Primary breast lymphoma – a case report

Primární lymfom prsu – kazuistika

Rajabto W.[1], Angkasa Y. K.[1], Harahap A.S.[2], Ham M. F.[2], Brahma B.[3]

[1] Division of Hematology-Medical Oncology, Department of Internal Medicine Dr. Cipto Mangunkusumo General Hospital/ Faculty of Medicine Universitas Indonesia, Jakarta, Indonesia
[2] Department of Anatomical Pathology, Dr. Cipto Mangunkusumo General Hospital/ Faculty of Medicine Universitas Indonesia, Jakarta, Indonesia
[3] Department of Surgical Oncology, Dharmais National Cancer Hospital, Jakarta, Indonesia

Summary

Background: Primary breast lymphoma is a rare disease and accounts for 0.4–0.5% of malignant breast neoplasms and 1.7–2.2% of extra-nodal lymphomas, with diffuse large B-cell lymphoma (DLBCL) as the most common histologic subtype. ***Case:*** A 47-year-old female with beta thalassemia presented with a lump of the left breast, redness, pain, and swelling of her left breast. Physical examination showed tender, red, swollen left breast. Laboratory findings show mild anemia and normal level of lactate dehydrogenase 329 U/L (normal range: 240–480 U/L). PET scan showed hypermetabolic mass with irregular margins covering the whole left breast quadrants with the size of 11.25 × 5.17 cm with left pectoralis major, left parasternal, and left axillary hypermetabolic nodules. Histopathology and immunohistochemistry staining showed a non-germinal center B-cell-like subtype of DLBCL CD20+. We administered the R-CHOP regimen (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednison) every 3 weeks for 6 cycles. The response was complete remission. The patient tolerated the chemotherapy well and achieved long term complete remission. ***Conclusion:*** Primary breast lymphoma is a rare disease with the most common subtype is diffuse large B-cell lymphoma. Systemic chemotherapy R-CHOP is the treatment option for primary breast diffuse large B-cell lymphoma.

Key words

primary breast lymphoma – diffuse large B-cell lymphoma – R-CHOP chemotherapy

Souhrn

Východiska: Primární lymfom prsu je vzácné onemocnění a tvoří 0,4–0,5 % maligních novotvarů prsu a 1,7–2,2 % of extranodálních lymfomů, přičemž nejčastějším histologickým podtypem je difuzní velkobuněčný B lymfom (diffuse large B-cell lymphoma – DLBCL). ***Případ:*** Žena ve věku 47 let s beta talasémií přišla s tím, že má v levém prsu bulku a prs je začervenalý, bolestivý a oteklý. Při fyzikálním vyšetření bylo potvrzeno, že levý přes je citlivý, zařervenalý a oteklý. Laboratorní vyšetření ukázala mírnou anemii a normální hodnotu laktát dehydrogenázy, a sice 329 U/l (normální rozmezí: 240–480 U/l). Na snímku PET byla patrná hypermetabolická masa s nepravidelnými okraji o rozměrech 11,25 × 5,17 cm s hypermetabolickými noduly v levém pectoralis major, levé parasternální čáře a levé axile. Histopatologické a imunohistochemické barvení prokázalo CD20+ podtyp DLBCL nepodobný B buňkám germinálního centra. Podávali jsme chemoterapii v režimu R-CHOP (rituximab, cyklofosfamid, doxorubicin, vinkristin a prednison) v 6 cyklech každé 3 týdny. Opdpovědí byla kompletní remise. Pacientka snášela chemoterapii dobře a bylo dosaženo dlouhodobé kompletní remise. ***Závěr:*** Primární lymfom prsu je vzácné onemocnění, přičemž nejčastějším podtypem je difuzní velkobuněčný B lymfom. Lékem volby u pacientů s primárním difuzním velkobuněčným B lymfomem je chemoterapie v režimu R-CHOP.

Klíčová slova

primární lymfom prsu – difuzní velkobuněčný B lymfom – chemoterapie R-CHOP

The authors declare they have no potential conflicts of interest concerning drugs, products, or services used in the study.

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Yohana Kusuma Angkasa, MD
Division of Hematology-Medical Oncology
Department of Internal Medicine
Dr. Cipto Mangunkusumo General Hospital/ Faculty of Medicine Universitas Indonesia
Jl. Pangeran Diponegoro no 71,
Kenari, Senen, RW 5
Kota Jakarta Pusat, Daerah Khusus Ibukota Jakarta 10430
Indonesia
e-mail: yohanaksma@gmail.com

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Introduction

It is estimated that approximately a third of patients with diffuse large B--cell lymphoma (DLBCL) present with an extra-nodal disease, with gastrointestinal tract, head and neck, and skin or soft tissue as the most common sites of involvement [1]. Primary breast lymphoma (PBL) is a rare disease and accounts for around less than 1–2% of non-Hodgkin lymphomas, with DLBCL as the most common histologic subtype [2,3]. The terminology PBL is used when the breast is the main site or, in most cases, the only site of lymphoma [4]. PBL is mainly found in female patients, with age distribution ranging widely from 17 to 95 years, and is commonly found in only one breast, especially in the upper quadrant of the right breast. The optimal treatment of primary breast DLBCL has not been defined well. Most patients received combination therapy, including surgery, systemic chemotherapy, or radiotherapy [5]. Here, we presented a case report of a patient with primary breast lymphoma who achieved a favorable response to rituximab, cyclophosphamide, doxorubicin, vincristine, and prednison (R-CHOP) chemotherapy.

Case

A 47-year-old female with beta thalassemia and good ECOG (Eastern Cooperative Oncology Group) performance status presented with a lump of the left breast which emerged one month before admission. She also complained of redness, pain, and swelling of her left breast. There was no fever, night sweat, or weight loss. Physical examination showed a tender, red, swollen left breast. Laboratory findings show mild anemia and a normal level of LDH, 329 U/L (normal range: 240–480 U/L).

Ultrasonography of the left breast showed thickening of the cutaneous and subcutaneous layers of the left breast. There was a solid hypoechoic lesion covering the whole quadrants of the left breast. Intralesional necrotic components were present. Color doppler imaging showed prominent intra-lesion vascularisation. Multiple axillary lymph nodes were also present. A PET scan was performed; it confirmed the abovementioned results and showed a hypermetabolic mass (standardized uptake value 43.2) with irregular margins covering the whole left breast quadrants with the size of 11.25 × 5.17 cm (Fig. 1). There were also left pectoralis major, left parasternal, and left axillary hypermetabolic nodules.

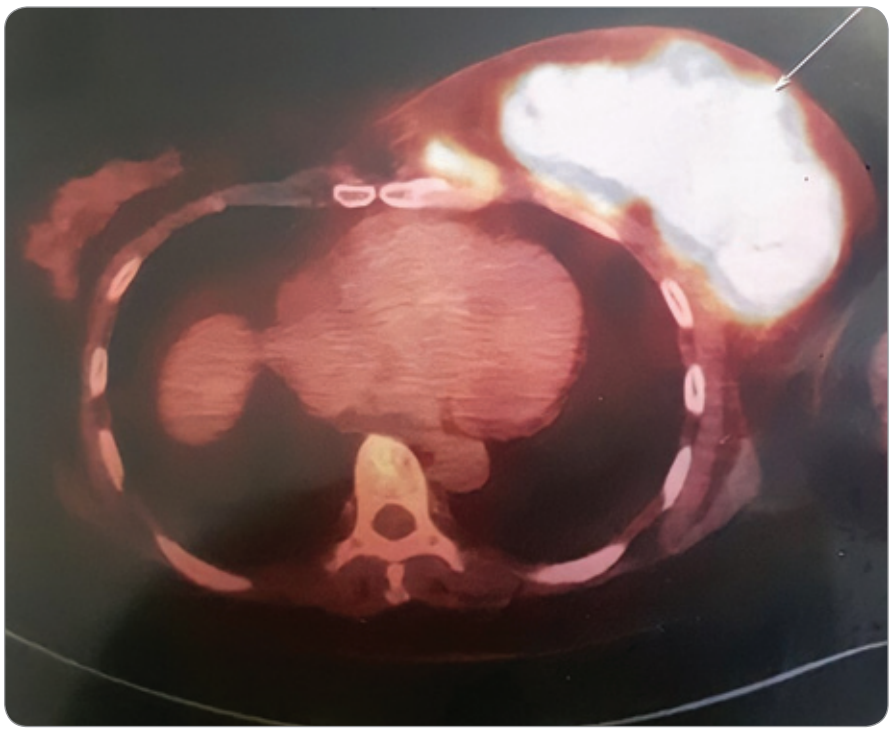

Fig. 1. PET scan of the left breast.

A core biopsy was performed, and histology showed diffuse proliferation of large tumor cells with centroblastic-like cells, with the conclusion of non-Hodgkin lymphoma. Immunohistochemical (IHC) staining results were positive for CD20, BCL6, MUM and BLC2, and negative for CD3, CD10, TdT, and C-myc. Ki67 proliferation index was positive in approximately 90% of the cells (Fig. 2). The IHC conclusion was a non-germinal center B-cell-like (non-GCB) subtype of DLBCL.

Based on history, radiology, histopathology, and immunohistochemistry, we established the diagnosis of primary breast diffuse large B-cell lymphoma, stage 2AE, age-adjusted IPI = 0. We administered the R-CHOP regimen every 3 weeks for 6 cycles. The response was complete remission (Fig. 3). The patient tolerated the chemotherapy well, although she developed neutropenia, nausea and vomiting, alopecia, and peripheral neuropathy during chemotherapy, which were all classified to grade 2 adverse events severity. The patient was still in complete remission after 6 years.

Discussion

Primary breast lymphoma accounts for 0.4–0.5% of malignant breast neoplasms and 1.7–2.2% of extra-nodal lymphomas. The most common PBL is diffuse large B-cell lymphoma which makes up to 60–85%. Wiseman first described the case in 1972 and defined PBL as the infiltration of breast tissue by lymphoma with or without regional lymph node [6,7]. Since breast lymphoma symptoms are nonspecific, the diagnosis of PBL is mainly based on histopathological biopsy and immunohistochemical staining [5]. We performed a core biopsy of left patient's breast, and the histopathological and immunohistochemical results were consistent with breast lymphoma due to non-GCB subtype of DLBCL.

There are only a few reports about beta thalassemia with malignancies in the literature. Theoretically, the correlation of beta thalassemia with Non-Hodgkin's lymphoma was because of the abnormal immune system after chronic

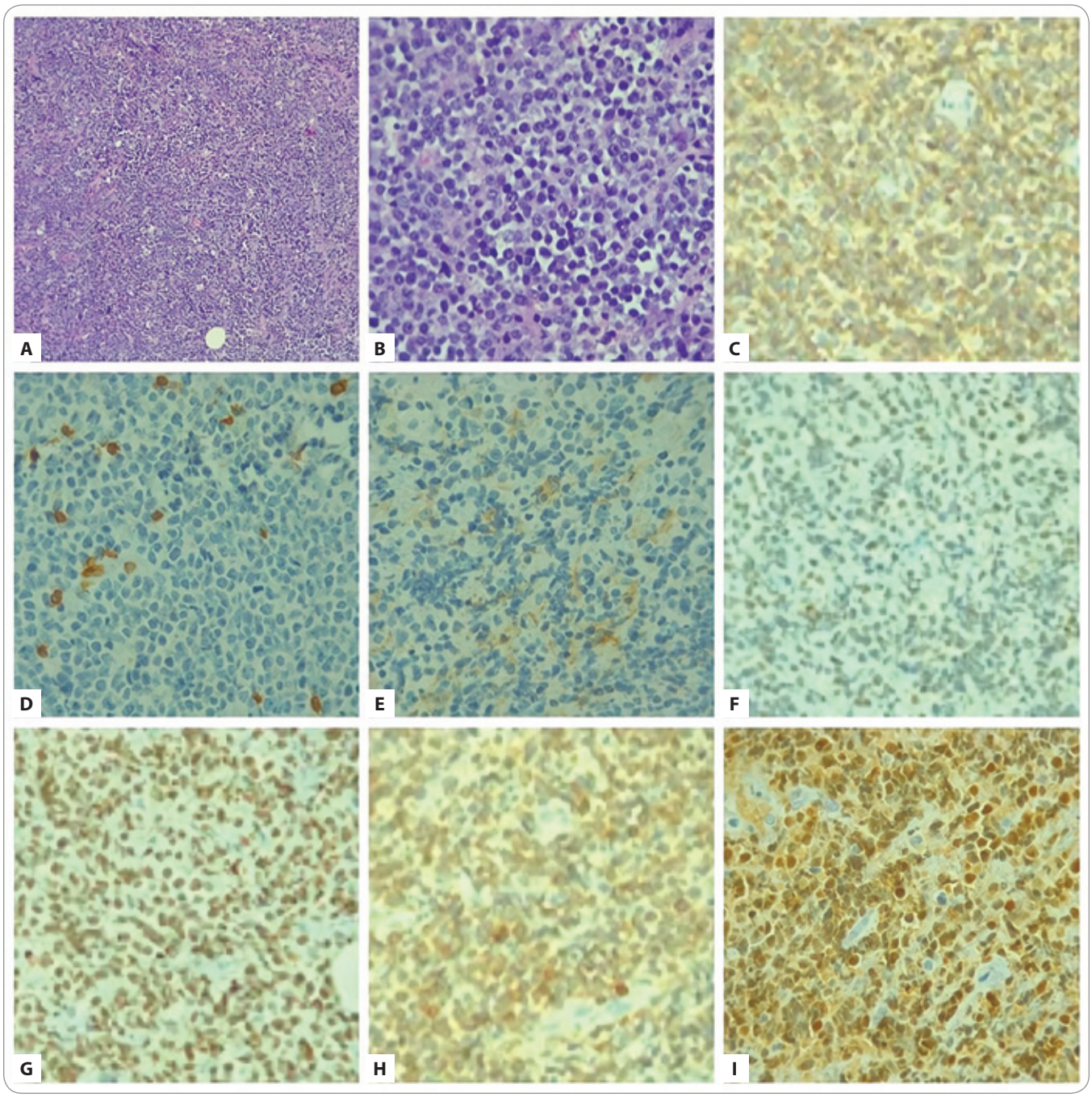

Fig. 2. Histopathology and immunohistochemistry results. A) Diffuse proliferation of lymphoid cells (hematoxylin-eosin (HE) 100×); B) large-sized tumor cells with centroblastic-like features (HE 400×); C) CD20+ (400×); D) CD3– (400×); E) CD10– (400×); F) BCL6+ (400×); G) MUM1+ (400×); H) BCL2+ (400×); I) High Ki67 proliferation index (400×).

antigenic stimulations, including recurrent blood transfusions, accompanied by the development of serum IgE level, anti-IgG, anti-IgA, and antileukocyte antibodies. Iron-induced oxidative injury in iron overload or deferoxamine carcinogenic effects also contributes to malignancies development in thalassemia patients [8–11]. However, this patient never received blood transfusion. Infection of Epstein-Barr virus (EBV) also contributes to the development of lymphoma in beta thalassemia patients [8,9,12]. We did not take EBV titer in this case.

There is no standard guideline for the treatment of PBL. Treatment strategies for PBL vary broadly, from surgical intervention, systemic chemotherapy, radiotherapy, or a combination of systemic chemotherapy and radiotherapy [4,7,13]. Several studies recommend that surgery is offered for diagnostic purposes only. Minimally invasive surgery is a preferable option because extensive surgery may carry a high risk of morbidity [4,13]. We used a surgical modality to perform core biopsy on the patient. Mastectomy was

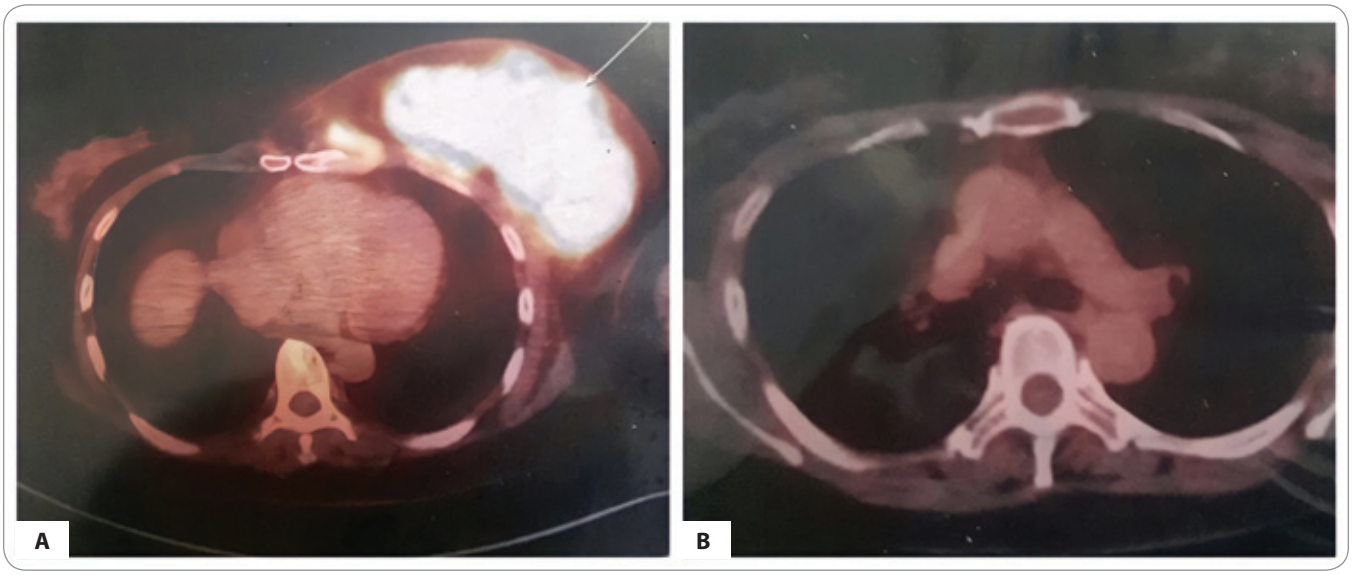

Fig. 3. PET/CT Scan. A) before therapy; B) after therapy.

not performed. Systemic treatment with chemotherapy remains the basis of management of PBL, with the schemes generally using R-CHOP. In a cohort from the Spanish Lymphoma Oncology Group, the 5-year overal survival was 76%, and the 5-year progression-free survival was 73%, with no statistically significant differences observed in the analysis by subgroups of treatment and histology [7]. This patient responded well to R-CHOP systemic chemotherapy and reached complete remission after 6 cycles. There was no disease, and she still survives after 6 years from the last dose of R-CHOP chemotherapy.

Conclusion

Primary breast lymphoma is a rare disease and the most common subtype is diffuse large B-cell lymphoma. Systemic chemotherapy R-CHOP is a treatment option for primary breast diffuse large B-cell lymphoma.

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