Case Report

Management and quality of life extranodal non hodgkin lymphoma of testis

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ABSTRACT

Extranodal non-Hodgkin lymphoma still seems to be a rare case and an issue to discuss a lot. Clinical evidence and guidelines on treatment have not yet been widely published and accessible. We present a case of a forty-five-year-old male with the chief complaint of a bulky and huge right mass in the testis with an ulcer on it. The patient underwent an orchietomy, and the biopsy showed a malignant round cell tumor, suspected as non-Hodgkin lymphoma. The patient then received the following treatment: chemotherapy with R-CHOP regimen every three weeks, consisting of 6 cycles showing shrinkage size of the testis by day 7 and final complete response after 4th cycle with ADE grade 0 no sexual activity disorder after chemotherapy. This raises hope in developing treatment modalities that the right choice on chemotherapy regimen with complete control on the drug effects may improve clinical outcome and patient’s quality of life.
INTRODUCTION

Extranodal Non-Hodgkin lymphoma (NHL) is an uncommon case. Approximately 30% of NHL are extranodal, which can arise from any organ. The most common extranodal lymphoma originates from the GI tract (4-20% cases). NHL of the testis is 1-9% of all cancer cases and 1-2% of NHL cases. The mean age of patients diagnosed with extranodal NHL is 63 years old and 66-68 years for NHL of the testis (Cheah, Wirth, & Seymour, 2014; Nanthakwang et al., 2019; Vannata & Zucca, 2015; Xu & Yao, 2019).

Extranodal NHL is mostly found during an advanced stage and on immunocompromised patients. It is a progressive and bulky disease that often reoccurs, has a poor prognosis, and rarely responds completely (Vannata & Zucca, 2015). Nevertheless, this report will discuss the diagnostic approach and therapy modalities in a young, sexually active man, followed by monitoring FSH and LH due to the awareness of NHL-induced secondary hypogonadism.

CASE REPORT

Forty-five-year-old male, married with two children, who lived in Lamongan, East Java, presented with a bulky and massive right mass testis, 20x20 cm in size, with an ulcer since four months ago. He lost approximately 13 pounds in 2 months. He did not have any history of hypertension, diabetes mellitus, or previously known malignancy. He had not been smoking for a year back and had no alcohol intake since married.

In May 2019, he came to a private hospital in Lamongan, East Java. The USG testis showed a solid mass with a solid line, positive vascularization, size 11 x 8.7 x 12.9 cm, suspect testicular tumor, suspicious metastatic process lymphadenopathy of right and left inguinal (Figure 1).
Case Report

Diabetes insipidus in patients with traumatic severe brain injury

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Traumatic severe brain injury is a fatal injury, with a mortality rate of up to 50%. About 1.5 million people experience severe brain injury in the United States. There are more than 50,000 deaths and 500,000 incidents of permanent neurological sequelae. About 85% of mortality occurs in the first 2 weeks after the injury. One complication of severe brain injury is diabetes insipidus. There are no definitive data on the incidence of diabetes insipidus in patients with traumatic severe brain injury. In this case report, a male, 45 years old, was taken to the emergency installation (IRD) after experiencing a severe brain injury during surgery, the signs of diabetes insipidus were presented by hypernatremia, polyuria of 300 cc/hour urine production and 149 mmol/l serum sodium. The patient received desmopressin treatment, the patient's clinical and hemodynamic were not shown any improvements. The patient passed away in the intensive care unit (ICU).

Figure 2a-d. MSCT demonstrated enhancing homogenous mass with the necrotic area, solid line, size 8.6x11.6x15 cm in the right scrotum, suspect testicular tumor multiple lymphadenopathy paraaortic size 1.3x1.5x2 cm, right inguinal 1.7x1.2x0.98 cm, left inguinal 1x1.5x1.6 cm.
Tumor marker level of germinal cell tumor showed normal (LDH 565 U/L; β-HCG < 0.6 mIU/ml; AFP 1.42 IU/ML); and not detected hepatitis viral and HIV infection (HbsAg negative; anti-HCV negative; and HIV test negative). MSCT demonstrated enhancing homogenous mass with a necrotic area, suspected testicular tumor multiple lymphadenopathies, and inguinal (Figure 2a-d).

Orchietomy unilateral right-sided testis was performed in June 2019 in a private hospital, and biopsy results showed suspect non-Hodgkin lymphoma. After orchietomy, the mass became larger with an ulcer, and the patient was then referred to Dr. Soetomo General Hospital, Surabaya, East Java, for further diagnostic process and treatment.

IHC result showed CD 20+ Ki index proliferation 30%, confirming NHL B cell type high grade. The patient was treated using the R-CHOP regimen every 21 days and six cycles. The evaluation was done after the first cycle of chemotherapy on day 7th showed shrinkage size of testis and no blood or pus found in the scrotal ulcer. After 4th and 6th cycle chemotherapy, the patient showed complete response with Adverse Event Drugs (ADE) grade 0. Evaluation level of FSH, LH, and Testosterone was performed after chemotherapy, mean level of FSH 39,48 mIU/ml, LH 16,59 mIU/ml, testosterone 165,12 ng/dl. No sexual activity disorder was found after chemotherapy. Radiotherapy was not performed for the patient.

**DISCUSSION**

NHL of the testis is an example of extranodal NHL, which is scarce and aggressive. According to Surveillance, Epidemiology, and End Results (SEER), the median age of patients with NHL of the testis is 70 years old. Histological subtype NHL of testis most commonly demonstrate diffused large B cell lymphoma (DLBCL) 82,9% and 68,6% of patients are diagnosed in early-stage (stadium I-II), 5% in stadium III, and 15,9% in stadium IV. Most frequent cases are found in the right-sided testis (49,1%) and rarely bilateral (5,3%). NHL of the testis is commonly found in Caucasians (Kuper-Hommel et al., 2012; Xu & Yao, 2019).

NHL of the testis is sometimes associated with hydrocele. Constitutional symptoms at admission are uncommon. They strongly suggest systemic disease in 20% to 30% of patients (Ellatif, Kumar, Weller, Katz, & Vrentzou, 2019; Nanthakwng et al., 2019; Sahu, Mishra, Lal, & Oshea, 2020; Shih et al., 2014; Xu & Yao, 2019).

Ultrasound of gonadal NHL demonstrated enlarged, heterogenous, and hyper-vascular testicles. Tunica albuginea and epididymis are infiltrated and presenting a hydrocele. The ultrasound imaging of epididymis and testis reveals hypervascularity and infiltrative mass; however, it will be excluded by orchietomy and biopsy. CT demonstrated testicular mass with soft tissue extending along the spermatic cord through the inguinal canal and cranially in the retroperitoneum along the gonadal vein to the level of its insertion into the inferior vena cava. It also infiltrated organs around the testis. Sporadic lymph node involvement and extranodal deposit finding in CT and ultrasound are strongly associated with lymphoma, infection, or germ cell tumor (Ellatif et al., 2019).

Modality of treatments of NHL of the testis is surgery, chemotherapy, immunotherapy, and radiotherapy. Inguinal orchietomy and debulking surgery aim to control the disease growth and simultaneously get pathological specimens as a diagnostic tool. Histopathologically, the NHL of testis shows a large lymphoid cell with the size of nucleus.
twice normal nucleus lymphocyte and no Reed Stenberg cell. It is challenging to distinguish NHL of testis from seminoma histopathologically since they look alike; however, Immunohistochemistry (IHC) will be useful to verify the diagnosis. IHC used to diagnose lymphoma is CD 20 and Ki67. The Ann Arbor system is used to stage NHL (Cheah et al., 2014; Marcus, Sweetenham, & Williams, 2014).

A standard treatment for NHL of testis has not yet been established since it is a rare disease and prospective randomized controlled trials were not yet available. In previous studies for NHL of the testis, orchietomy has been used as a diagnostic and a therapeutic tool; however, the outcomes of patients who undergo this surgery alone or in combination with radiotherapy are not satisfactory (Xu & Yao, 2019).

Following the introduction of Rituximab in 2006, the prognosis of patients’ NHL of testis has significantly improved. A retrospective review involving 75 patients with NHL of testis from MD Anderson Cancer Centre revealed that the addition of Rituximab to anthracycline-based chemotherapy significantly improves the 5-year overall survival. In addition, a retrospective analysis by the British Columbia Cancer Agency demonstrated that the five-year-progressive-free survival (PFS) and OS of patients treated with Rituximab were similar (Jia et al., 2014; Xu & Yao, 2019).

Chemotherapy regiment used to NHL of testis mainly are CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone). There are some conditions that, if CD 20 results positive, Rituximab will be given every 21 days for 6-8 cycles. The regimen came with or without prophylaxis for the central nervous system, methotrexate, administrated intravenously or intrathecally. The regimen comes with the recommended dose, which is: Rituximab 375 mg/m²; Cyclophosphamide 750 mg/m²; Doxorubicin 50 mg/m², and Vincristine 1.4 mg/m²; The other NHL of testis regimen for patients 18-60 years old are VCAP (vincdesine, doxorubicin, cyclophosphamide, prednisolone), VECP-bleo (vindesine, epirubicin, cyclophosphamide, prednisolone, bleomycin), or R-CEOP (Rituximab, cyclophosphamide, epirubicin, vincristine, prednisone) every 14 days (Cheah et al., 2014; Marcus et al., 2014; Skeel & Khleif, 2011).

A single-center study in China showed a complete response of stage I NHL subtype DLBCL after 4-6 cycles of R-CHOP or CHOP. Most patients at stage II had demonstrated partial response for 6-8 cycles using CHOP or RCHOP. Progressive disease and partial response were seen in stage III and IV. International Prognostic Index (IPI) ≤ 1 in the stadium I and II refer to complete response and better prognosis (Jia et al., 2014; Zhou et al., 2017).

A new study using SEER data from 1,165 NHL of testis cases from 1973 to 2013 had demonstrated the 5-year cause-specific survival (CSS) rates improving significantly after the Rituximab era (after 2006), 44% during 1973-99, 62,4% during 1998-2005, and 70,4% during 2006-2013, respectively. Patients under 70 years old that are diagnosed and treated earlier show a more promising prognosis. The 5-year CSS rates were 60,2% for DLBCL, 57,8% for indolent B-NHL, 40,4% for other aggressive B-NHL, and 53,4% for malignant NHL that was not otherwise specified. All patients underwent surgical intervention, and patients who had received radiotherapy had a five-year CSS rate of 67,5% compared with 54,3% for patients who did not undergo radiation therapy. According to stadium NHL of testis, the 5-year CSS and OS of stadium I is (70.9% & 70.5%); stadium II (58.2% & 58.1%); stadium III (48.1% & 49%); and stadium IV (34.7% & 35.5%) (Deng et al., 2016; Xu & Yao, 2019).

In the DLBCL subtype, Rituximab had been
remarkably improving the prognosis of stage I-IV. Patients at the earlier stages who receive Rituximab manifest better outcomes and prognosis. The complete response showed in the early stages (stages I and II), but no data represented the long-term effect of chemotherapy (Ma et al., 2018; Xu & Yao, 2019).

The effect of orchiectomy and chemotherapy for infertility and the occurrence of hypogonadism in NHL of testis patients is debatable. The orchiectomy unilateral showed some dynamic effects in fluctuating FSH, LH, and testosterone hormones in patients with tumor testis. However, a study from Wiechno et al., 2017, did not include NHL of the testis as a sample; therefore, there is still not enough evidence on infertility and hypogonadism following NHL of the testis. Nevertheless, RCHOP or CHOP regimen < 8 cycles demonstrated lower gonadotoxic effect and impaired quality of sperm (Kumar et al., 2018). However, a satisfying result has been seen in a patient showing complete response to the therapy with grade 0 adverse drug effect (ADE) and normal gonadal hormones. The absence of disturbance in the sexual activity was also paramount considering the patient’s quality of life.

CONCLUSION

Testicular LNH has been reported in a 45-year-old male. He was diagnosed with LNH B cell type high-grade CD 20 + with stage II EB. A right unilateral orchiectomy was performed, the mass still enlarged and formed a scrotal ulcer after orchidectomy, and then chemotherapy followed. The chemotherapy regimen used was a 6-cycle R-CHOP regimen every 21 days. After six cycles of chemotherapy, complete therapeutic response with an ESÖ grade 0 was gained. There were no signs of hypogonadism, and the FSH, LH, and testosterone levels were within normal limits. No disturbance of sexual activity was reported.

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REFERENCES


Tidak ada data pasti tentang kejadian diabetes insipidus pada pasien dengan cedera otak traumatis pertama setelah cedera. Salah satu komplikasi dari cedera otak yang parah adalah diabetes insipidus.

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Hypernatremia corrections are the keys to the successful experience severe brain injury in the United States. There are more than 50,000 deaths and 500,000 incidents of neurological permanent disability. About 85% of deaths occur within 2 weeks after the injury. One complication of brain injury requires complicated treatment. Therefore, treatment of diabetes insipidus. Diabetes insipidus in cases of severe brain injury is diabetes insipidus. There are no definite data on the incidence of diabetes insipidus in traumatic severe brain injury patients of Indonesia of the traffic accident 12 hours before being hospitalized. After surgery, the signs of diabetes insipidus were presented by polyuria of 300 cc/hour urine production and 149 mmol/l.


