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Primary Breast Burkitt's Lymphoma: A Case Report

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ABSTRACT

We report the case of a 59-year-old Mexican woman who was treated in the emergency department (ED) on two occasions, the first one for a gastroenteritis episode, during which a tumor mass was found in the upper outer quadrant of her right breast along and ipsilateral axillary adenomegaly, both painful, with a three-month evolution. After the patient's discharge, she was unable to continue the diagnostic protocol on an outpatient basis, as she was readmitted 15 days later due to a convulsive episode in conjunction with severe hyponatremia. Relevant prior findings to this admission included episodes of fever and a weight loss of eight kg. During the physical examination, the presence of the tumor was ratified, and an excisional biopsy was performed. On the sixth day of hospitalization, she began to experience progressive neurological deterioration. A cranial tomography revealed a hypodense lesion in the right occipital lobe of the brain. Due to the imminent need for cardiopulmonary resuscitation measures, the family's request was denied, and the patient passed away shortly after. Histopathological examination of the biopsy identified a lymphoid neoplasm with a diffuse growth pattern composed of medium-sized, monotonous, discohesive cells with evident nucleoli, frequent atypical mitosis, and abundant macrophages—findings suggestive of a Burkitt lymphoma, ratified six days after the death with immunohistochemical studies that identified positive CD20 and CD10, negative bcl-2 and CD3, and 90% for Ki-67 and 90% for MYC. The patient did not receive any type of chemotherapy.

Keywords: Invasive breast cancer; Burkitt lymphoma; Starry sky image; B-type lymphoid cells; CD10 and CD20 markers.

INTRODUCTION

Due to the variety of primary neoplasms that can develop in the female mammary gland (MG), breast cancer (BC) is more than a unique pathological entity, has been considered a generic term that comprehends a range of diseases, including the 21 histological subtypes and four molecular subtypes known [1]. These can be classified by their histological origin as epithelial and non-epithelial neoplasms, belonging to the epithelial, ductal and lobular invasive types, as well as 14 to 21 subtypes called rare, which, together with non-epithelial subtypes, account for 10-35% of BC [1-3].

Among non-epithelial mammary neoplasms are sarcomas, phyllodes tumors, and lymphomas, whose prevalence does not exceed 1%, with primary breast lymphoma (PBL) having the lowest prevalence (0.04% to 1%), representing <2% of non-Hodgkin lymphomas (NHL) of extranodal location [3-5]. To accept PBL as primary and not secondary, the criteria of Wiserman and Liao [6] must be met, specifically that the neoplasm is confined to the breast, that both mammary and lymphoid tissues coexist intermixed, there is no disease disseminated beyond the axillary lymph nodes, and the patient has never been diagnosed with lymphoma before.

These neoplasms predominantly present in patients aged 60 to 65 years; They are composed of T or B lymphocyte lineage cells, with predominantly mature B cells identified in up to 90% of PBL cases, more than 50% of which are diffuse large B-cell lymphomas (DLBCL), as reported by James et al. [4], who cited prevalences of 39.6% to 76.6%, followed by extranodal marginal zone lymphoma (6.7% to 28%), follicular lymphoma (10% to 15.9%), and Burkitt lymphoma of the breast (BLB) (2%). The experience with a case treated in October 2023 at a hospital of the Mexican Social Security Institute in Cancun, Quintana Roo, Mexico, is presented here.

CASE PRESENTATION

It was about a 59-year-old Mexican patient who was brought to the emergency department (ED) for a *de novo* convulsive crisis. She had a history of chronic diabetes and hypertension and had undergone three uncomplicated abdominopelvic surgeries in her adult life, in addition to a previous hospitalization prior to this one.

Regarding her gynecological-obstetric history, she reported menarche at age 12, having had five pregnancies, five deliveries, and breastfed each child, without mentioning the duration of each episode. She denied the use of any type of hormonal contraceptives; she reported menopause at age 49 without any hormone replacement therapy. At age 51, she had a mammogram that resulted in BI-RADS 0 and a normal breast ultrasound.

Her previous hospitalization occurred 15 days prior due to a severe gastroenteritis episode, during which she reported pain in the right breast and axilla of moderate intensity, of three months duration. The physical examination identified a tumor mass in the upper outer quadrant, approximately 10x6 cm, extending to the Spencer tail, not attached to deep layers, with no erythema, skin changes, or nipple discharge, and it was painful to both superficial and deep palpation, radiating to the ipsilateral axilla and upper extremity. After gastroenteritis was

controlled, she was discharged with plans to further investigate the breast and axillary findings on an outpatient basis. However, two weeks later, the convulsive episode occurred.

Upon current admission, episodes of fever and a weight loss of up to eight kg were reported, along with hepatomegaly and bilateral inguinal adenomegaly. Laboratory results showed normal hemoglobin and white blood cell counts. The only abnormal biochemical parameters were sodium (118 mmol/L), glucose (163 mg/dL), triglycerides (296 mg/dL), and lactate dehydrogenase (LDH) (917 IU/L). A central venous catheter was placed for treatment of the electrolyte imbalance. Cranial tomography revealed a hypodense lesion in the right occipital region.

Ulterior stabilization, she was admitted to the Gynecology service to continue treatment and initiate diagnostic protocols given the suspicion of BC. She complained of burning and intense pain in the affected breast and axilla and continued with febrile episodes. Ultrasound identified a mass of 52x49 mm with poorly defined and irregular borders, no calcifications, and poor vascularity on Doppler, classified as BI-RADS 5. Ultrasound of both axillae showed reactive adenopathy. A contrast-enhanced abdominal-pelvic tomography identified a hepatic adenoma, splenomegaly, and bilateral inguinal adenopathy.

She underwent an excisional biopsy of the tumor, which reported a lymphoid neoplasm with a diffuse growth pattern composed of medium-sized, monotonous, discohesive cells with evident nucleoli, frequent atypical mitosis, and abundant macrophages, suggestive of a BL (image 1), confirmed with immunohistochemical tests (IHC) (table, images 2,3, and 4).

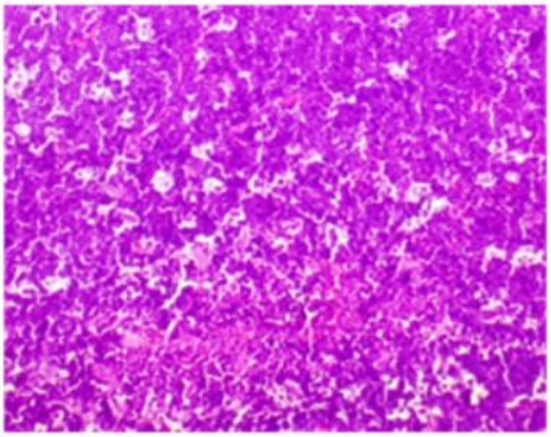

Image 1. Burkitt lymphoma. Hematoxylin – Eosin staining. A diffuse neoplasm composed of medium, monotonous lymphocytes with nuclear molding, round nuclei with fine granular chromatin, frequent mitoses, apoptotic bodies, and abundant macrophages with tingible bodies (starry sky pattern).

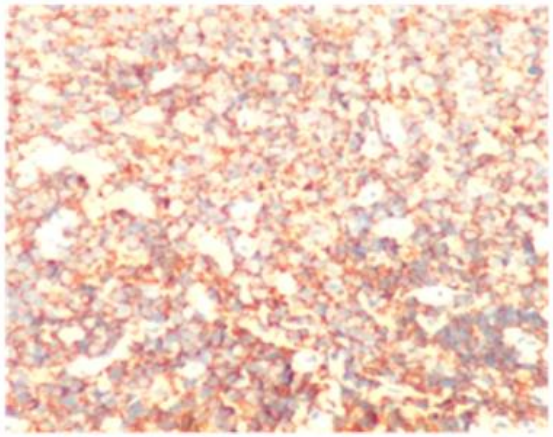

Image 2. Immunohistochemical reaction with CD20 in breast tissue infiltrated by Burkitt lymphoma. Strong and diffuse marking in neoplastic B lymphocytes.

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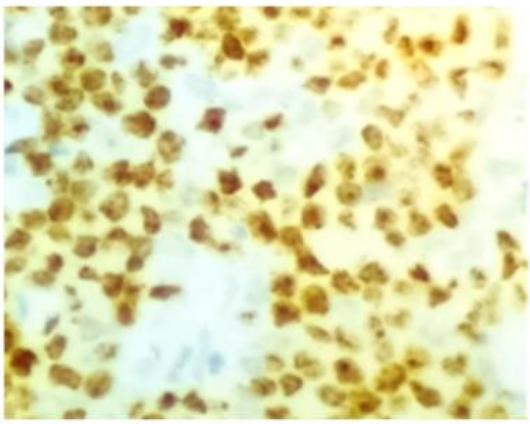

Image 3. Immunohistochemical reaction with Ki-67 in breast tissue with Burkitt lymphoma. Almost all cells are proliferating, characteristically with a proliferation index greater than 90%, intermediate density in patches in breast tissue infiltrated by the tumor.

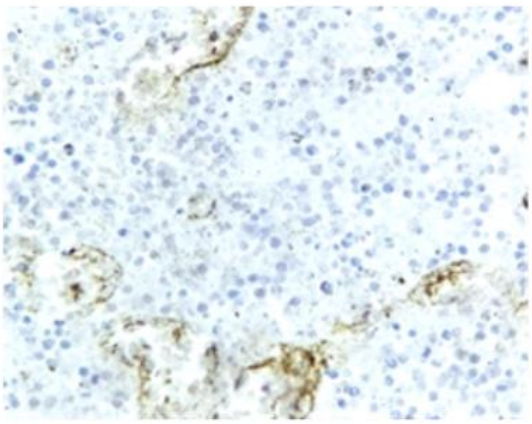

Image 4. Immunohistochemical reaction with GCDFP15 in breast tissue infiltrated by Burkitt lymphoma. Weak multifocal positivity in residual breast tissue.

Table. Interpretation of indirect immunohistochemistry.

Marker	Interpretation
CD20	Positive for neoplasm
CD3	Negative for neoplasm
CD10	Positive for neoplasm
Bcl-2	Negative for neoplasm
CMYC	Positive in 90% for neoplasm
Ki67	Positive in 90% for neoplasm
GCDPF15	Multifocal positive in residual breast tissue

She began with progressive neurological deterioration until reaching deep coma, and did not receive life support as per the family's request, passing away on the sixth day of admission. Histopathological and immunohistochemical results were received posthumously, and therefore, she did not receive any oncological treatment.

DISCUSSION

As far as we have investigated, the clinical case presented here would be the first described in many years in the southeastern region of Mexico, reflecting the epidemiology of this subtype of lymphoma, whose prevalence among NHLs ranges from 1% to 5% [7]. The frequency in Mexico is reported as 2.5% in an epidemiological study describing trends in different types and subtypes of over 4 thousand NHLs gathered over ten years [8].

Its extranodal presentation as BLB appears to be limited to isolated cases [9-14], defining the non-endemic or sporadic category in the World Health Organization's classification of this lymphoma subtype [7], which seems to predominate in women of reproductive age [4,9-14], but has also been identified in the MG of an adolescent [11], during the perinatal period [8,9,14], and even in the breast of a young, African man [15].

Rapidly evolving (from three weeks to three months) [9-14], it is characterized by affecting one or both MGs and clinically, the patient, whether male or female, may notice an increase in

volume and distortion of breast anatomy because the neoplasm develops as a diffuse, painful, pruritic, erythematous lesion, with or without skin hyperpigmentation, serohematic nipple discharge, B symptoms, and axillary adenopathy, painful or not [9-15].

However, it may also present with systemic clinical data alongside breast findings, such as those characterizing systemic inflammatory response syndrome, acute renal and hepatic failure, and acute neurological involvement, manifested as seizures and hemicorporal motor deficits [13,14,16]. Basic lab tests may show elevated uric acid and LDH in serum due to rapid tumor cell turnover. Any type of electrolyte disturbances and acid-base imbalances are also part of the clinical presentation at admission and during hospital evolution [13,14,16].

Some of these data conglomerate coincide with what was observed in the case presented here, a postmenopausal woman, under 60 years of age, who during her two hospital admissions reported severe pain in the affected breast and ipsilateral upper extremity, along with B symptoms, increased LDH, and severe hyponatremia—an abnormality commonly seen in patients with various hematological cancers, including lymphomas, and which may have contributed to the convulsive event at admission [16].

Like its abdominal presentation as ileocecal disease—most common in the sporadic BL category— difficult to diagnose, the same happens when diagnosing BLB due to the clinical presentation's similarity to infectious breast processes [9-11] or primary ductal epithelial breast cancer [12], especially when the clinical data pointing to a mammary NHL are not considered [6]. In the presented case, such biases may have occurred when the ED decided to discharge the patient and defer her care to an outpatient clinic, which would have delayed her diagnostic workup by at least two weeks, this being the biopsy.

Fine needle aspiration, cutting needle [11], or excisional biopsy are the ways to obtain breast tissue, with excisional biopsy being the most efficient—considered the gold standard—due to the amount of material available for histopathological and immunohistochemical studies [7,17]. In this case, the excisional biopsy was performed at the second admission, and the histopathological analysis revealed the cellular pattern characteristic of B-cell NHLs [7,11,15], classified by IHC as a PBL subtype BL [4,18-20].

This technique, of limited access in not few countries' healthcare systems [20], including Mexico, relies on the use of specific antibodies to identify the presence, absence, germinal origin, and concentration (percentage) of various protein antigens synthesized at different stages of the neoplastic cell cycle, many of which, when combined in minimal (<10 markers) or extended panels (10 or more markers), allow for more precise lymphoma classifications [4,7,18-20]. In this case, a seven-marker panel identified the characteristic markers for BLB, including CD20 (B-cell marker), CD10 (germinal center marker), 90% cMYC gene translocation, 90% Ki67 (rapid cell turnover), and the absence of CD3 and bcl-2, which are characteristic of T-cell NHL and DLBCL [18-20].

This IHC panel is like those found in other clinical cases, with differences that would determine the interpopulation variability of clinical BLB presentations. For instance, in the Iranian case [9], CD19 and CD20 were identified, but not CD10. Negahban et al. [10] structured their panel with CD10, CD20, Ki-67, and IGH-MYC gene translocation-fusion. Kato and Solomon [15]

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identified CD20, CD10, and Ki-67, with CD45 detected by flow cytometry. Mitala et al. [11] identified CD45, c-MYC, and 100% Ki-67, but no CD3 or bcl-2. A Mexican case did not provide an IHC panel [14].

As a panel for IHQ, which could be used as a reference, Rymkiewicz et al. [18] state that most MYC-positive BL are CD20+/CD10+/BCL6+/BCL2−/MUM1−/MYC+/CD44−/CD43+/Ki-67 >95%, which allows them to be differentiated from other aggressive MYC-negative B-cell lymphomas, such as BL-like Brittney et al. [7] describe the BL panel as CD20, CD19, CD10, CD79a, CD45, CD5, MUM1, Bcl2, BCL6, and Ki-67, but not the cytokeratin cocktail, which identifies epithelial neoplasms [5,15]. Cho [19] proposes an essential (or minimum) panel consisting of the markers CD20, CD10, CD3, BcL-2, and Ki-67, and an optional panel composed of 13 markers.

Disanto et al. [20] state that using three antibodies results in the correct identification of 69% of B-cell lymphomas. For BL, they propose five: CD20+, CD10+, BCL2(−), TdT(−), and cyclin D1(−). Cho [19] mentions that confusion in interpretation is a fact, since when the histopathological sample of an DLBCL is positive for CD10, negative for Bcl-2, and the mitosis index is >95%, the possibility of the neoplasm being an BL is high and should be confirmed through fluorescent in situ hybridization of the MYC oncogene.

Unfortunately, the patient passed away due to neurological deterioration before the IHQ results were known and thus had not started any anti-neoplastic treatment. This was the expected outcome, considering that cerebral infiltration is a characteristic with high mortality in BL and DLBCL [21,22]. In the case presented here, it would have acted as an epileptogenic focus or as a cause of intracranial hypertension [22], although it has also been observed that the neoplasm induces severe metabolic changes—the patient arrived at the ER with severe hyponatremia, one of the clinical signs being precisely the seizure episode—resulting from multiple organ failure and the cause of death in this clinical scenario [13,23].

Durodola [23] describes the immediate causes of death in 41 patients with BL of any location, three (7.3%) of whom had BLB. In five (12.2%), the cause was heart failure (one with BLB), seven (17.1%) died from liver failure (one with BLB), kidney or adrenal failure, ten (24.4%) from hemorrhage of the necrotic tumor, twelve (29.3%) from miscellaneous causes (one with BLB), died from adhesive fibrous pleuritis), and in seven (17.1%), no precise cause was identified. Based on these results, the author suggests that effective supportive treatment can be a life-saving adjunct to the oncological treatment regimen and should be instituted as soon as the diagnosis is made, or even earlier.

CONCLUSIONS

Clinical cases teach a lot. The one presented here, the only known one in hospitals in southeastern Mexico, raises questions about whether the medical actions or decisions made both in the ER and in Gynecology service delayed the diagnosis and adversely changed its outcome, or if it was the expected outcome for a rare neoplasm like BLB. On her first discharge, referring her to the Breast cancer consultation—medical decision that the patient was unable to access—rather than hospitalizing her, could have been a determining factor in the progression of the neoplasm by delaying the diagnostic approach by 15 days. On the second admission, already in a precarious general state and after the biopsy was taken, the waiting

time for the immunohistochemical results would also be significant, as it would have prevented the patient from receiving oncological treatment and, therefore, further deteriorated her condition.

Confronting this case—practically an oncological emergency—reveals, on the one hand, how medical interpretation biases can affect the efficiency of care, which would also be compounded by the limitations or deficiencies in high-level infrastructure that hospitals suffer from, such as the lack of a histopathology service and, even more so, an IHQ laboratory. These circumstances often prolong waiting times, as biological samples, such as biopsies, must be processed and analyzed externally, contributing to the vulnerability of patients with rare—and not so rare—aggressive pathologies, as would have occurred in the case presented.

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