Obstructive jaundice as manifestation of relapsing Hodgkin’s Lymphoma: the success of chemotherapy (case report)

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ABSTRACT

Background: Hodgkin’s lymphoma is a hematologic malignancy of lymphocyte cells. Intrahepatic or extrahepatic disorders can cause jaundice associated with lymphoma. An extrahepatic obstructive jaundice due to lymphoma is still rarely reported, the incidence is only 1.3% out of 370 patients.

Case Description: A male patient, 44 years old, admitted to the hospital because his eyes and all over his body became yellowish. He also felt itchy on his skin, and his stool color was pale. The patient was diagnosed with a post-chemotherapy relapse of Hodgkin’s lymphoma twice with different regimens. The first chemotherapy was with the CHOP regimen. We evaluated the patient nine months after the chemotherapy with abdominal CT-scan, and we found paraaortic lymphadenopathy with infiltration to the spleen and gaster. Then, the patient was re-chemotherapy using Mesna’s ICE regimen. Seven months after the second chemotherapy, the patient was re-admitted to the hospital with jaundice throughout his body.

The diagnosis is difficult to establish because many other things can also cause obstructive jaundice. The laboratory results in three weeks post-chemotherapy were, 5.87 mg/dl for direct bilirubin, 21.5 for total bilirubin, 213 U/L for ALT, 199 U/L for AST, 469 mg/dl for ALP, and 6,400/mm3 for leukocytes. We found gall bladder hydrops and Intra-Hepatic Bile Duct Dilatation (IHBD) during an abdominal ultrasound examination. The results of the PET-scan showed multiple metastases to the peritoneal/omentum and diffuse lymphomatous infiltration in the gastric. After that, the patient was given the third chemotherapy with gemcitabine and vinorelbine regimens. His laboratory results were 25.3 mg/dl for total bilirubin, 21.5 for direct bilirubin, 82 U/L for AST, and 36 U/L for ALT. We also found significant clinical improvement after the third chemotherapy.

Conclusion: The diagnosis is difficult to establish because many other things can also cause obstructive jaundice. Chemotherapy is one therapeutic choice in the management of obstructive jaundice related to Hodgkin’s lymphoma.

INTRODUCTION

Lymphoma is a hematologic malignancy originating from the lymphatic system, which divides into Hodgkin’s Lymphoma (HL) and Non-Hodgkin’s Lymphoma (NHL). HL is derived from lymphocyte cells, which can be clinically manifested with varied manifestations in several parts of the body, according to the distribution of lymph glands, which are around 600 lymph glands in the whole body. HL can infiltrate surrounding organs, including the spleen. The most common cause of jaundice in HL is due to extrahepatic biliary obstruction due to suppression caused by HL itself.1

Hodgkin’s lymphoma is a disease affecting the lymph glands and can present with complaints of fever of unknown origin. Jaundice is one of the symptoms that are common in patients with Hodgkin’s lymphoma,2 but the specific etiology is often difficult to figure out. Intrahepatic or extrahepatic abnormalities can cause jaundice associated with lymphoma. The incidence of patients with Hodgkin’s lymphoma accompanied by jaundice is reported in the medical literature between 3% and 68%. Hodgkin’s lymphoma with obstructive jaundice is rarely reported, which is only 1.3% of 370 patients. Because of the small number of its incidence, it is rarely considered in patients who present with obstructive jaundice.3 Based on the medical records obtained from dr. Zainoel Abidin Hospital Banda Aceh, the incidence of jaundice in HL patients, has never been found. Because of the incidence and the number of misdiagnosis cases, the author interest in elaborating more about this case.

CASE DESCRIPTION

A male, 44 years old, came with complaints of jaundice in his eyes and all over his skin since one month ago, but the complaint was getting heavier one week before being admitted to the hospital. The jaundice was initially seen in the eyes, then sooner, it was seen throughout the body. The patient also complained that his skin became itchy but without rash, and his stool color became pale. The patient was previously diagnosed with Hodgkin’s lymphoma in April 2017. At that time, the patient...
complained that there was a lump in his right neck with a size of about 10 × 10 cm, and there were three other lumps in his left and right axillae with a diameter of 2 cm. The biopsy results were Hodgkin’s lymphomas.

This patient also experienced fever with the Pel-Ebstein pattern for the past one year, which is typical for Hodgkin’s Lymphoma. The rising temperature occurred for three to four days, then decreasing to a standard temperature. The patient also complained of frequent night sweats, even though the weather was not hot as well as eight kilograms weight loss in the past year with unknown causes and without a strict diet program.

The patient had previously been on chemotherapy twice with different regimens. The first chemotherapy was with the ABVD regimen (Adriamycin, Bleomycin, Vinblastine, Dacarbazine) for six cycles from May to October 2017. The evaluations of chemotherapy were conducted for eight months after chemotherapy. Since the sixth month after chemotherapy, there were no signs of recurrence.

Abdominal ultrasound examination at nine months post-chemotherapy showed signs of mass in the left hypochondriac region. This patient was treated with the second chemotherapy using the Mesna ICE regimen (Ifosfamide, Carboplatin, Etoposide). Six months after the second chemotherapy, an abdominal CT-scan was performed, and the result was paraaortic lymphadenopathy with infiltration to the spleen and gastric. Seven months after the second chemotherapy, the patient was rehospitalized because of jaundice throughout the body. The abdominal ultrasound showed hydrops gall bladders and Intrahepatic Bile Duct (IHBD) dilatation. PET-scan showed multiple metastases to the peritoneal/omentum and diffuse lymphomatous in the gastric.

The patient’s blood pressure was 110/80 mmHg, his pulse was 92 times per minute, his respiratory rate was 18 times per minute, and his body temperature was afebrile. The assessment of pain status with a visual analog scale was two, scleral jaundice was positive, and no edema in both lower limbs. The abdominal examination was concluded as lymphocyte depletion, based on the following basis:

- CD45RO (T-cell) : Positive
- CD20 (B-cell) : Positive
- CD30 : Positive

The definitive diagnosis was obstructive jaundice et causa suppression of relapsing Hodgkin’s lymphoma stage IV. The management of this patient was to be treated with the third chemotherapy with gemcitabine and vinorelbine regimens. The total bilirubin at three weeks after the third chemotherapy was 6.4 mg/dl, and direct bilirubin was 5.87 mg/dl, AST was 82U/L, ALT was 36 U/L. Significant clinical improvements were observed in this patient until the patient was discharged from the hospital.

**DISCUSSION**

Hodgkin’s lymphoma is classified as a lymphoreticular malignancy with histopathological characteristics of Reed-Sternberg cells. PCR analysis shows that Reed-Sternberg cells are derived from B cell follicles that have structural disorders of immunoglobulin. Hodgkin’s lymphoma clinically appears as an enlarged painless lymph node with a rubbery consistency. Systemic symptoms appear in the form of fever (Pel-Ebstein type), night sweats, weight loss, weakness, and pruritus. From the physical examination, we can find splenomegaly and massive gland enlargement as well as bone pain due to local destruction. Signs of obstruction can also be found such as limb edema, vena cava syndrome, spinal cord compression, and hollow visceral dysfunction.³
In this patient, systemic complaints and symptoms are obtained from Hodgkin's lymphoma. History of swelling in the neck with a size of $10 \times 10$ cm and several lumps in both axillae, which have now disappeared after six cycles of chemotherapy at Cut Meutia District Hospital, North Aceh. This patient also experienced fever with the Pel-Ebstein pattern for the past one year, which is typical for Hodgkin's Lymphoma. The rising temperature occurred for three to four days, then decreasing to average temperature. The patient also complained of frequent night sweats, even though the weather was not hot as well as eight kilograms weight loss in the past year with unknown causes and without a strict diet program.

The patient has done radiological examinations to confirm the result of the history taking and physical examination that lead to Hodgkin's lymphoma. A chest X-ray was done to see the hilar and mediastinal lymphadenopathy, pleural effusion, or pulmonary parenchymal lesions. Ultrasonography (USG) is less sensitive to diagnose lymphadenopathy (Figure 2). Thoracic CT-scan is able to detect lung parenchymal abnormalities and mediastinum. Additionally, abdominal CT-scan could determine the presence of lymphadenopathy in the retroperitoneal, para aorta, mesenteric. A tumor mass can be detected by radiological examination of body tissues or organs outside of the lymph nodes.

In the REAL (the Revised European-American Lymphoma) classification in 1994, Hodgkin’s lymphoma was divided into two categories, namely Classic Hodgkin Lymphoma (CHL) and Lymphocyte predominant Hodgkin Lymphoma (LP-HL). The classical Hodgkin Lymphoma (CHL) is further divided into four subtypes, namely: nodular sclerosis (NS-CHL), mixed cellularity (MC-CHL), lymphocyte depletion (LD-CHL) and lymphocyte rich CHL (LRCHL). The classical HL has the highest incidence, reaching 95% of all Hodgkin’s lymphoma cases, with 70-80% successful therapy showing longer life.

| Lymphoma Subtypes             | Expressed Proteins | Unexpressed Proteins |
|-------------------------------|--------------------|----------------------|
| Classical Hodgkin lymphoma    | CD30, CD15         | CD10                 |
| Mantle cell lymphoma          | CD20, CD5          | CD10                 |
| Anaplastic large cell lymphoma| CD30, ALK          | CD10                 |
| Diffuse large B cell lymphoma | CD10, CD20         | CD5, CD30            |

The gold standard for lymphoma diagnosis is an excisional biopsy of the lymph nodes. A biopsy is performed only in one representative gland, superficial and peripheral gland. If there is a representative peripheral or superficial gland, there is no need for an intra-abdominal or intra-thoracic biopsy. If an excisional biopsy cannot be performed, Fine Needle Aspiration Biopsy (FNAB) examination can be performed for specific indications, although the results are not better than the biopsy. Histopathological picture of Hodgkin’s lymphoma is the discovery of Reed-Sternberg cells which is the name of the two researchers who discovered the cells for the first time, which were Carl Sternberg and Dorothy Reed.

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expectancy. To determine the type of lymphoma, in addition to histopathology biopsy examination, immunophenotype or immunochemistry examination is also needed.

The examination is able to determine the origin of lymphoma tumor cells, whether from B cells, T cells, or Natural Killer cells. The Classical Hodgkin Lymphoma has classic Reed-Sternberg cells that express CD15 and CD30 but are not markers for specific B cells. The CD30 molecules are found in 98% of CHL cases, although their intensity can vary from one case to another, whereas CD15 is detected in 80% of CHL cases. B cells express CD20, CD45, and CD79a on immunophenotype examination. The CD20 molecule is a B cell marker found in 30-40% of cases of CHL which are usually with negative EBV (Tables 1 and 2).

An abdominal ultrasound examination, which is done eight months after initial chemotherapy, did not show any abnormalities. This result is in accordance with the theory that states that the abdominal ultrasound examination is not sensitive to detect the presence of lymphadenopathy.

The abdominal CT-scan of the patient showed a mass in the outer wall of the major and minor curvature of the gaster and infiltrating to the spleen with paraaortic lymphadenopathy. This result is in line with the literature, which states that lymphoma masses can be detected by radiological examination of body tissues or organs outside of the lymph nodes (Figure 1). The biopsy of this patient showed lymph nodes tissues in the neck with many Reed-Sternberg cells, acidophilic nucleoli, and an increase in the process of abnormal mitosis leading to the Hodgkin’s Lymphoma diagnosis. Biopsy performed on the patient was originated from neck lymph nodes; it is theoretically representing abdominal or paraaortic lymph nodes found from the results of CT-scans as superficial lymph nodes. Immunophenotype examination revealed the presence of CD30, CD20, and CD45 molecules. Following the theory stating that CD30 is a molecule expressed by Reed-Sternberg cells and found in 90% of cases of CHL. While CD20 and CD45 are protein molecules expressed by B lymphocyte cells, which are the origin of cells from Hodgkin’s lymphoma, the CD20 supports the diagnosis of CHL explicitly by its etiology rather than being caused by an Epstein-Barr virus infection. Based on the results of biopsy and immunophenotype, the type of Hodgkin's Lymphoma in this patient is Lymphocyte depletion, which is theoretically only found in 4% of all Hodgkin's Lymphoma cases and has a poor prognosis.

Figure 2  Abdominal USG 7 months after the second chemotherapy showed hydrops gall bladers and Intrahepatic Bile Duct (IHBD) dilatation.

Figure 3  PET-Scan post-chemotherapy cycles. PET-scan showed multiple metastases to the peritoneal/omentum and diffuse lymphomatous in the gastric.

Figure 4  Liver function test after chemotherapy
Staging is essential to determine the therapy and prognosis of Hodgkin’s lymphoma. Staging is carried out according to the Cotswolds in 1990, which is a modification of the Ann Arbor classification (1974). The following are the stages of Hodgkin’s lymphoma according to Cotswolds:

- **Stage I**: Involvement of one lymph node region or lymphoid tissue structure (spleen, thymus, Waldeyer ring) or involvement of one extralymphatic organ.
- **Stage II**: Involvement of ≥ 2 lymph nodes regions on the same side of the diaphragm (hilar gland when occurred on both sides is included to stage II); local involvement of one extranodal organ or one place and lymph node on the same side of the diaphragm. The number of anatomic regions involved is written in numbers.
- **Stage III**: Involvement of the lymph node region on both sides of the diaphragm, can include Spleen (III_1) or involvement of one extranodal organ (III_2) or both (III_E).
  - III_1: With or without the involvement of splenic, hilar, celiac or portal lymph nodes
  - III_2: With the involvement of paraaortic, iliak and mesenteric lymph nodes
- **Stage IV**: Diffuse involvement of one or more extranodal organs or tissues with or without lymph nodes.

The staging of this patient is in accordance with Hodgkin’s lymphoma stage IV. Based on the result of the abdominal CT-scan, the involvement of several extranodal organs were found, namely infiltration of the gastric and spleen, as well as the presence of multiple liver nodules accompanied by paraaortic lymphadenopathy.

The diagnosis of obstructive jaundice due to lymphoma is indeed difficult to establish. Biliary tract can be pressed by lymphoma in any position, but the most common location is the hilar of the liver or peripancreatic head. The mechanism of obstruction can occur due to decreased biliary duct motility caused by the pressure of Hodgkin’s lymphoma. Management of obstructive jaundice due to Hodgkin’s lymphoma consists of chemotherapy, surgery, and biliary drainage. In this patient, jaundice was not caused by infection based on clinical and laboratory results. Severe jaundice has improved both clinically, and laboratory and obstruction symptoms also begin to disappear after chemotherapy.

**CONFLICT OF INTEREST**

The authors declare no conflict of interest.

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**AUTHOR CONTRIBUTION**

All authors contributed to the reporting and analysing of the case as well as writing the manuscript.

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