

## MEDIASTINAL MASS AS A PROGNOSTIC FACTOR OF HODGKIN LYMPHOMA – CASE REVIEW

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Many studies have researched the prognostic factors of Hodgkin disease. Up date, seven most important prognostic factors have been defined.

Among them, as an important negative prognostic factor, the dissemination of the disease at the moment of diagnosis stands out. The aim of this study was to determine the influence of the presence of mediastinal mass greater than a third of the chest diameter in Hodgkin lymphoma on the disease outcome. In this study, an 18-year-old patient P.A. was presented. At the time of diagnosis, the patient had Bulky disease. Mediastinal mass was observed by radiography, computed tomography, ultrasound of the heart.

The patient was treated with ABVD, GDP, BEACOPP, miniBEAM protocol and mediastinal radiation. In this patient, the mediastinal mass persisted in spite of the therapy.

The course of disease deteriorated due to the presence of resistant pericardial effusion, and the patient died three years after. *Acta Medica Medianae 2008;47(4):25-28.*

**Key words:** mediastinal mass, Hodgkin disease, prognostic factor

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### Introduction

Lymphomas belong to the group of diseases associated with chronic lymphocytic leukemia and immunoproliferative diseases. There are two main types of lymphoma: non-Hodgkin lymphoma (NHL) and Hodgkin lymphoma (HL)(1).

Mediastinal lymph gland is present in about 60% of HD patients whereas approximately 20% in patients with NHL (2,3). The most frequent Hodgkin lymphoma involving mediastinum is a nodular sclerosis type, non-Hodgkin lymphoma and primary mediastinal B cell lymphoma (PMBCL). Their presence is accompanied by fever, night sweating, dyspnea, whizzing, pain in the chest, the superior vena cava syndrome (SVCS) and pleural effusion. In the clinical practice the most important procedure after diagnosis is to determine clinical stages of the disease (CS). Therefore, Ann Arbor classification is used for staging Hodgkin lymphoma. As far as stages I and II are concerned, Bulky disease is mentioned with regards to the poor prognosis alongside sedimentation rate of more than 50 (if the patient is asymptomatic in more than three regions), the presence of B symptoms and the existence of

extra-nodal disease. As far as patients with stages III and IV of the disease, the international prognostic index (IPI) is used (4).

Ann Arbor staging classification includes the following stages:

- CS I Involvement of one region in lymph glands or an extra-lymphatic organ.
- CS II Involvement of two or more lymph regions on the same side of the diaphragm or a localized involvement of extra-lymphatic organ and one or more lymph regions on the same side of the diaphragm.
- CS III Per continuitatem positive lymph regions are adjacent.
- CS IV Although positive regions are not adjacent they are still on the same side of the diaphragm.
- CS V Involvement of the lymph glands regions on both sides of the diaphragm.
- CS VI Diffuse or disseminate involvement of one or more extra-lymphatic organs or tissues with or without the involvement of lymph glands. All of the aforementioned stadiums are marked as follows:
  - A. Af there are no general symptoms
  - B. In the case of the occurrence of the unexplicable increase of the body temperature of more than 38°C, night sweating or loss of more than 10% of the body weight for 6 months.
  - E. Localized involvement of extra-lymphatic organ
  - S. Involvement of the spleen
  - X. Indicates the involvement of the mediastinum Bulky disease, spreading of mediastinum to more than one third of the chest diameter.

Many studies have investigated the prognostic factors of Hodgkin disease. In the beginning sex, age, histological type, presence of the general symptoms, mediastinal mass, sedimentation rate, the level of serum albumin and hemoglobin were all mentioned (5).

However, in 1998 the seven prognostic factors for the treatment of lymphoma were defined: patients over 45 years of age, male sex, clinical stage IV, the number of leukocytes higher than  $15 \times 10^9/l$ , the number of lymphocytes lower than 600, serum albumin less than 4 g/hemoglobin less than 10,5 g/l (6,7). Duration of remission (FFP) is in correlation with the number of these prognostic factors (7).

The most important prognostic factor is the dissemination of the disease when diagnosed alongside negative factors: a large mediastinal mass, extra-nodal involvement and/or massive spleen contraction (1,8). For the treatment of Hodgkin lymphoma the clinical stadium is the most important as opposed to the NHL (9,10,6).

In the first or second clinical stage, Hodgkin disease has a very unfavorable outcome in the case of mediastinal mass existence on the computerized tomography of the lungs of more than one third in transverse diameter on the fifth and the sixth chest disc (Th5/6) or 10 cm, Bulky disease (11).

For patients in the third or fourth stage the outcome is unfavorable in case of more than four factors according to IPI prognostic index (7).

The presence of mediastinal mass larger than the third of the chest diameter is a very important determinant of the future disease prognosis than the Ann Arbor staging or clinical prognostic factors (12). Apart from the existence of pleural effusion, the presence of the extra-thoracic disease is also considered an unfavorable outcome (13).

The size of mediastinal mass that is steadily over than 10 cm after the completion of chemotherapy is a predictor of a relapse (14).

The treatment of Hodgkin disease with the involvement of mediastinum with chemotherapy prolongs a patient's life up to 5 years (14).

Recent research points to other prognostic markers of Hodgkin's lymphoma such as the level of serum interleukin 9, (IL- 9) (15). What has also been indicated is the prognostic significance of position emission tomography (PET) for the evaluation of the residual mass after Hodgkin lymphoma and non- Hodgkin lymphoma treatment. A positive finding is in a significant correlation with the disease relapse (16).

### Aim

The aim of this study was to show the importance of mediastinal mass that is larger than the third of the chest diameter in Hodgkin lymphoma for the disease outcome in the examined patient.

### Case review

An 18 year old patient visited a hematologist because of the enlarged lymph glands in the neck

in January 2005. Examination of the lymph glands in the left supraclavicular package was performed and their enlargement was evident. Laboratory examination found the following CBC values: Le  $6,6 \times 10^9/l$ , Er  $5,78 \times 10^{12}/l$ , Hb 145g/L, Hct 47,4 Tr  $404 \times 10^9/l$  fibrinogen 7,1 g /l LDH 242 ,4 U/l.

Upon the ultrasound examination a left supraclavicular hypoechoic vascular solid formation size 6x30 mm was discovered which clearly corresponded to the lymph nodi. Radiography of the lung and the heart showed mediastinal lymphadenopathy - Bulky disease. Ultrasound of the heart revealed a swelling in the right ventricular walls. Separation sheets of the pericardium were also noted in front of the apex and the right ventricular up to 5 mm. Paracardially, a mass was detected that did not belong to the heart. It was clearly outlined and made of the soft tissue and multilokular, size 37x 67 mm. Pathohistological findings showed that lymph glands in the neck indicating the case of Hodgkin disease of nodular sclerosis type. After a thorough examination, the disease was classified as the clinical stage CS IIB.

The treatment was conducted by substituting the ABVD protocol (Adriablastin 50 mg, Bleomycin 15 mg, Vinblastin 10 mg, Dacarbazine 700 mg) with three cycles; after the radioscopy of the mediastinum three more cycles of ABVD were included.

After the primary evaluation, there was an obvious remission of the disease which lasted 5 months. Afterwards, the radiography of the lungs and the heart again confirmed mediastinal lymphadenopathy and relapse of the primary disease.

The patient was treated with GDP (Gemcitabine 2000 mg, Dexamthason 40 mg, Platinex150 mg) protocol. The patient received six cycles of this protocol. During the reassessment, mediastinoscopy was performed and pathohistological diagnosis confirmed Hodgkin disease, nodular sclerosis with a mixed cellularity with immunophenotype: CD 20-,CD 15+,CD 30+/-, high expression of EBV. Radiography of the lungs and the heart revealed pericardial effusion behind the rear wall of the left ventricle up to 5 mm as well as 5 mm in the left lateral wall of the left ventricular which showed solid formation that did not match the heart configuration. A partial remission of the primary disease was achieved with the aforementioned therapy; the performance was ECOG=0. According to IPI there was only one negative prognostic factor. Afterwards, earlier in 2007, the patient was sent to the autologous stem cells hemathopoesis transplantation in the Clinical Centar of Novi Sad that was abandoned in the end.

The doctoral team decided to continue the treatment with maximized protocol BEACOPP (Bleomycin 15 mg, Etoposide 300 mg, Doxorubicin 50 mg, Cyclophosphamide 2000 mg, Vincristin 2 mg, Procarbazine 200 mg, Prednisone 80mg).The treatment with this protocol was followed by a febrile neutropenia. Hence, the patient was treated with antibiotic therapy and

granulocito column stimulative factor (GCS -F). After the repeated disease evaluation after three cycles of this protocol a relaps was found in the mediastinum which resulted in the patient's treatment with paliative radiotherapy of eight sessions with 20 Gy. The therapy was continued but with a mini BEAM protocol (Carmustine 1000mg, Etoposide 100 mg, Cytosar 200 mg, Melpahalan 60 mg). Before the application of this therapy, pathohistological pericardial fluid comprized a fresh and hemolyzing erithrocite lymphoid mononuclear cells, rare netrophili and scarce mesothelial reactive cells; tumor cells were not present. After the first cycle of this protocol a complete radiological regression of pleuropericardial effusion was accomplished. The patient was treated with hepatothoprotective therapy. However, after the completion of the last treatment and the evaluation of the disease that followed, the worsening of the disease was noticed which was accompanied by radiological finding of the enlargement of the hilar lymph nodi on the left side by an ultrasound reduced ejection fraction EF 48%, as well as pericardial drain around the heart - the largest after the last and lateral wall of 18 mm. The treatment was continued with the cardiological therapy, cortocosteroids and non-steroidal anti-inflammatory drugs. In January 2008, the radiological finding confirmed the existence of the previosly found enlarged hilar left lymph glands as well as bilateral pleural effusion. The ultrasound again showed the pericardial effusion behind the rear wall LK of 10 mm. Computerized tomography of mediastinum performed in January 2008 showed the existenece of bilateral pleural effusion, pericardial effusion with left and right paracardial calcification with the presence of conglomerates of the lymph nodi of 55x56x85 mm in diameter. Future suggested therapy was cardiological. Despite of that the repeated radiological examination in February 2008 showed the presence of the bilateral inhomogenic shadow that matched parenchyma inflammation as well as the shadow corresponding to the effusion on the right. The ultrasound view of the heart confirmed the presence of the effusion of 9 mm along the lateral wall LK. The patient was treated with cardiological therapy without improvement and in February 2008 it ended with a leathal outcome.

## Discussion

In this paper the diagnosis of lymphoma was confirmed after biopsy of lymph glands in the neck. It was the second clinical stage with mediastinal mass wider than the third of the chest (4). Bulky disease presence in the second stage was an indicator of the unfavorable (lethal) outcome (11). The patient was treated with ABVD protocol. After the three cycles of the protocol, the patient was treated with mediastinal radiation and received three cycles of ABVD. Disease remission lasted five months. After this period of time there was a relapse of the disease which corresponded to the literature data that the presence of mediastinal mass after chemotherapy was a predictor of the relapse (14). Early relapse, after the induction therapy, is the standard for referal of patients to high doses of chemotherapy with transplation prospects. The patient was treated with GDP protocol and was sent to transplation but in the end it was decided to continue only with chemotherapy treatment with the BEACOPP protocol. The treatment with this protocol did not lead to remission because of the persistent mediastinal mass that was treated with paliative radiotherapy and miniBeam protocol. The data obtained correspond to those in literature that the mediastinal mass is the most important indicator of Hodgkin's disease more than Ann Arbor classification. Not a single way of treatment lead to regression of the mediastinal mass. On the contrary, it only produced pleuropericardial effusion resistant to therapy that resulted in the patient's demise.

## Conclusion

The size of mediastinal mass significantly influences the prognosis of Hodgkin disease as well as the unfavorable outcome of the primary disease. Mediastinal mass proved to be a very important indicator of the Hodgkin's disease outcome even more than Ann Arbor classificaton.

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## **MEDIJASTINALNA MASA KAO PROGNOŠTIČKI FAKTOR HODGKINOVOG LIMFOMA – PRIKAZ BOLESNIKA**

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Mnoge studije su izučavale prognostičke faktore kod bolesnika obolelih od Hodgkinovog limfoma (HB). Danas je definisano sedam najvažnijih prognostičkih faktora. Među njima, kao značajan negativni prognostički faktor izdvaja se stepen raširenosti bolesti u momentu dijagnoze. Cilj rada bio je da pokažemo značaj prisustva mediastinalne mase veće od trećine dijametra grudnog koša u Hodgkinovom limfomu na tok bolesti. Prikazan je slučaj bolesnika P.A. starosti 18 godina. Bolesnik je u momentu dijagnoze bolesti imao zahvaćenost mediastinuma. Pomenuta mediastinalna masa praćena je radiografijom pluća i srca (RTG), kompjuterizovanom tomografijom mediastinuma (CT) i ehokardiografskim pregledom srca (UZ). Bolesnik je lečen protokolima ABVD, GDP, BEACOPP, mini BEAM i zračenjem mediastinuma. Kod ovog bolesnika, mediastinalna masa se održala uprkos lečenju. Tok bolesti pogoršalo je prisustvo rezistentnog perikardnog izliva i bolesnik je tri godine nakon postavljene dijagnoze preminuo. *Acta Medica Medianae* 2008;47(4):25-28.

***Ključne reči:*** Mediastinalna masa, Hodgkinova bolest, prognostički faktor