The Turkish Journal of Pediatrics 2024; 66(6): 781-785
https://doi.org/10.24953/turkjpediatr.2024.4681

Case Report

Primary breast Burkitt lymphoma with lactic acidosis in a child: a case report

Eren Müngen[1], Nilgün Kurucu[1], Tezer Kutluk[1], H. Nursun Özcan[2], Selman Kesici[3], Diclehan Orhan[4]

[1]Department of Pediatric Oncology, Faculty of Medicine, Hacettepe University, Ankara; [2]Department of Pediatric Radiology, Faculty of Medicine, Hacettepe University, Ankara; [3]Department of Pediatric Critical Care Medicine, Life Support Center, Faculty of Medicine, Hacettepe University, Ankara; [4]Department of Pathology, Faculty of Medicine, Hacettepe University, Ankara, Türkiye.

ABSTRACT

Background. Primary breast lymphoma is extremely rare and constitutes approximately 1% of all non-Hodgkin's lymphomas (NHL). Only 1-5% of them are Burkitt type. We present a case of childhood primary breast Burkitt lymphoma (BL).

Case presentation. A 16-year-old female patient was referred to our hospital for bilateral breast swelling and respiratory distress. She had lactic acidosis. Despite aggressive dialysis support, lactic acid levels started to decrease only after the combination chemotherapy treatment was started and returned to normal. Histopathological examination of the biopsy was consistent with the diagnosis of BL. The case was classified as stage 4 disease. EICNHL Mature B NHL protocol, Group C3 chemotherapy was given and a very good partial response was achieved. However, the patient died due to fungal septicemia.

Conclusion. Type B lactic acidosis in aggressive malignancies indicates a poor prognosis. In such cases, as in our case, lactic acidosis improves only with appropriate and sufficient chemotherapy, and its improvement is an important indicator that the case is responsive to treatment.

Key words: breast Burkitt lymphoma, lactic acidosis, childhood.

Lymphoma constitutes 17.6% of all childhood cancers in Türkiye.[1] Approximately 20%–40% of patients with non-Hodgkin lymphoma (NHL) arise from primary extranodal sites. The most common site of primary extranodal disease is the gastrointestinal tract followed by skin, testis, bone, and central nervous system (CNS); rarely, the kidney, prostate, bladder, ovary, orbit, heart, breast, salivary glands, thyroid, and adrenal glands may be involved.[2,3]

Primary breast lymphoma (PBL) arises from breast lymphoid tissue. It is an extremely rare disease, which constitutes 2% of extranodal NHLs and approximately 1% of all NHL.[4–6] Diffuse large B cell lymphoma is the most common histopathological subtype of PBL. Only 1-5% of them are Burkitt type.[4,5,7,8]

In this context, herein we present a case of childhood primary breast Burkitt lymphoma (PB-BL).

Case presentation

A 16-year-old female patient was referred to our hospital due to bilateral breast swelling and respiratory distress. It was learned that she had been admitted to a regional hospital with the complaint of swelling in her right breast 40 days

✉ Eren Müngen ▪ mungeneren@gmail.com

Received 10th Jun 2024, revised 26th Aug 2024, accepted 12th Sep 2024.

before. In physical examination, there had been no pathological finding except for swelling, induration and tenderness in the breast. The diagnosis of mastitis had been made and antibiotic therapy started. Since there was no improvement of the symptoms with antibiotics, she underwent to the surgery in that hospital with the diagnosis of a breast abscess, debridement of the tissues thought to be infected, and a tru-cut biopsy was performed. Later on she was referred to our hospital. It was seen that both breasts, especially right one, turned into giant purplish-blue masses with diffuse nodularity. There was a tissue defect and seropurulent discharge on the biopsy area in the right lower lateral quadrant of the right breast. There was lymphadenopathy of 3×2 cm in the right axillary region. In the laboratory examination, hemoglobin was low at 9.5 g/dL, platelet count was $689x10^3$ /mm^3, white blood cells $8.3x10^3$ /mm^3, lactate dehydrogenase (LDH) 3505 U/L, renal and liver function tests were in normal limits. Her blood pH was 7.25, bicarbonate 14.6 mmol/L, lactate 22 mmol/L, anion gap was 20.8. In thorax computed tomography, the size of both breasts was increased and there were diffuse infiltrative soft tissue lesions which was more obvious in the right breast (Fig 1a). Breast ultrasonography demonstrated hypoechoic ill-defined breast masses with soft tissue edema (Fig 1b). Pathological lymphadenopathies along the bilateral parasternal intermammarian chain on the anterior chest wall and in the right axillary region were observed. Abdominal computed tomography revealed prominent diffuse thickening of small intestinal wall and colonic segments (Fig 2), intraabdominal free fluid, and a soft tissue lesion in the left pelvic lesion, consistent with peritoneal thickening.

The patient underwent hemodialysis after sodium bicarbonate deficit treatment for the lactic acidosis. Despite intermittent hemodialysis lactic acidosis persisted and continuous veno-venous hemodiafiltration was started. Daily two sessions of 4 hours intermittent hemodialysis, and 16 hours continuous veno-venous hemodiafiltration was continued for 3 days. Wide spectrum antibiotics were started, since purulent discharge from biopsy site was observed. Despite aggressive dialysis support, lactic acid levels started to decrease only after the cancer specific treatment was started and returned to normal on the third day. Histopathological examination of the biopsy was consistent with the diagnosis of BL. Bone marrow biopsy was normal. Cytological examination of cerebrospinal fluid showed central nervous system (CNS) involvement. The case was classified as stage 4 disease and EICNHL Mature B NHL protocol, Group C3 chemotherapy was started. At the end of the third course very good partial response was achieved. Radiological response evaluation

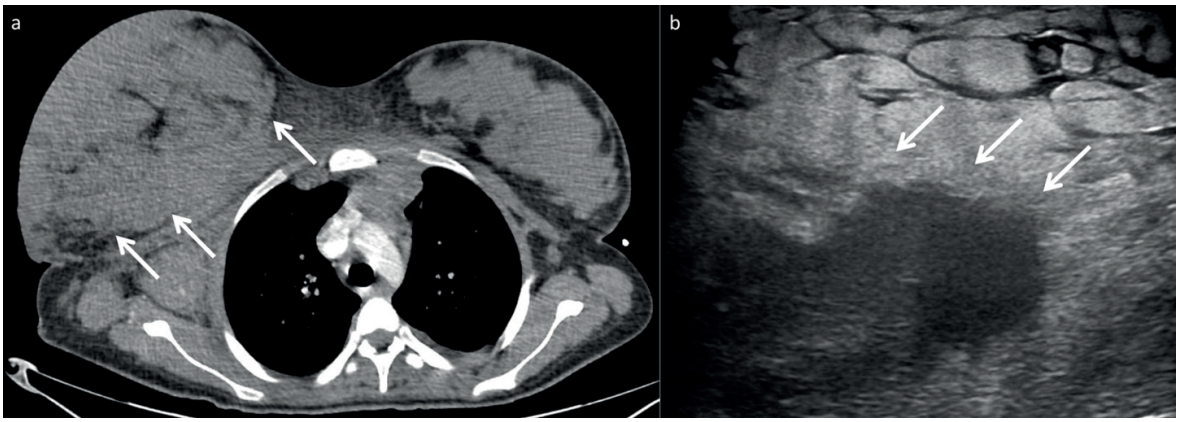

Fig. 1a-b. A 16-year-old girl with Burkitt lymphoma. **(a)** Axial contrast enhanced chest computerized tomography shows large heterogeneous breast mass (arrows). **(b)** Breast ultrasonography demonstrates hypoechoic ill-defined breast mass (arrows) with soft tissue edema.

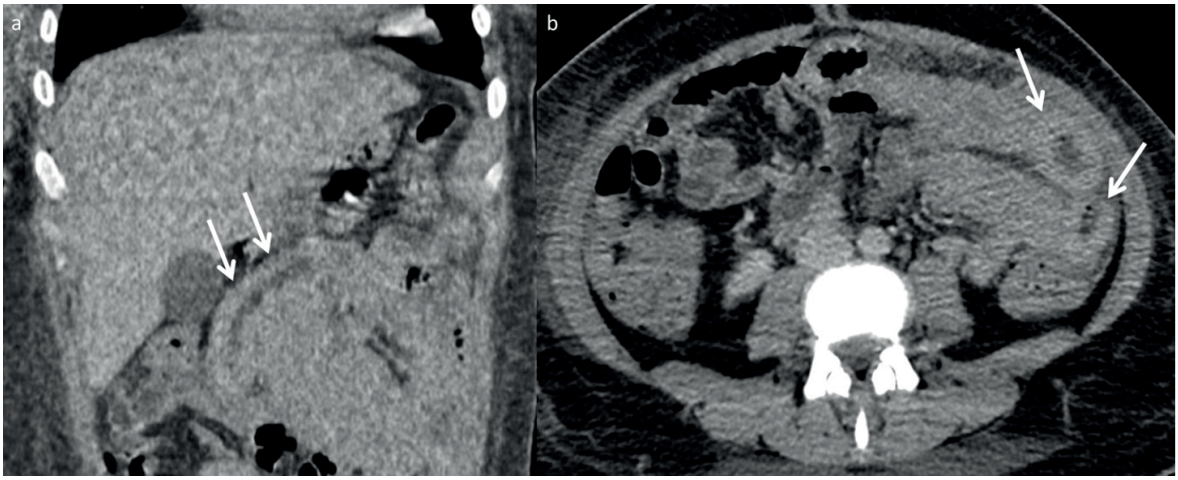

Fig. 2. A 16-year-old girl with Burkitt lymphoma. Coronal reformatted **(a)** and axial **(b)** contrast enhanced abdomen computerized tomography shows diffuse bowel wall thickening (arrows).

showed regression in the entire affected area except for heterogeneous nodularity in the right breast, which was thought to be due to infection rather than tumoral residue. She was diagnosed with neutropenic sepsis at the end of this course. Mold fungus belonging to *Aspergillus spp.* and *Mucoralis spp.* and *Stenotrophomonas maltophilia* were isolated from the pus culture obtained from the biopsy site, where the breast infection had drained through the skin. Amphotericin and voriconazole were started. Wide surgical debridement was planned. However, pulmonary and femoral venous thromboembolism developed during this period. Anticoagulant treatment was started. Respiratory distress and circulatory failure developed, and the patient died from septic shock three months after the diagnosis. Consent was obtained from the patient and the parents for the publication of this case report.

Discussion

Breast cancer arising from epithelial cell components is the most common cancer in women. Lymphoma rarely involves breast tissue either as a part of disseminated disease or as primary location.[4]

Primary breast lymphoma accounts for only 0.04% of breast neoplasms. It mostly affects adult women between fourth and sixth decade.[9] Its onset in childhood is exceptionally rare. Restivo et al.[10] reviewed 11 cases reported in the literature. These were mostly adolescent females with a median age of 14.5 years. There was only one boy. There was a slight right breast predominance and only one bilateral involvement.

Over 90% of reported adult PBL cases are of B cell origin. More than 50% were diagnosed as diffuse large B cell lymphomas, while Burkitt lymphomas were the less common B cell variants. However, anaplastic large cell lymphomas and mature B-cell lymphomas were reported with equal frequency in children.[10]

Burkitt lymphoma in adults is a highly uncommon subtype of PBL. PB-BL primarily affects young women in their reproductive years. It has been observed that PB-BL often presents in pregnancy or post-partum during lactation, which has led to the suggestion that hormonal changes may play a role in its development.[4] Very few cases of PB-BL have been reported in childhood. The most common presentation of PB-BL is a diffuse and rapid bilateral enlargement of the breasts along with associated symptoms such as pain, redness, itching, fever, and axillary lymphadenopathy.[4]

A high incidence of CNS involvement was reported in patients with breast lymphomas.[11]

CNS involvement occurs in 6 percent of pediatric NHL with rates ranging from 8.8% in BL to < 3% in diffuse large B cell lymphoma[12], while this ratio reached 50% in PBL.[11]

Most common presentation of BL is rapidly growing tumor masses and frequent spontaneous tumor lysis. Tumor lysis syndrome, a condition resulting from the massive lysis of tumor cells and the subsequent release of large quantities of potassium, phosphate, and uric acid into the systemic circulation, is a potential oncologic emergency. The deposition of uric acid or calcium phosphate crystals in the renal tubules can lead to acute renal failure.[13] When our patient was admitted to our hospital, serum uric acid, potassium, and phosphate levels were normal, and serum LDH level was 3505 U/L. There was no sign of tumor lysis despite the heavy tumor burden. However, she had severe lactic acidosis. Renal involvement, which is a risk factor for the development and severity of tumor lysis syndrome and common in Burkitt lymphoma, was not present in our case.

Type A lactic acidosis is a serious complication occurring in critically ill patients and is associated with the underlying shock state resulting from tissue hypoperfusion and dysoxia. If lactic acidosis occurs in a person with normal hemodynamic parameters and adequate tissue oxygenation, this condition is called type B lactic acidosis. Type B lactic acidosis is a rare complication in cancer patients. Malignant cells increase glycolysis and lactate production to allow for uncontrolled proliferation, also called the Warburg effect. Lactogenic cancers exhibit increased aerobic glycolysis and lactate production in parallel with the aggressiveness of the cancer.[14] The occurrence of type B lactic acidosis in cancer cases is considered an indicator of a poor prognosis. If the serum LDH level is 2-3 times higher than the standard value, it suggests a poor prognosis.[15] In our case, the serum LDH level was 3505 U/L at the time of admission to our hospital. When appropriate chemotherapy is started, acidosis is corrected.[16] In fact, it is the only treatment method that leads to sustained remission. Lactic acidosis was reported to resolve within 15 h to 3 days after starting chemotherapy. In cases whose tumors are unresponsive to chemotherapy, lactic acidosis will not improve.[16,17] The resolution of lactic acidosis with chemotherapy could be considered a herald of the onset of remission. In the case of lactic acidosis, besides reducing the production of lactic acid, it is important to remove lactic acid extracorporeally in order to keep the patient alive during this period and to prevent irreversible damage to the organs due to acidosis. Although hemodialysis is the best method for this purpose, continuous veno-venous hemodiafiltration may be used in the case of persistent lactic acidosis despite hemodialysis or to prevent recurrence after hemodialysis. In our patient, both dialysis modes were successfully used in combination until the third day when chemotherapy started to take effect.

Surgical interventions should be avoided in these cases because the recovery process after surgery may delay the initiation of systemic therapy, which is needed urgently. Burkitt's lymphoma responds very well to combination chemotherapy. In children and adolescents, risk-adapted treatment approaches are required. These are high-dose intensive chemotherapy protocols that penetrate the CNS. In high-risk patients rituximab improves outcome and should be given to all patients.[13] Although our patient has all kinds of negative risk factors for the outcome; with early initiation of treatment and selected effective chemotherapy, she was in remission rapidly. Unfortunately, she died due to secondary fungal infections and sepsis.

In conclusion, primary childhood breast Burkitt lymphoma (BL) is a very rare disease, frequently associated with tumor lysis syndrome and rarely with type B lactic acidosis. Its prognosis is poor and early initiation of appropriate combination chemotherapy is crucial for the cure of both lactic acidosis and lymphoma.

Ethical approval

Informed consent was obtained from the parents of the child.

Author contribution

The authors confirm contribution to the paper as follows: Study conception and design: EM, NK; data collection: EM; analysis and interpretation of results: EM, NK, TK, HNO, DO, SK; draft manuscript preparation: EM, NK, TK. All authors reviewed the results and approved the final version of the article.

Source of funding

The authors declare the study received no funding.

Conflict of interest

The authors declare that there is no conflict of interest.

REFERENCES

1. Kutluk MT, Yeşilipek A. Pediatric cancer registry in Turkey 2002-2023: 22 years of achievement (TPOG & TPHD). J Clin Oncol 2024; 42(Suppl 16): 10051. https://doi.org/10.1200/JCO.2024.42.16_suppl.10051
2. Minard-Colin V, Brugières L, Reiter A, et al. Non-Hodgkin lymphoma in children and adolescents: progress through effective collaboration, current knowledge, and challenges ahead. J Clin Oncol 2015; 33: 2963-2974. https://doi.org/10.1200/JCO.2014.59.5827
3. Chung EM, Pavio M. Pediatric extranodal lymphoma. Radiol Clin North Am 2016; 54: 727-746. https://doi.org/10.1016/j.rcl.2016.03.004
4. James ER, Miranda RN, Turner SD. Primary lymphomas of the breast: a review. JPRAS Open 2022; 32: 127-143. https://doi.org/10.1016/j.jpra.2022.01.004
5. Feng K, Zhao S, Shang Q, et al. An overview of the correlation between IPI and prognosis in primary breast lymphoma. Am J Cancer Res 2023; 13: 245-260.
6. Talwalkar SS, Miranda RN, Valbuena JR, Routbort MJ, Martin AW, Medeiros LJ. Lymphomas involving the breast: a study of 106 cases comparing localized and disseminated neoplasms. Am J Surg Pathol 2008; 32: 1299-1309. https://doi.org/10.1097/PAS.0b013e318165eb50
7. Miyoshi I, Yamamoto K, Saito T, Taguchi H. Burkitt lymphoma of the breast. Am J Hematol 2006; 81: 147-148. https://doi.org/10.1002/ajh.20321
8. Elgaafary S, López C, Nagel I, et al. Molecular characterization of Burkitt lymphoma in the breast or ovary. Leuk Lymphoma 2021; 62: 2120-2129. https://doi.org/10.1080/10428194.2021.1907374
9. Gholam D, Bibeau F, El Weshi A, Bosq J, Ribrag V. Primary breast lymphoma. Leuk Lymphoma 2003; 44: 1173-1178. https://doi.org/10.1080/1042819031000079195
10. Restivo GA, Pillon M, Mussolin L, et al. Primary breast lymphoma of childhood: a case report and review of literature. BMC Pediatr 2021; 21: 530. https://doi.org/10.1186/s12887-021-03002-6
11. Yamazaki H, Hanada M, Kitada M, et al. Four cases of central nervous system involvement of breast malignant lymphoma. Jpn J Clin Oncol 2003; 33: 399-403. https://doi.org/10.1093/jjco/hyg072
12. Salzburg J, Burkhardt B, Zimmermann M, et al. Prevalence, clinical pattern, and outcome of CNS involvement in childhood and adolescent non-Hodgkin's lymphoma differ by non-Hodgkin's lymphoma subtype: a Berlin-Frankfurt-Munster Group Report. J Clin Oncol 2007; 25: 3915-3922. https://doi.org/10.1200/JCO.2007.11.0700
13. Roschewski M, Staudt LM, Wilson WH. Burkitt's lymphoma. N Engl J Med 2022; 387: 1111-1122. https://doi.org/10.1056/NEJMra2025746
14. Looyens C, Giraud R, Neto Silva I, Bendjelid K. Burkitt lymphoma and lactic acidosis: a case report and review of the literature. Physiol Rep 2021; 9: e14737. https://doi.org/10.14814/phy2.14737
15. Cairo MS, Sposto R, Gerrard M, et al. Advanced stage, increased lactate dehydrogenase, and primary site, but not adolescent age (≥ 15 years), are associated with an increased risk of treatment failure in children and adolescents with mature B-cell non-Hodgkin's lymphoma: results of the FAB LMB 96 study. J Clin Oncol 2012; 30: 387-393. https://doi.org/10.1200/JCO.2010.33.3369
16. Friedenberg AS, Brandoff DE, Schiffman FJ. Type B lactic acidosis as a severe metabolic complication in lymphoma and leukemia: a case series from a single institution and literature review. Medicine (Baltimore) 2007; 86: 225-232. https://doi.org/10.1097/MD.0b013e318125759a
17. Chan FH, Carl D, Lyckholm LJ. Severe lactic acidosis in a patient with B-cell lymphoma: a case report and review of the literature. Case Rep Med 2009; 2009: 534561. https://doi.org/10.1155/2009/534561