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Multidisciplinary management of a patient with synchronous neoplasms: A case report of breast cancer plus pheochromocytoma

Manejo multidisciplinario de paciente con neoplasias sincrónicas: reporte de un caso clínico de cáncer de mama y feocromocitoma

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ABSTRACT

Introduction: Synchronous neoplasms are a rare phenomenon. It is reported that patients with breast cancer and synchronous neoplasms most frequently develop malignant tumors in the thyroid gland (71%) or the gynecological tract (9.7%). There is no established association with pheochromocytoma, as the presence of both synchronous neoplasms is extremely rare. This case describes an atypical association of two neoplasms and their multidisciplinary approach in a public institution in Peru. **Case report:** Postmenopausal patient who presented with a breast tumor compatible with malignant neoplasm. Extension studies incidentally evidenced an adrenal mass with characteristics of malignancy, initially suspecting a focus of secondary metastasis. Complementary studies evidenced elevated serum and urinary metanephrines, leading to the diagnosis of pheochromocytoma. Initially, a right adrenalectomy was performed, followed later by a radical mastectomy, obtaining high-risk pathology (grade II with lymphovascular invasion, perineural invasion, and nodal macrometastases). **Discussion:** Synchronous neoplasms present a challenge in the diagnosis and treatment of the oncological patient. In this case, the surgical management of pheochromocytoma was prioritized due to the risk of cardiovascular complications. Delay in the management of breast pathology is a factor associated with the presence of high-risk scenarios, characterized by disease in more advanced stages, a greater probability of tumor progression, and worst oncological outcomes. **Conclusions:** The management of multiple neoplasms should be individualized according to the characteristics of each neoplasm and risk of complications. It is necessary to report cases of atypical associations of multiple neoplasms to broaden the diagnostic spectrum and improve the therapeutic approach for patients.

Keywords: Synchronous neoplasms, pheochromocytoma, breast cancer, clinical case.

RESUMEN

Introducción: Las neoplasias sincrónicas son poco frecuentes. Se reporta que los pacientes con cáncer de mama y neoplasias sincrónicas desarrollan con mayor frecuencia tumores malignos en la glándula tiroidea (71 %) o en el tracto ginecológico (9,7 %); pero no existe ninguna asociación establecida con el feocromocitoma, ya que la presencia de ambas neoplasias sincrónicas es extremadamente rara. Este caso describe una asociación atípica de dos neoplasias y su abordaje multidisciplinario en una institución pública de Perú. **Caso clínico:** Paciente posmenopáusica consulta por tumoración en la mama compatible con una neoplasia maligna, en estudios de extensión se evidencia incidentalmente una masa suprarrenal con características de malignidad, con sospecha inicial de un foco metastásico. En estudios complementarios se evidencia elevación de metanefrinas séricas y en orina. El diagnóstico fue feocromocitoma. Inicialmente, se realizó una adrenalectomía derecha y luego la

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mastectomía radical; el resultado histopatológico fue de alto riesgo (grado II con invasión linfovascular, perineural y macrometástasis ganglionar). **Discusión:** Las neoplasias sincrónicas representan un desafío al diagnóstico y tratamiento del paciente oncológico. En este caso se priorizó el manejo quirúrgico del feocromocitoma ante el riesgo de complicaciones cardiovasculares. La demora en el manejo de la patología mamaria es un factor asociado a presencia de escenarios de alto riesgo, caracterizados por enfermedad en estadios más avanzados, mayor probabilidad de progresión tumoral y peores resultados oncológicos. **Conclusiones:** El manejo de neoplasias múltiples debe ser individualizado según las características de cada neoplasia y riesgo de complicaciones. Es necesario reportar casos de asociaciones atípicas de neoplasias múltiples para ampliar el espectro diagnóstico y mejorar el abordaje terapéutico de los pacientes.

Palabras clave: neoplasias sincrónicas, feocromocitoma, cáncer de mama, caso clínico.

1. Introduction

Synchronous neoplasms are defined as two or more malignant tumors of different histopathological origins diagnosed within the first six months. This is considered a rare phenomenon; the presence of multiple primary neoplasms is estimated to range between 0.73% and 11.7%. [1,2]. LV et al. [3] described the incidence of synchronous neoplasms in 161 patients, demonstrating a high frequency of synchronism in gastric cancer (13%), lung cancer (12%), and esophageal cancer (11.8%). Some studies report the prevalence of synchronous neoplasms ranging from 15% to 34% in patients with breast cancer [4,5]. Other studies report a worse prognosis in this group of patients varies according to clinical stage, histological grade, and treatment [6–8]. Chen et al. [9] described a difference greater than 10% in overall survival among patients with colorectal cancer with synchronous tumors compared to patients with a single primary tumor (61.9% vs. 73.7%, respectively).

The development of multiple neoplasms is associated with extrinsic patient-related factors, such as harmful habits, occupational risks, level of physical activity, or a combination of both. It is also associated with intrinsic factors, including immune system alterations or genetic mutations in susceptibility genes, for instance, BRCA and PTEN. [2, 10–11] In breast cancer, the presence of synchronous neoplasms has been associated with radiotherapy and cytotoxic agents, which controversially constitute part of its treatment. [2, 10]. A study conducted in Korea reports that patients with breast cancer and synchronous neoplasms more frequently develop malignant tumors of the thyroid gland (71%) or the gynecologic tract (9.7%) [12]. Additionally, other studies have reported a higher rate of synchronism in luminal breast cancer and advanced-stage disease [13].

Herein, we present the case of a patient with two synchronous neoplasms—an atypical combination of breast cancer and pheochromocytoma—and its multidisciplinary therapeutic management.

2. Case Report

A 47-year-old postmenopausal woman with no relevant personal medical or surgical record and no first-degree family history of cancer presented with a one-year palpable mass in the right breast, associated over the past five months with sporadic episodes of tachycardia and hot flashes.

On physical examination, a 4 × 4 cm, mobile, non-tender mass was palpated, with no skin or nipple changes. Mammography revealed dense breasts, BI-RADS 2, and breast ultrasound showed a solid hyperechoic lesion in the right breast with irregular margins, measuring 17 × 15 mm, with no axillary lymphadenopathy.

Core needle biopsy revealed invasive breast carcinoma of no special type (NST). Immunohistochemistry showed estrogen receptor positivity of 90%, progesterone receptor positivity of 80%, HER2-negative status, and Ki-67 of 3%. As part of the preoperative workup, a contrast-enhanced breast MRI was requested (Figure 1), revealing a lesion in the right breast measuring 5.6 × 4.2 × 2.8 cm, with no infiltration of the skin or the nipple–areola complex.

Staging computed tomography scans revealed a right adrenal mass measuring 52 × 43 mm, with 30-mm hypodense areas within the lesion. Subsequently, a contrast-enhanced abdominal MRI described

a right adrenal tumor measuring 5.4 × 3.8 × 3.8 cm, transverse–anteroposterior–craniocaudal diameters (T-AP-CC), with a T1 hyperintense component and progressive T2 hypointensity, which suggested hemorrhagic metastatic disease (Figure 2).

The patient was evaluated by the urologic oncology and endocrinology services, who requested additional diagnostic studies. Tests revealed elevated serum and urinary metanephrines, as well as increased chromogranin A levels. Those findings were consistent with the diagnosis of pheochromocytoma. Cardiovascular evaluation revealed no abnormalities in blood pressure or cardiac rhythm.

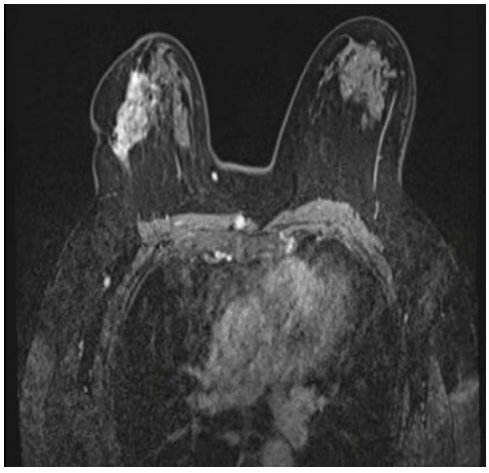
Given the potential for cardiovascular complications caused by catecholamine release from pheochromocytoma—such as tachyarrhythmias, hypertensive crises, among others—surgical management was prioritized, and a right adrenalectomy via exploratory laparotomy was performed. A combined surgical approach for both neoplasms was not undertaken due to the patient's personal preference. The surgery was uneventful, and histological confirmation of pheochromocytoma was obtained. Histopathological examination revealed a mitotic index of 2 mitoses per 10 high-power fields, with no evidence of necrosis or capsular or lymphovascular invasion. Immunohistochemistry showed synaptophysin positivity, chromogranin positivity, focal S-100 positivity, and inhibin negativity.

Three months after the first surgery, a modified radical mastectomy was performed. The pathological examination revealed an invasive breast carcinoma of no special type (NST), with macroscopic measurements of 60mm, histological grade II, with presence of lymphovascular invasion, probable perineural invasion, and lymph node involvement (seven lymph nodes involved by neoplasia, three with macrometastases and four with extranodal extension), staged as pT3 pN2 M0 (clinical stage IIIA and clinical prognostic stage IIA).

Adjuvant chemotherapy was initiated with an anthracycline-based regimen. The patient received four cycles of the AC regimen (Doxorubicin 60 mg/m² and Cyclophosphamide 600 mg/m²) and experienced gastrointestinal toxicity (grade 3 nausea and grade 2 emesis), as well as grade 2 asthenia.

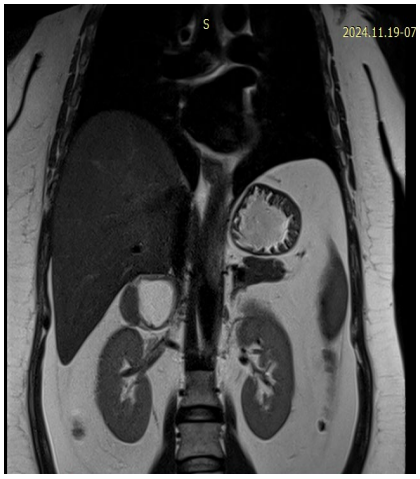
She is currently receiving weekly Paclitaxel at a dose of 80 mg/m², with good tolerance and no toxicities reported to date (a total of four cycles are planned). Subsequently, hormone therapy with Anastrozole was indicated for a minimum of 5 years, along with radiotherapy to the chest wall and axillary region.

Figure 1. Contrast-enhanced breast MRI: In the right breast, upper outer quadrant, anterior and middle thirds (between the 8 and 12 o'clock positions and 2 cm from the nipple) a mass-type lesion with irregular margins is identified. The lesion shows intermediate T2 signal intensity, diffusion restriction, and early contrast enhancement with a heterogeneous pattern and a persistent kinetic curve (type I). Peritumoral edema is noted as adjacent to its posterior aspect. The lesion measures 5.6 × 4.2 × 2.8 cm (AP × T × L diameters).



Source: Hospital Nacional Cayetano Heredia, Lima, Peru

Figure 2. Contrast-enhanced abdominal MRI: A mass arising from the lateral limb and body of the right adrenal gland is identified, measuring approximately 5.4 × 3.8 × 3.8 cm (T × AP × CC diameters). The lesion shows a heterogeneous signal, with a central T1 hyperintense and T2 hypointense component, suggesting a hemorrhagic component. The periphery demonstrates diffusion restriction and contrast enhancement predominantly in the venous phases. No signal drop is observed on out-of-phase T1 gradient-echo sequences, suggesting the absence of intralesional fat content.



Source: Hospital Nacional Cayetano Heredia, Lima, Peru.

3. Discussion

This is the first case reported in South America of a patient with synchronous neoplasms of breast cancer and pheochromocytoma. This is an atypical event since only a few cases have been reported in Europe and the United States [14,15]. Those patients presented with hormone receptor–positive breast cancer at stages amenable to curative surgical management, like our patient.

Following the radical mastectomy, the patient presented with lymphatic dissemination. A possible contributing factor is the delay in surgical management of this neoplasm, as adrenalectomy had to be prioritized due to the cardiovascular risks associated with pheochromocytoma. Given a 60-mm tumor with lymph node metastasis, the patient is a candidate for adjuvant therapy with cyclin-dependent kinase inhibitors, such as Abemaciclib [16,17] or Ribociclib [18,19], which have demonstrated a reduction in the risk of invasive disease recurrence (33% at 5 years and 25% at 3 years, respectively) when combined with endocrine therapy. Surgical management remains the best curative option for pheochromocytoma [20]. There is no indication for chemotherapy in early-stage disease, and even in advanced stages, no consistent overall survival benefit has been observed, with overall response rates (ORR) below 40% [21,22].

The patient's breast cancer was initially an early-stage disease with estrogen receptor positivity and a low proliferative index, making a metastatic adrenal lesion less likely. In the natural history of ductal breast carcinoma, metastases most frequently occur in the bone (30%–62.5%), lung (11%–34%), liver (7.3%–32%), and central nervous system (2%–16%); however, lobular histology may disseminate to more atypical sites, such as the peritoneum or adrenal gland [23,24]. Nevertheless, a case of ductal breast cancer with solitary adrenal metastasis has been reported [25]. Despite this rare association, pheochromocytoma should always be considered as a diagnostic possibility.

4. Conclusion

Synchronous neoplasms pose a significant challenge for the diagnosis and management of oncologic patients. Moreover, they are known to be associated with a poorer prognosis and reduced survival. Understanding metastatic patterns and the natural history of malignancies is essential to consider a broader spectrum of differential diagnoses, as reports of patients with an association of these two neoplasms remain scarce.

The incidental detection of pheochromocytoma through imaging studies performed for staging, together with its biochemical confirmation and timely surgical treatment, highlights the importance of a multidisciplinary evaluation from the outset. Furthermore, additional information is needed regarding the clinical presentation, diagnostic process, and individualized management of these neoplasms to facilitate early identification and optimize therapeutic strategies for patients.

5. Patient Perspective

In the first months following her diagnosis, the patient described in this case report experienced depressive symptoms. She received therapy through the oncology psychology service, resulting in improvement in her mood and mental health. According to the patient, the most challenging aspect of her illness has been recovery from consecutive surgeries. She is currently experiencing postoperative complications (abdominal incisional hernia/eventration) secondary to the first surgery.

She experienced multiple toxicities during the initial cycles of chemotherapy; however, she currently reports a sense of well-being and demonstrates good tolerance to systemic treatment.

6. Abbreviations

- No Special Type (NST)
- Magnetic Resonance Imaging (MRI)
- Transverse (T)
- Anteroposterior (AP)
- Craniocaudal (CC)
- Longitudinal (L)

7. Administrative Information

7.1 Supplementary Files

None.

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7.3 Author Contributions

- Sheila María Huertas Tirado: Conceptualization, writing – original draft, investigation, manuscript review and editing, and final approval of the manuscript.
- José Luis Vargas Mejía: Conceptualization, investigation, reference management.
- Ciro Bryan Espejo Alencastre: Writing – original draft.

7.4 Funding

None.

7.5 Availability of Data and Materials

Data are available upon reasonable request from the corresponding author. No additional materials are reported.

8. Declarations

The authors declare no conflicts of interest. Written and verbal informed consent was obtained from the patient for publication of this case report.

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