A wound that failed to heal: high-grade ovarian serous carcinoma associated with chronic schistosomiasis

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In 1858, Rudolph Virchow initially proposed his irritation theory for cancer. According to his observation, irritation of any type, including mechanical, chemical, or thermal, was the essential factor in neoplastic tissue proliferation. With the premise that long-standing inflammation secondary to chronic infection predisposes to cancer by promoting an environment that cultivates genomic lesions and tumor initiation, does chronic infection with Schistosomiasis also predispose to ovarian malignancy?

CASE REPORT

The patient is a 54 year-old, Gravida 3 Para 3 (3003) from Eastern Samar, Philippines who was admitted due to progressive abdominal distention for the past three years. She was first diagnosed with Schistosomiasis in 1992, had reinfection and complication of compensated liver cirrhosis in 2010. Abdomen was globularly enlarged, with abdominal girth of 103 cm, tense but not tender, with positive fluid wave. On pelvic examination, the adnexa cannot be fully assessed due to ascites. On transvaginal ultrasound, the right ovary was converted into an irregular solid mass, measuring 3.14 x 2.48 x 2.36 cm, no intratumoral flow, with non-benign sonomorphologic features. Cancer antigen (CA-125) and Human Epididymis Protein 4 (HE4) were elevated at 942.4 U/mL and 1165.1 pmol/L, respectively. Admitting diagnosis was Ovarian New Growth, Right probably Malignant.

INTRAOPERATIVE FINDINGS

Total abdominal hysterectomy with bilateral salpingo-oophorectomy, with frozen section of the right ovary and right fallopian tube were done. Intraoperatively, ascites was noted and amounted to 9 liters. The right ovary was converted to an irregularly shaped, solid multinodular mass, measuring 4.5 x 2.5 x 3 cm while the right fallopian is cystically enlarged measuring 8 x 4 x 2 cm with noted adhesion to the omentum. Frozen section revealed High-grade serous carcinoma of the right ovary and right fallopian tube with incidental finding of schistosomiasis on the left ovary and right fallopian tube.

CASE REPORT

Infestation with schistosomiasis is referred to as ectopic when the eggs or the adult form of the parasite is found outside the portal system. Adult schistosomes inhabit the blood vessels for years and evades the immune system while excreting thousands of ova daily with subsequent deposition in adjacent tissues. As the adult parasites migrate to the pelvic veins, they usually travel in an opposite direction to that of the blood flow, thus reaching the terminal portal venules and other tissue sites. In the patient, ectopic migration occurred in the right fallopian tube leading to an undetected chronic infection.

Hoang, Brindley, Meyer and Velavan (2016) proposed a mechanism by which infection like schistosomiasis induces carcinogenesis.

First, the chronic inflammatory response during infection leads to the activation of signaling pathways including p53, nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB), janus/knase (Jak/Stat) and retinoblastoma protein (Rb) that could produce somatic mutations and/or activate oncogenes. The production of fluke-derived products and metabolites also causes oxidative stress. Lastly, physical damage of host tissues during the development of parasites concurrent with the active wound healing process leads to increased cell transformation and proliferation.

In this case, the right ovary and fallopian tubes were positive for tumor. However, infection was evident only in the right fallopian tube as documented by biopsy. What's more interesting is the finding of schistosomiasis in the left ovary. If chronic inflammation can lead to malignant transformation, how come the left ovary with evident schistosomiasis did not develop carcinoma? On the same note, it was the right ovary that developed the cancer.

Recently, it has been hypothesized that the fimbriated end of the fallopian tube, being in close proximity to the ovarian surface is the origin of high-grade serous carcinomas of the ovary. This is supported by the discovery of a lesion called Tubal Intraepithelial Carcinoma (TIC) detected at the fimbriated end of the fallopian tube which has the cytologic appearance of high-grade serous carcinoma of the ovary. The TIC then developed into a high-grade serous carcinoma that clinically and grossly appears to be an ovarian primary tumor. This is further strengthened with the fact that although the left ovary has evident infection, it did not undergo malignant transformation since the fimbriated end of the fallopian tube was free from any lesion unlike its contralateral counterpart.

CONCLUSION Chronic infection with schistosomiasis might be a potential cause of carcinoma by promoting general inflammation and subsequently affecting key cellular processes. However, in this case, the mechanism involved with inflammation may not be the only factor contributing in the malignant transformation of the right ovary. If it did, the left ovary found to harbor schistosome eggs, should have developed the cancer as well. Based on the concept of the tubal intraepithelial carcinoma (TIC) detected at the fimbriated end of the fallopian tube, we can assume that the primary site is the right fallopian tube. As this was found to be infested with schistosome and based on proximity could have seeded on the right ovary leading to neoplasia.

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