a high proliferative rate that may be fatal within months if not treated promptly. We presented a very aggressive and fatal case of a Double-Hit Lymphoma. 18 years old male patient referred Ear-Nose-Throat outpatient clinic due to swelling under the chin and an excisional biopsy was performed. High grade Burkitt like lymphoma CD20 (+) was reported. Approximately 12 months after diagnosis patient who was accepted as a stage IIIB according to Ann-Arbor staging system died of disease progression despite the various treatment protocols of high dose chemotherapy followed by autologous bone marrow transplantation. Double-Hit lymphoma is aggressive and can be fatal. Therefore, treatment should be initiated without delay after diagnosis.

Key Words: Double-Hit Lymphoma; Burkitt Like Lymphoma; Aggressive; Bone Marrow Transplantation.

Agresif Seyreden Double-Hit Lenfoma: Bir olgu sunumu

Özet

Double-Hit lenfoma acil tedavi edilmez ise aylar içinde ölümcül olabilen kötü seyirli B hücreli lenfomadır. Biz burada kötü seyirli giden fatal seyreden Double-Hit Lenfomalı erişkin bir olguyu sunduk. 18 yaşındaki erkek hasta Kulak Burun Boğaz polikliniğine çene altındaki şişlik nedeni ile başvurdu ve eksizyonel biopsi yapıldı. Hastanın biyopsisi CD20(+) Burkitt-like lenfoma olarak rapor edildi. Ann-Arbor evreleme sistemine göre evre IIIB kabul edilen hasta tedavi protokolündeki kemoterapotiklere ve yüksek doz kemoterapi eşliğinde otolog kemik iliği nakline cevap vermedi. Hastamız tanı konulmasından yaklaşık 12 ay sonra kaybedildi. Double-Hit lenfoma agresif gidişli olabilir ve fatal seyirli seyredebilir. Bu yüzden tanıdan sonra zaman kaybetmeden tedavi başlanmalıdır.

Anahtar Kelimeler: Double-Hit Lenfoma; Burkitt Like Lenfoma; Agresif; Kemik İliği Nakli.

INTRODUCTION

Double-hit lymphoma (DHL), atypical Burkitt lymphoma, Burkitt-like Lymphoma and gray zone lymphoma are expressions used to describe the same kind of lymphomas. DHL, unclassifiable, with features intermediate between Burkitt lymphoma (BL) and diffuse large B-cell lymphoma (DLBCL) (intermediate BL /DLBCL), is a heterogeneous group with some features resembling BL and others resembling DLBCL (1). DHL coverages translocations of both *MYC* and *BCL2* and are generally refractory to standard chemotherapy regimens and have a poor prognosis (2-4). Separation from the DLBCL for Double-hit lymphoma is important especially due to particularly since a high proportion of cases of BL can be cured with short, intensive, multiagent chemotherapy (e.g.Hyper-CVAD(course A: cyclophosphamide, vincristine, doxorubicin (also known as adriamycin), and dexamethasone. Course B consists of methotrexate and cytarabine.), CODOX-M (cyclophosphamide, vincristine, doxorubicin, high-dose methotrexate)/IVAC (ifosfamide, etoposide, high-dose cytarabine) usually with the anti-CD20 monoclonal antibody rituximab) and central nervous system prophylaxis, whereas conventional chemotherapy (R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone) is considered inadequate therapy for BL but represents a standard of care regimen for DLBCL (5). Bone marrow transplantation has proven feasible in many patient populations with DHL (6). We describe to agressive and fatal progression of DHL.

CASE REPORT

18 years old male patient was admitted to ENT (Ear, Nose, Throat) Clinic due to swollen mass in the right jaw (Figure 1).

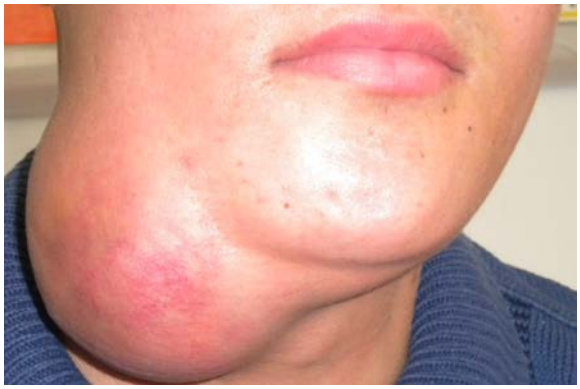

Figure 1. This patient presented with neck swelling on the right side of the neck**.**

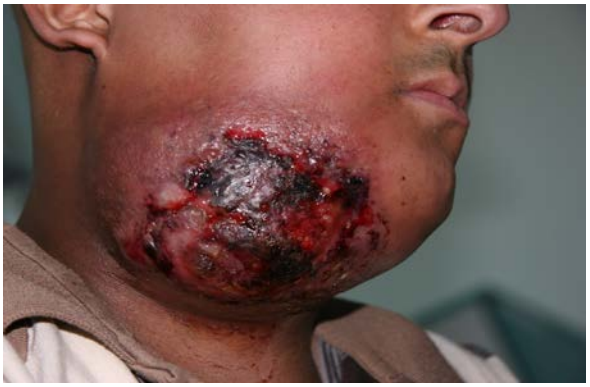

Figure 2. After treatment, photograph of a gross specimen shows necrotic-appearing mass lesion.

Solid mass was operated by the ENT clinic as excisional biopsy and a Ebstein Barr Virus (EBV)-negative, CD20(+), CD79A(+), CD10(+), Ki67 PI:%80-90(+), high-grade Burkitt-like lymphoma was reported. In the right submandibular region 4x3 cm solid lesion was detected by neck computed tomography (CT), appearance of conglomerate lymphadenopathy was detected in mesenteric by abdominal CT. There was no evidence with lymphoma in thorax CT and bone marrow. Patient with DHL who is accepted as stage IIIB according to Ann-Arbor was treated with 4 cycles of R-CHOP (Rituximab 600 mg on day 1, cyclophosphamide 1200 mg on day 1, adriamisin 80 mg on day 1, vincristine 2 mg on day 1, prednisone 100 mg on days 1 to 5). After chemotherapy patient whose neck mass no regression was accepted refractor and CODOX-M/IVAC protocol was planned to be administered. One cure CODOX-M (cyclophosphamide (1250 mg on day 1, 320 mg on days 2 to 5), doxorubicin 64 mg on day 1, vincristine 2 mg on days 1 and 8, high-dose methotrexate 4700 mg on day 10, intrathecal teratment (cytarabine 70 mg on days 1 and 3, methotrexate12 mg on day 15) / IVAC (etoposide 96 mg on days 1 to 5, ifosfamide 2400 mg on days 1 to 5, mesna 4000 mg on days 1 to 5, cytarabine 2x3200mg on days 1 to 2, intrathecal teratment (methotrexate 12mg on day 5) was given. Then, neck ultrasound was taken and seen as an approximately 6.4 x 4,7 cm sized heterogeneous, irregular, solid mass (Figure 2).

This situation was commented favor of progression. ICE(ifosfamide 8000mg on day 1, mesna 8000 mg on day 1, carboplatin AUC:5 760 mg on day 1, etoposide 160 mg on days 1 to 3) therapy was given as rescue therapy. The mass was not seen to regress at the end of the ICE treatment. CODOX-M/IVAC protocol was given again. Ultrasonography revealed a 1.7 x0,7 cm mass at the end of this treatment, this was evaluated as partial remission. High-dose chemotherapy (BEAM, karmustin 480 mg on day 1, etoposide 320mg on days 2 to 5, cytarabine 2×320 mg on days 2 to 5, melphalan 220 mg on day 6) followed by autologous stem cell transplantation was applied due to the mass which was chemosensitive. There was no sufficient regression after autologous stem cell transplantation. Therefore, radiotherapy was applied for the tumor mass (total dose 2400cGy). Patient was considered refractory DHL and allogeneic stem cell transplantation was planned. The mass was seen to progress quickly, increased respiratory distress and worsened general condition and patient died due to the progression.

DISCUSSION

DHL is an emerging disease concept in which concurrent BCL-2 and MYC translocation. Burkitt's and DHL (BL/DHL) are aggressive B-cell malignancies with a high proliferative rate that may be fatal within months if not treated promptly (6). The cases classified as DHL Lymphoma by the 2008 World Health Organization (WHO) Classification of Tumors of Hematopoietic and Lymphoid Tissue were thought to represent a continuum between BL and diffuse DLBCL. The optimal therapeutic strategy for this provisional

entity was not definitively established. Several retrospective studies suggest poorer outcome if atypical BL/DHL is treated with regimens designed for DLBCL instead of those typically used for BL (7). Clinical trials have demonstrated that short duration, multi-agent, dose-intensive chemotherapy regimens (e.g. CODOX-M/IVAC) combined with aggressive central nervous system therapy results in long-term survival rates in children and young adults near 70% to 80%, whereas long-term disease-free survival rates in older adults remains suboptimal at 15% to 25%. Autologous bone marrow transplantation has proven feasible in many patient populations with BL/DHL and may lead to cure in selected patients and in literature two cases of DHL successfully treated with an aggressive immunochemotherapy regimen, autologous bone marrow transplantation and radiation (6,8). At the same time, NCCN 2012 Guideline recommended allogeneic or autologous transplantation as consolidation regimen for the treatment of Burkitt's lymphoma. Our patient did not respond to conventional chemotherapies. Autologous stem cell transplantation was applied due to the mass which was be chemosensitive. However be progressed again, allogeneic bone marrow transplantation was planned, but it could not be performed. Early recognition of DHL is important for considering up-front total body irridation-based hematopoietic stem cell transplantation (9). DH lymphomas generally tended to have a poor survival, with a median overall survival of only 0.2-1.5 years (10). Our case died approximately 12 months after diagnosis. DHL is an emercing disease and should be think bone morrow transplantation. DH lymphoma, there is no standard therapy, but allogeneic SCT may have an advantage over autologous SCT at relapse. Transplantation is rarely successful for relapsed patients unless they are chemosensitive and ideally in a second CR

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