

Abstract

Cancer during pregnancy occurs in approximately 1 in 2000 pregnancies, which is recently increasing. However, metastasis to the placenta is very rare and the number of cases of malignant tumors that metastasize to the placenta and the fetus is reported to be approximately 70 cases in worldwide so far. Reported cases that have metastasized to the placenta include melanoma, lymphoma, leukemia, breast, lung, gastric, and gynecologic cancers. We report a case of placental metastasis of invasive breast cancer in a pregnant woman.

Case Presentation

A 35-year-old pregnant woman (gravida 2, para 1) without past medical history was referred to Severance Hospital at 27 week's gestation with biopsy-proven breast malignancy. She visited the breast clinic complaining of a palpable breast mass. Breast ultrasonography (USG) showed a 3cm-sized ill-defined mass of right breast and invasive carcinoma of no special type was diagnosed in the histopathologic examination of the needle aspiration biopsy.

At our hospital, initial work-up for primary breast cancer was done. USG showed ① proven malignancy in right breast with subareolar extension and multifocality(category 6), ② low suspicion for malignancy in right 5-o'clock area(category 4a), and ③ low suspicious lymph node in right axilla level 1. Axillary lymph node biopsy was done and the result was positive for malignancy, metastatic carcinoma. For the work-up for distant metastasis, liver USG and whole body MRI was conducted. Two hyperechoic lesions in both lobes was found in liver USG, suggesting probable hemangiomas. Whole body MRI showed bone marrow hyperplasia at whole spine, pelvic bone, proximal femur, which were not specific findings.

She was diagnosed with invasive breast cancer without distant metastasis and was decided to receive 2 cycles of neoadjuvant chemotherapy (NAC) with doxorubicin and cyclophosphamide before delivery. NAC was performed at 29 and 33 week's gestation. During work-up for breast cancer and 2 cycles of NAC, fetal surveillance including fetal USG and nonstress test, as indicated, was conducted at 27, 29, 33, 36 week's gestation and there were no abnormal findings on antenatal fetal surveillance. At 36 week's gestation, 3 weeks later after the 2nd cycle of NAC, induction of labor was done. She delivered a healthy male baby without any complication. He weighed 2850g, and there were no abnormalities except cryptorchidism. The histopathologic examination of the placenta showed metastatic carcinoma (Figure 1), which was originated from the breast based on the clinical information and immunohistochemical staining (Figure 2). Scattered tumor cell clusters were found in the intervillous space (Figure 1).

When she received 2 more cycles of NAC after delivery, follow-up work-up (abdomen CT, chest CT, whole body bone scan, and PET-CT) to evaluate the response of NAC and to investigate distant metastasis was done, which indicating residual primary malignancy in right breast with multiple bone metastasis and liver metastasis. After received 2 cycles of palliative chemotherapy with doxorubicin, cyclophosphamide, and demasumab, she was referred to other hospital on her request. She died 4 years after the diagnosis. The baby is doing well without specific problems.

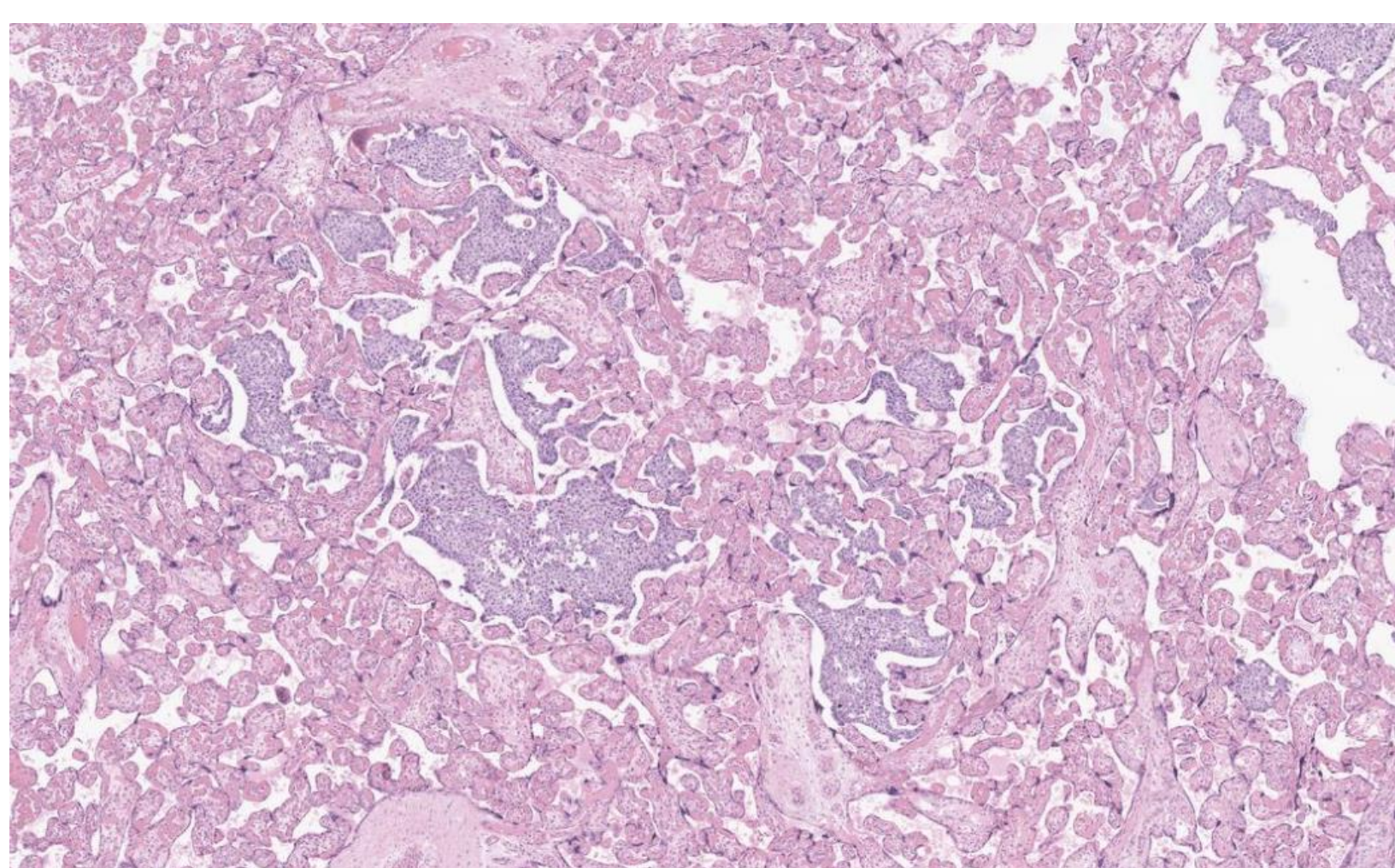


Figure 1-1. 2.5x, Hematoxylin and eosin
Several clusters of atypical cell clusters in intervillous spaces were noted.

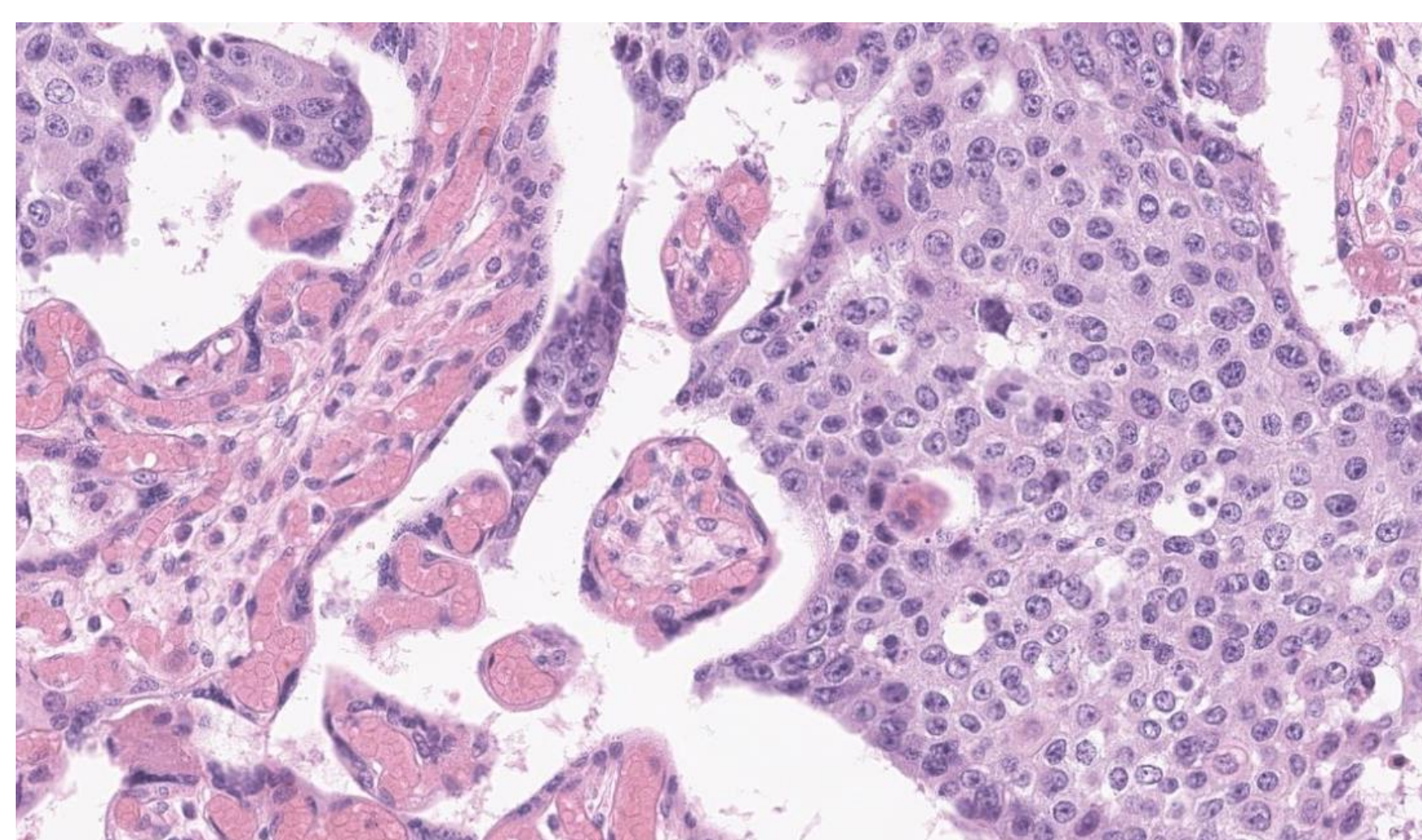


Figure 1-2. 20x, Hematoxylin and eosin

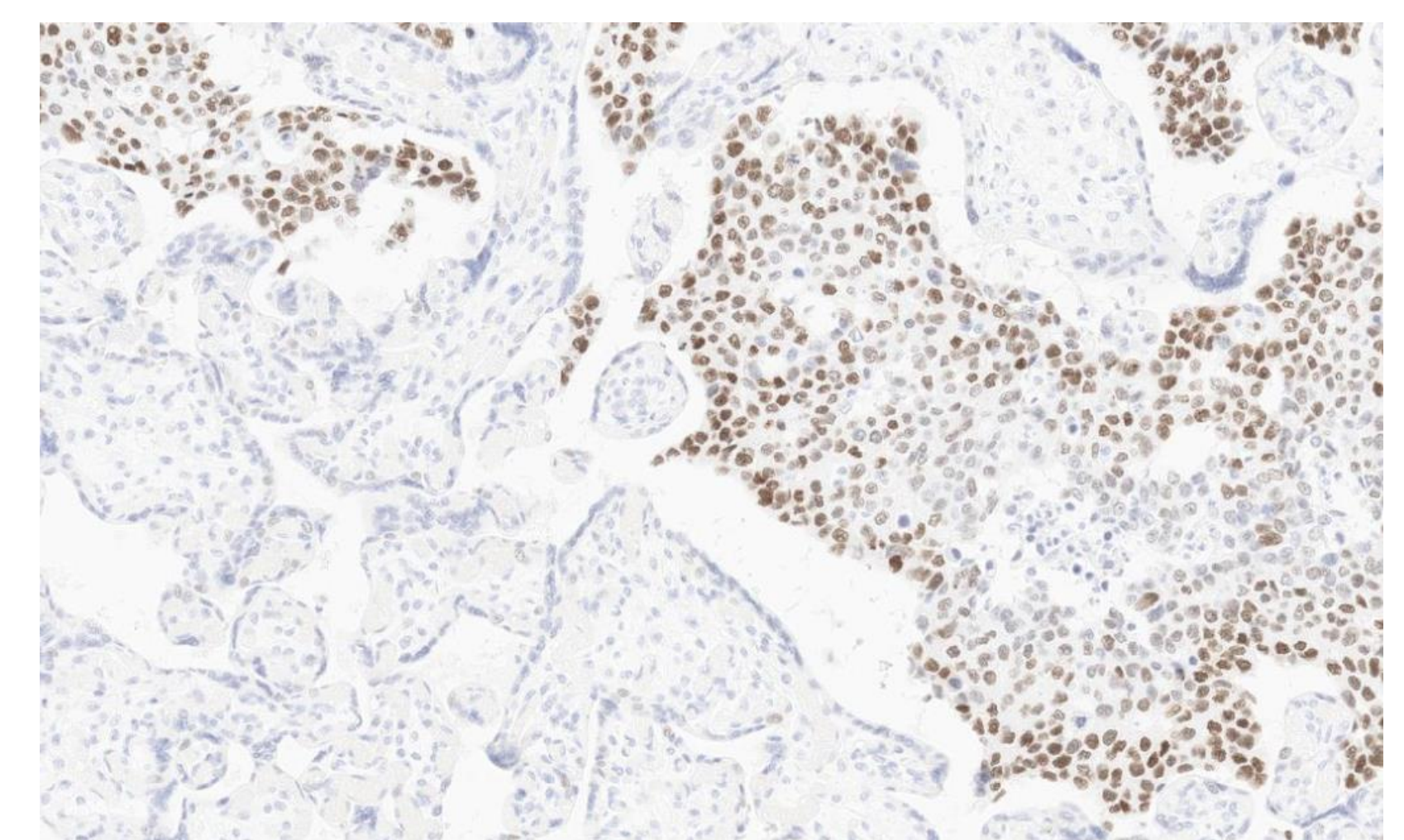


Figure 2. 10x, Immunohistochemical staining for GATA-3. GATA-3 was diffusely positive in atypical cell clusters, supporting the diagnosis of metastatic breast carcinoma

Discussion

Diagnosis of breast cancer during pregnancy is associated with poor prognosis compared to nonpregnant breast cancer, as breast cancer during pregnancy is diagnosed later, resulting in the diagnosis at an advanced stage. Because of the physiological changes of the breast during pregnancy, the breast become enlarged and the presence of normal nodules makes difficult to palpate the mass. Also the examination is limited because of the risk of radiation exposure to fetus, which makes more difficult to diagnose breast cancer during pregnancy.¹

Although the placenta has a high blood flow, the metastasis to the placenta and the fetus is very rare due to the role of immune response in the chorionic villi space and chorionic cells, which filter the cancer cells. The intervillous space acts as a filter for malignant cells, and most malignant cells are confined to the maternal vascular space. This prevents cancer cells transfer through the bloodstream from the mother to the fetus, which lowers the risk of fetal metastasis.² Also, the immune response of the fetus may prevent fetal metastasis.³ Nevertheless, placental metastasis, if found, infers that the cancer cells move through the bloodstream, which increases the possibility of distant metastasis of maternal cancer and indicates a poor prognosis of the mothers. Few cases of the metastasis to the fetus are reported, the significance of which is yet to be determined.²⁻⁵

This case emphasizes the importance of analyzing the pathology of the placenta when cancer is diagnosed during pregnancy. Also, a long-term follow-up evaluation for the babies with placenta metastasis will be needed.

References

1. Byun YJ, et al. A case of pregnancy-associated breast cancer. *Korean Journal of Obstetrics and Gynecology* 2004;47:1814-1818.
2. Sebire NJ, Jauniaux E. Fetal and placental malignancies: prenatal diagnosis and management. *Ultrasound Obstet Gynecol* 2009;33:235-244.
3. Micco RD, et al. Rare sites of breast cancer metastasis: a review. *Translational Cancer Research* 2019;8(Suppl 5):S518-S552.
4. Lee HS, et al. Placental metastasis of maternal gastric adenocarcinoma. *Korean J Pathol* 1999;33:214-216.
5. Ouh YT, et al. Overview of malignancy in pregnancy. *Perinatology* 2020;31(4):161-165.