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Case Report

Merkel Carcinoma and Advanced Synchronous Ovarian Cancer, A Rare Presentation: Case Report and Literature Review

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Abstract:

Objective: To report a rare case of synchronicity, Merkel carcinoma, and high-grade ovarian cancer (EC IV). We reviewed the literature and determined the clinical and pathological characteristics and treatment.

Case presentation: A 62-year-old female patient with a 1-month history of disease characterized by a rapidly growing axillary tumor. The tumor was biopsied with the result: neuroendocrine carcinoma compatible with Merkel carcinoma. During the extension imaging studies, tumor lesions were identified in both ovaries. A diagnostic laparoscopy was performed, revealing evidence of multiple implants in the omentum, ovaries, and mesogenital tract. The biopsy and report were: primary high-grade serous carcinoma of the ovary. She underwent surgery at another institution for a right axillary tumor, which was reported as Merkel carcinoma, with clear margins, a tumor size of 14 cm, and subsequently received chemotherapy with subsequent interval cytoreduction and a report of complete pathological response. Currently undergoing follow-up.

Conclusions: Synchronicity between Merkel carcinoma and metastatic serous ovarian carcinoma is extremely rare. Cases of metastasis of Merkel carcinoma to the ovary have been reported in only 02 cases, but the presence of both malignant neoplasms synchronously has not been reported in Latin America. Despite the concurrence of both neoplasms and the reserved prognosis, surgical and systemic treatment has allowed control of both neoplasms and after 8 months of follow-up, no local or distant recurrence is evident.

Key words: merkel carcinoma; ovarian cancer; synchronicity

Introduction

Merkel carcinoma is an extremely rare and aggressive malignant cutaneous neuroendocrine tumor characterized by granular neuroendocrine cells very similar to Merkel cells. It is common in men, older adults, patients with immunosuppression, immune treatment, and chronic radiation exposure. Its worldwide incidence is low; in Europe, it is estimated to represent less than 1% of malignant skin lesions, and in the US, 1,500 cases are reported annually [1,2]. In Latin America and Peru, it is even less common (approximately 75 cases over an 18-year period – National institute neoplastic diseases, Perú). Clinically, they are characterized by rapidly growing, purplish, firm nodular lesions located in sun-exposed areas. They rarely ulcerate, and up to 30% can metastasize to regional lymph node groups.

They also metastasize distantly, mainly to the lungs, adrenal glands, pancreas, liver, among others. Within the etiology of this neoplasia, it may be associated with Polyomavirus infection or exposure to UV radiation [2,3]. Surgical treatment is the treatment of choice in early stages, with a 2-3 cm margin. Due to the potential for lymph node involvement, a sentinel lymph node biopsy can be performed, and if evidence of lymph node disease is present, lymph node dissection is performed. Adjuvant RT remains important to reduce local recurrence and improve overall survival in patients with clinical stages I and II. Chemotherapy remains controversial; various studies have not shown an improvement in overall survival, and therefore, it is not a standard protocol for treatment [4, 5, 6, 7, 8].

High-grade serous ovarian carcinoma is one of the most aggressive and fatal gynecological tumors. The high-grade subtype accounts for 70% of serous tumors and is diagnosed in stages III or IV, which confers a lower overall survival rate. First- line chemotherapy (platinum) has a good

response, and resistance is rarely seen (9, 10). No cases or relationship between the two pathologies have been reported in Latin America; the synchronous presentation of both is an unexpected finding.

Case Presentation

A 62-year-old female patient from Lima presented with a 1-month history of illness characterized by pain in the axillary region and right breast. Physical examination revealed a 7 x 7 cm, hard, slightly mobile mass in the right axillary region that did not infiltrate the skin (Figure 1). CT scan of the chest and abdomen with contrast (Figures 2 and 3): In the right axilla, a tumor with lobulated contours measuring 60 x 76 mm was seen, with no vascular involvement; in the abdomen, a right adnexal cyst was seen, increased fat density of the greater omentum and mesenteric microadenyae, low free fluid, and multiple nodules in the cul-de-sac suggestive of carcinomatosis. An ultrasound-assisted CORE biopsy of the axillary tumor was performed: Neuroendocrine carcinoma infiltrating soft tissue SYNAPTOPHYSIN: Positive (+++) Chromogramin A: Positive (+++) Nse: Positive (++) Ck7: Negative Ck20: Negative Cd3: Focal Positive Cd20: Focal Positive.

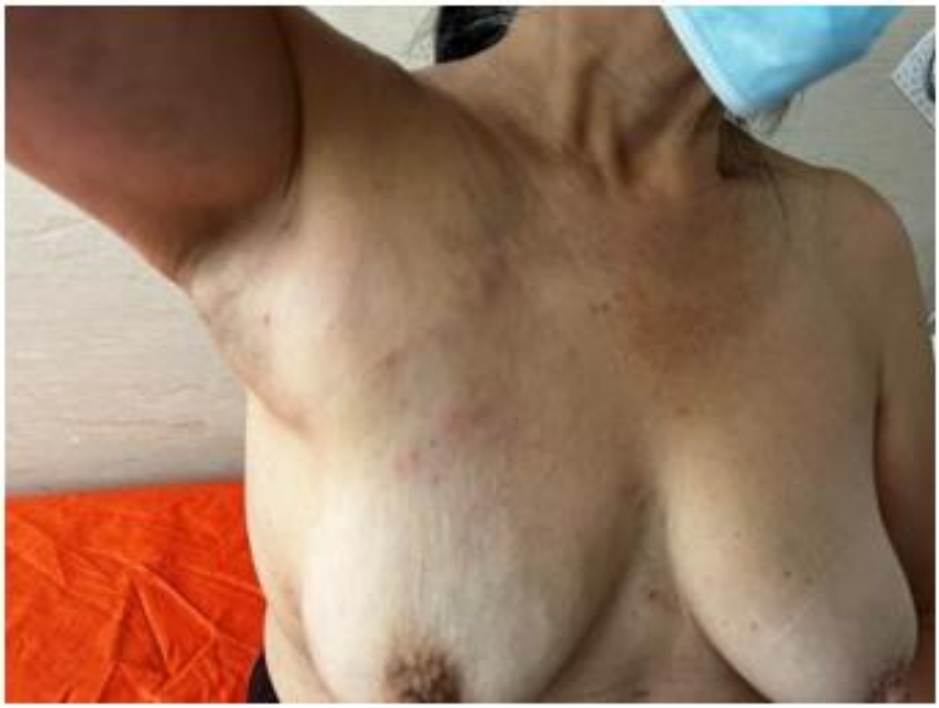

Figure 1: Tumor in the right axillary region.

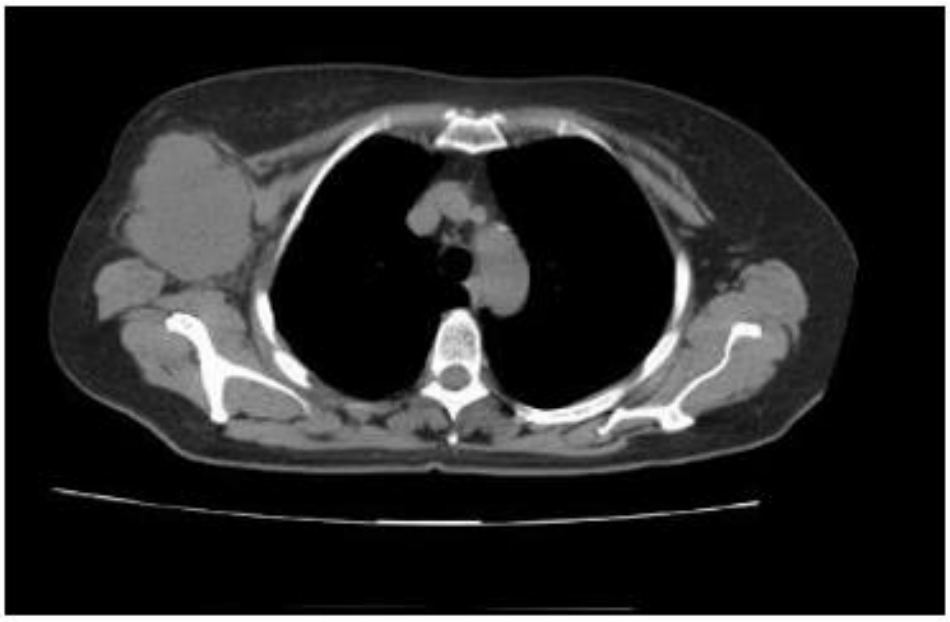

Figure 2: Chest CT scan with contrast: Right axillary mass measuring 60 x 76 mm.

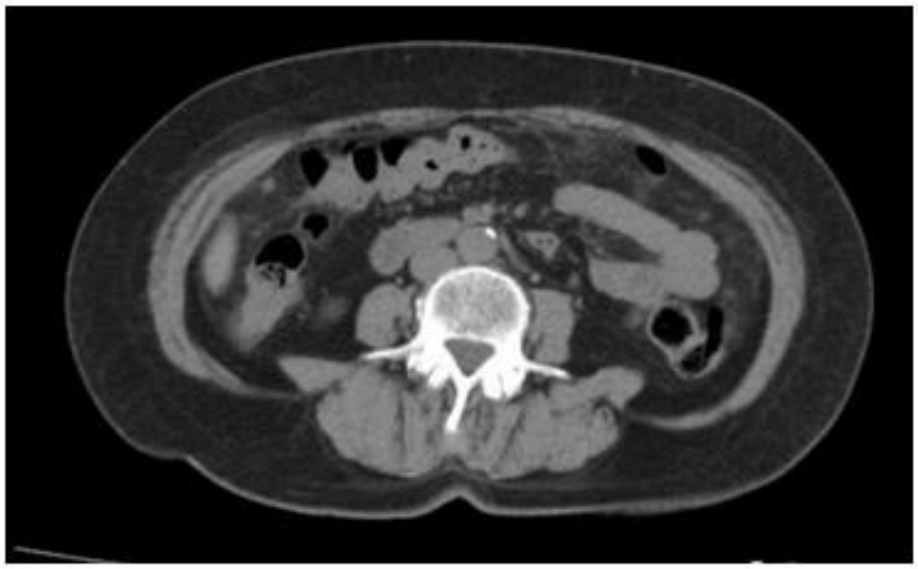

Figure 3: Abdominal CT scan with contrast, increased fat density in the omentum, nodules suggestive of carcinomatosis.

She was evaluated by Gynecology with a transvaginal ultrasound that reported lesions in both ovaries with d/c Metastasis, with a Ca 125: 29.9. She underwent diagnostic laparoscopy: multiple peritoneal implants and lesions in both ovaries were identified. Multiple biopsies were performed: HIGH-GRADE SEROUS CARCINOMA IN OMENTAL IMPLANTS, IN THE RIGHT AND LEFT OVARY, AT THE PARATUBAL AND UTERINE TUBE LEVEL, AND IN DOUGLAS'S FORNUS OF SAC. P16: POSITIVE - P53: 3+ - ER: 2+, 30% - Ki67: 90%. Ca 125: 48 was controlled prior to systemic treatment. He had wide local resection of a lesion in the right axillary region: Neuroendocrine carcinoma, compatible with Merkel Carcinoma, Synaptophysin: Positive (+++) Chromogramin A: Positive (+++) Nse: Positive (++) Ck7: Negative Ck20: Negative Cd3: Focal Positive Cd20: Focal Positive, Tumor size of 14 cm (Figure 4).

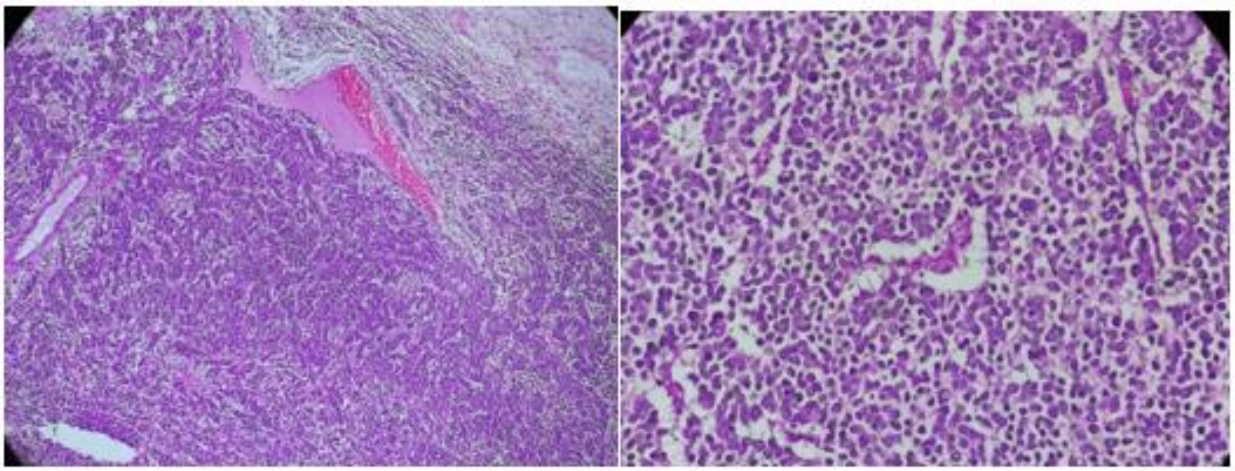

Figure 4: Poorly circumscribed tumor showing an expansive, nodular, and infiltrative growth pattern in the dermis. Small, round, blue tumor cells with a high N:C ratio, round/oval nuclei, finely dispersed chromatin (salt and pepper), indistinct nucleoli, and scant cytoplasm.

She received three courses of carboplatin and paclitaxel chemotherapy. Post- chemotherapy follow-up studies showed a Ca 125:12.9 level, and abdominal and chest CT scans were negative for metastatic lesions. She underwent interval cytoreduction: no evidence of malignancy in the uterus, cervix, omentum, or cecal appendix. She is currently resuming chemotherapy: four and five courses of carboplatin and paclitaxel. Her general condition is good and there is no evidence of recurrent disease 8 months after treatment.

Merkel carcinoma is a rare skin malignancy, ranking second among causes of mortality from skin malignancy after melanoma. It primarily affects older adults (75- 79 years of age), but can also affect younger individuals associated with immunosuppression. Factors linked to its etiopathogenesis are exposure to UV radiation and polyomavirus infection, the latter being the causative agent in 80% of cases (1,3). Clinically, it is characterized by a nodular, painful, and violaceous lesion, predominantly located in the extremities, head, and neck. The presence of lymph node involvement as the onset of the disease without an evident cutaneous lesion has not been reported. There may be locoregional (8.9%) and distant (4.3%) involvement, detected by imaging; Likewise, the possibility of regional lymph node disease that is not evident clinically or on imaging can reach up to 30% (20-40%), therefore the sentinel lymph node biopsy is useful (5,6,7). Among the organs affected by metastasis: lungs, adrenal glands, pancreas and liver. Overall survival varies according to the different stages: EC I (62.8%), EC II (34.8-64%), EC III (26.8- 40%) and EC IV (13.5%). Treatment will depend on the clinical stage and condition of the patient. Surgery is the best option for early-stage lesions, with wide local resections performed with 1-2 cm margins. Mohs surgery is an important tool to ensure clear margins without

extensive resections (2,4). Radiotherapy is also a relevant treatment, having implications for local recurrence following surgical resection. It can also be applied to the affected regional nodal area following lymph node dissection. It is an important tool for local control treatment in patients who are classified as inoperable. The post-surgical recurrence rate is 40%, with a higher incidence during the first 2 years after treatment (2,16).

Chemotherapy is a controversial treatment due to chemotherapy resistance, toxicity,

and cost-benefit ratio. Targeted cell inhibitors such as Nivolumab, Pembrolizumab, and Avelumab are highly effective in advanced stages. Metastasis of Merkel carcinoma to the ovaries is very rare, with only a few case reports (2014, 2019) and the possibility of a synchronous second primary is even more remote (1, 16).

Serous ovarian carcinoma is one of the most aggressive gynecological tumors. Type II, or high-grade, is associated with mutations in the P53 and BRCA 1/2 genes; it has also been linked to some viral infections: HPV 16-18, as well as some families: Paramyxoviridae, Poxviridae, and Polyomavirus, as in the case of Merkel carcinoma. Among the most commonly used tumor markers are Ca 125 and Ca 72-4 (12, 13, 14, 15).

Conclusions

The presence of both types of malignant neoplasms (synchronous) is a very rare event. The aggressiveness of both neoplasms leads to higher mortality and complications in patients. However, in our patient, R0 resective surgical treatment for axillary disease and systemic treatment for ovarian disease with a complete pathological response allow us to assess the importance of timely treatment and the probable benefit of systemic treatment for skin malignancy. This is the first case reported in Peru, and it is important to use the information regarding treatment for subsequent similar cases.

Conflicts Of Interest

None of the authors declare any conflicts of interest.

Financial Declaration

self-financing

Informed Consent (Case Reports Only)

The patient's consent is obtained for the publication of her case and related medical information, as well as photographs.

Author contributions:

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