

Erythematous Nodules and Plaques on the Neck: A Quiz

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A 48-year-old woman presented with a 2-month history of asymptomatic and rapidly growing nodules on the neck. Clinical examination revealed erythematous, hard nodules and plaques covered by superficial telangiectasia on the left side of the neck (Fig. 1). Laboratory studies showed an elevated cancer antigen 125 (CA-125) level of 89.7 U/mL and a CA-153 level of 43.6 U/mL. Histopathological evaluation demonstrated that the tumour cells exhibited high-grade nuclear atypia and were organized in solid architectural patterns, with readily identifiable mitotic figures. The nuclei appeared enlarged, hyperchromatic and contained conspicuous nucleoli, accompanied by an elevated nuclear-to-cytoplasmic ratio (Fig. 2). Immunohistochemistry revealed positive staining for CA125, cytokeratin (CK), PAX-8, CK7 and WT1 (Fig. 3). In contrast, staining for GATA3, CK20, Napsin and P40 was negative. The Ki-67 proliferation index was approximately 70% (Fig. 3).

What is your diagnosis?

- 1: Cutaneous metastasis from ovarian serous adenocarcinoma.
- 2: Squamous cell carcinoma.
- 3: Cutaneous lymphoma.

4: Cutaneous metastases from breast carcinoma.
See next page for answer.



Fig. 1. Erythematous, hard nodules and plaques on her neck.

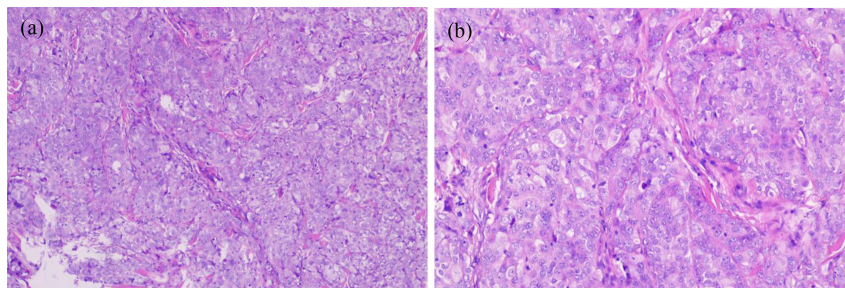


Fig. 2. Histopathology revealed the tumour cells exhibited high-grade nuclear atypia and are arranged in solid structures, with mitotic figures observed (HE staining, a:100×, b:200×).

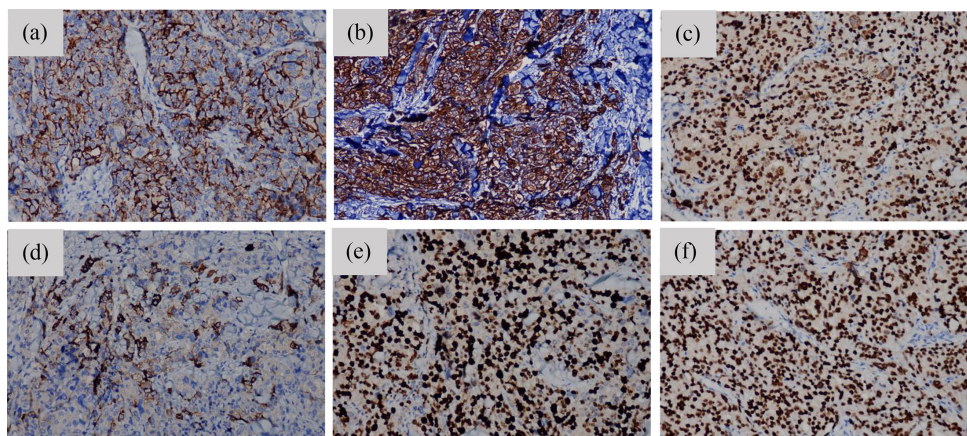


Fig. 3. Immunohistochemistry (a, b, c, d, e, f:200 x) a: CA125(+); b: CK(+), c: PAX-8(+), d: CK7(+), e: Ki67(70%), f:WT1(+).

ANSWERS TO QUIZ

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Diagnosis: Cutaneous metastasis from ovarian serous a denocarcinoma

Her past medical history was notable for stage IIIc serous ovarian carcinoma diagnosed 5 years prior, for which she underwent total abdominal hysterectomy, bilateral salpingo-oophorectomy, radical pelvic and abdominal lymphadenectomy with excision of pelvic implant lesions, followed by 6 cycles of carboplatin and paclitaxel chemotherapy. On immunocytochemistry, the tumour cells showed positivity for PAX-8, WT1, CA125, CK and CK7. Thus, a diagnosis of cutaneous metastasis from ovarian serous adenocarcinoma was rendered.

The majority of patients diagnosed with ovarian serous adenocarcinoma present with or eventually develop metastatic disease (1). Metastasis typically involves the peritoneum and intraperitoneal organs, with the lung being the most frequent site of extraperitoneal spread (2). Cutaneous metastases of serous ovarian carcinoma are exceptionally rare. In a review of 206 patients with ovarian and fallopian tube carcinomas, skin metastases were identified in only 12 cases, among which just 6 were of serous histology (3). The classic presentation of cutaneous metastasis in ovarian carcinoma is the development of solitary or multiple umbilical nodules, known as Sister Mary Joseph nodules (SJN) (3). Non-SJN metastatic skin lesions may manifest in diverse forms, including ulcerated herpetiform or zosteriform lesions, reticulate erythema, indurated plaques, cellulitis or lymphangitis (3–6). The patient in this case presented with erythematous nodules and plaques on the neck, which is an extremely rare presentation of cutaneous metastases. The mean time to diagnosis of skin metastasis was 28 months (range 4–84) (7). In our patient, cutaneous metastasis appeared 5 years after her initial diagnosis.

The precise mechanism underlying skin metastasis in ovarian cancer remains incompletely elucidated. The development of cutaneous metastases in ovarian carcinomas is thought to result from a complex interplay among tumour subtype, disease severity, metastatic pathways and the patient's prior medical and surgical history. Metastasis most commonly occurs via intraperitoneal seeding within the peritoneal cavity but may also involve lymphatic spread to pelvic and para-aortic lymph nodes or haematogenous dissemination to distant sites (8). Prior laparoscopic surgery, especially in the presence of malignant ascites or intraperitoneal metastases, can facilitate direct tumour implantation along surgical tracts, potentially increasing the risk of cutaneous spread (9). Furthermore, the use of anti-vascular endothelial growth factor (VEGF) therapies, such as

bevacizumab has been associated with an increased propensity for cutaneous metastases (3). This is attributed to acquired drug resistance and subsequent compensatory angiogenesis, which may promote metastatic seeding in the skin.

The prognosis of cutaneous metastases in ovarian cancer is generally poor, with a median survival of approximately 1 year following diagnosis (3). The most significant prognostic factor appears to be the interval between the initial diagnosis of ovarian carcinoma and the development of skin lesions. A longer latency period exceeding 40 months is associated with a more favourable outcome (4). Additionally, the Ki-67 proliferative index serves as a valuable marker for assessing tumour aggressiveness and prognosis.

The management of cutaneous metastasis from ovarian serous adenocarcinoma is based on the location of metastasis, patient comorbidities and individual care goals. The optimal treatment approaches include systemic chemotherapy, surgical excision and localized radiation therapy. A series of nine patients reported a median survival of 35 months in patients treated with surgical resection plus chemotherapy, compared to only 2 months in patients treated with chemotherapy alone (3). Besides disease eradication, surgical resection often offers symptomatic relief. In the current case, our patient was treated with multiple chemotherapeutic agents such as liposomal doxorubicin, cisplatin and bevacizumab and survived 1 year from the diagnosis of skin metastases.

In conclusion, cutaneous metastasis should remain in the differential diagnosis for patients with a history of cancer and unexplained dermatologic lesions, as it is often associated with late-stage internal malignancies and typically indicates a poor prognosis.

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