Ref: Ro J Med Pract. 2023;18(1)
DOI: 10.37897/RJMP.2023.1.5

Classic Hodgkin Lymphoma – mixed cellularity – case report and review of literature

Mihaela OPREA-LEBEDENCO[1,3], Nicoleta BERBEC[1], Oana STANCA[1], Andrei TURBATU[1], Stefan MARIN[3], Camelia DOBREA[2], Mihaela ANDREESCU[4], Anca Roxana LUPU[1]

[1]Department of Hematology, Coltea Clinical Hospital, Bucharest, Romania
[2]Department of Hematology, Fundeni Clinical Institute, Bucharest, Romania
[3]Ambulatory of Hematology, "Sf. Ioan" Emergency Clinical Hospital, Bucharest, Romania
[4]Department of Hematology, Colentina Hospital, Bucharest, Romania

Abstract

Hodgkin's lymphoma, formerly known as Hodgkin's disease, is a type of cancer of the lymphatic system, an important part of the site where immune processes take place. The disease can affect people of any age, but it is much more common in the age range of 20-40 years and in people over 55 years old. In Hodgkin's lymphoma, cells in the lymphatic system multiply uncontrollably and can spread outside of it. Advances in the diagnosis and treatment of Hodgkin's lymphomas present a chance for patients to achieve a complete remission of this type of cancer. The prognosis is constantly improving for people with this diagnosis.

This article will present the case of a 27-year-old patient with classic Hodgkin's lymphoma - histological subtype mixed cellularity - chemorefractory.

Keywords: Hodgkin lymphoma, mixed cellularity, chemorefractory

INTRODUCTION

Compared to many malignancies, Hodgkin's lymphoma has a very good prognosis, with a 10-year survival rate of 90% for early stages and 75% for advanced stages. Correct staging is essential in defining the patient groups that will benefit from more aggressive treatments. In this paper, we aimed to analyze the choice of targeted chemotherapy for the treatment of a case of chemorefractory Hodgkin's lymphoma [1-3].

CASE PRESENTATION

26-year-old patient, former smoker, underweight, with no significant personal pathological history, noticed the appearance of an inguinal adenopathy on the right side in 2015 - which progressively increased in size. In March 2016, he was admitted to the Surgery Clinic of "St. Ioan" Hospital, where excision of the right inguinal adenopathic block and the neighboring lymph nodes was performed, the histopathological and immunohistochemical examinations gave the diagnosis of classic Hodgkin's lymphoma, histological subtype mixed cellularity, stage II B [4].

The patient had night sweats and skin itching; in the rest - clinical examination within normal limits.

It was decided to initiate polychemotherapy courses, performing 4 ABVD type courses - with obtaining complete remission, remission confirmed by PET-CT.

The patient maintained complete remission for 18 months.

Corresponding author:
Mihaela Lebedenco
E-mail: mihaela.lebedenco@yahoo.com

Article History:
Received: 6 February 2023
Accepted: 14 February 2023

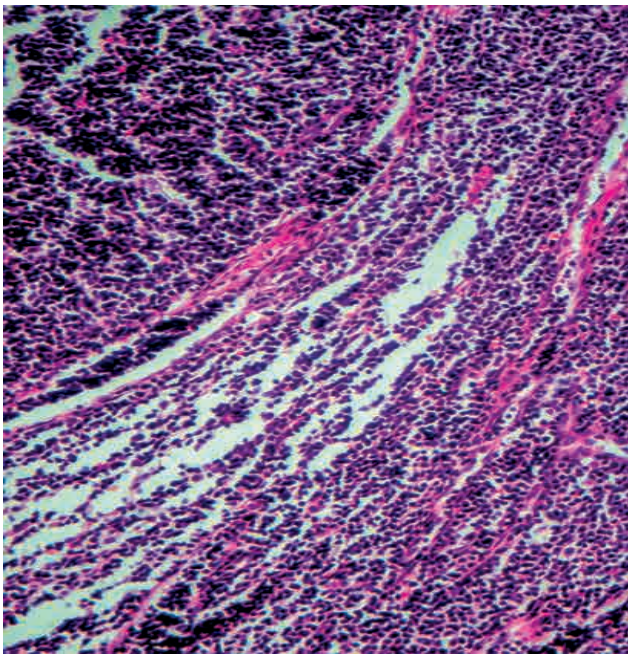

FIGURE 1. *PAS positive traves delimited by areas of classical Hodgkin lymphoma*

In January 2018, he was admitted to the Surgery Clinic of Coltea Hospital for the appearance of a tumor formation on the right side of the groin, which was biopsied, the histopathological and immunohistochemical examinations giving the same diagnosis: Hodgkin's lymphoma - mixed cellularity. The relapse was in stage IV B (with multiple bone lesions and subdiaphragmatic adenopathies).

It was decided to carry out BEACOPP polychemotherapy treatments, the control PET-CT examination in September 2018 revealed metabolically active lesions. MRI of the spine detects disease lesions.

It is decided that the disease is chemorefractory and chemotherapy is resumed in December 2018, performing 16 administrations of Brentuximab.

The PET-CT evaluation after the 16 administrations of Brentuximab highlights the progressive disease.

At this moment, the diagnosis is: Hodgkin's lymphoma - mixed cellularity, stage IV B, refractory to chemotherapy (no salvage treatment so far) and progression under Brentuximab.

On June 15, 2020, the patient had a second opinion with the following conclusions:

Nivolumab is only advisable for patients who have had a transplant and Brentuximab afterwards and have relapsed after these lines of treatment.

I don't believe Brentuximab and Nivolumab can be associated, as the patient has already had 16 infusions of Brentuximab.

Considering that the disease has progressed after being treated with Adcetris (Brentuximab), the advisable treatment would be **PEMBROLIZUMAB** or **CAR-T cell**.

The doctors initiated treatment with Pembrolizumab, with 9 infusions so far, during which the patient developed significant thrombocytosis (T>1000000/mm^3). The PET-CT performed on March 26, 2021 showed metabolically active lymphomatous determinations in the bones, metabolic progression in the splenic lymphomatous determinations and in the adenopathies situated above the clavicle, in both armpits and in the abdomen/pelvis. The PET-CT aspect suggests a disease in progression (Deauville 5).

A consultation is requested in the Hematology Department of the University Hospital of Turin-Italy, where the initiation of V-line treatment with chemotherapy according to the BeGEV scheme is indicated. 4 cycles with BEGEV are performed, with a positive response, which is why treatment with FEAM+ ASCT is initiated (hospitalization between 01.20.2023 and 02.06.2023). Chemotherapy was initiated with a view to the transplant, which included an infusion of Fotemustine 504 mg on 20.01.2023, Cytarabine 336 mg every 12 hours and Etoposide 168 mg every 12 hours between 21.01-24.01.2023, Melphalan 235.2 mg on 25.01.2023. The treatment was well tolerated, and on 27.01 peripheral stem cells were administered in the amount of 3.31 x 10'6/kg CD34 positive cells [5-8].

Pegfilgastrim was administered on 28.01.2023. The next stage of aplasia was complicated by grade I-II gastro-intestinal mucositis which involved parenteral nutrition for several days and an episode of hyperthermia on 30.01.2023 with a positive blood culture for E Coli nonESBL; chest x-ray within normal limits, Covid-negative test; treatment was carried out with Piperacillin/Tazobactam and Amikacin. The fever went down on 31.01. During the hospitalization, sampling was performed for the patient's HLA.

Latest analyzes (04.04.2023): Leukocytes = 3940/mm^3, Hb=13.2 g/dl, Platelets = 177000/mm^3; biochemistry – within normal limits.

CT-TAP from 21.03.2023: stationary appearance, no disease progression, no active disease.

DISCUSSIONS

The patient did not undergo rescue chemotherapy: IGEV or DHAP and then auto-transplant, and I do not know if performing them after the administration of 16 courses with Brentuximab could have brought the patient any benefit. Nivolumab is only indicated for patients who have had a transplant and subsequently Brentuximab and have relapsed after these mentioned lines of treatment, so the patient is not eligible for this type of treatment. I don't think that combining Brentuximab+Nivolumab in the conditions where the patient has already performed the 16 administrations of Brentuximab would have brought any benefit. Consid-

ering that the patient had progressive disease after Adcetris, he was indicated for Pembrolizumab or CAR-T cell outside the country [9-12].

CONCLUSIONS

Diagnosis of pluri-refractory Hodgkin's lymphoma, already subjected, starting from 2016, to treatment with ABVD, BEACOPP, Brentuximab and Pembrolizumab, disease in evolution subjected to treatment with Pembrolizumab. Treatment with BEGEV is initiated, performing 4 cycles. Later FEAM+ASCT- with good evolution.

Conflict of interest: none declared
Financial support: none declared

REFERENCES

1. Ferry JA, Linggood RM, Convery KM et al. Hodgkin disease, nodular sclerosis type. *Implication of histologic subclassification.* Cancer 1993;71:457-463.
2. Gociu M. Hodgkin's disease. In Paun R, ed. Treatise on internal medicine Hematology part II. *Bucharest: Medical Publishing House;* 1999. p. 367-393.
3. Greenlee RT, Hill-Harmon MB, Murray T, Thun M. Cancer statistics, 2001. *CA Cancer J Clin.* 2001 Jan-Feb;51(1):15-36.
4. Hueltenschmidt B, Sautter-Bihl ML, Lang O, Maul FD, Fischer J, Mergenthaler HG, Bihl H. Whole body positron emission tomography in the treatment of Hodgkin disease. *Cancer.* 2001 Jan 15;91(2):302-10.
5. Jemal A, Thomas A, Murray T, Thun M. Cancer statistics, 2002. *CA Cancer J Clin.* 2002 Jan-Feb;52(1):23-47.
6. Jemal A, Murray T, Samuels A, Ghafoor A, Ward E, Thun MJ. Cancer statistics, 2003. *CA Cancer J Clin*. 2003 Jan-Feb;53(1):5-26.
7. Jemal A, Tiwari RC, Murray T, Ghafoor A, Samuels A, Ward E et al. American Cancer Society. Cancer statistics, 2004. *CA Cancer J Clin*. 2004 Jan-Feb; 54(1):8-29.
8. Jemal A, Murray T, Ward E, Samuels A, Tiwari RC, Ghafoor A et al. Cancer statistics, 2005. *CA Cancer J Clin.* 2005 Jan-Feb;55(1):10-30.
9. Josting A, Engert A, Diehl V, Canellos GP. Prognostic factors and treatment outcome in patients with primary progressive and relapsed Hodgkin's disease. *Ann Oncol.* 2002;13 Suppl 1:112-6.
10. Masih AS, Weisenburger DD, Vose JM et al. Histologic grade does not predict prognosis in optimally treated, advanced-stage nodular sclerosing Hodgkin's disease. *Cancer* 1992; 69:228-232.
11. Pileri SA, Ascani S, Leoncini L, Sabattini E, Zinzani PL, Piccaluga PP et al. Hodgkin's lymphoma: the pathologist's viewpoint. *J Clin Pathol.* 2002 Mar;55(3):162-76.
12. Zander T, Wiedenmann S, Wolf J. Prognostic factors in Hodgkin's lymphoma. *Ann Oncol.* 2002;13 Suppl 1:67-74.