Multiple metastases from ovarian cancer

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Epithelial ovarian cancer is one of the most common ovarian tumours. Ovarian cancer affects women in the age group >60 years much more frequently than younger women. At the time of diagnosis, cancer will already have spread beyond the ovaries in approximately 75% of cases. We report a case of epithelial ovarian cancer presenting with liver and thoracic vertebral metastases 4 months after completion of treatment, as part of distant spread. The patient was then treated with gemcitabine-based chemotherapy. Palliative radiotherapy was given for the involved spine.

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The incidence of ovarian cancer is 6.1/100 000 population (3.6% of all cancer) worldwide. In India, the World Health Organization reports that the crude incidence rate of this cancer is 4.9/100 000 women, 5% of all malignancies in women.[1] Ovarian cancer is primarily a disease of postmenopausal women, the highest number of cases being concentrated in the age group 50 - 70 years.

To metastasise, a tumour cell must overcome a number of factors including entrance into the vascular system, travel to a distant site while avoiding immune surveillance, localisation in the microvasculature of the future metastatic site, growth, and evolution of a blood supply.[2,3] The main route of dissemination in ovarian cancer is by transcoelomic spread and through the lymphatic system. Haematogenous spread is uncommon. Ovarian cancer usually presents with widespread intra-abdominal metastases. However, the disease remains confined to the peritoneal cavity at presentation and throughout its course in approximately 85% of cases. Occasionally patients present with aggressive disease, manifested by parenchymal liver or lung metastases, or develop metastases to distant sites such as the brain and bone during disease progression. Metastasis to bone from these tumours is rare (0.1 - 0.12%).[4-7] We report a rare case of thoracic vertebral metastasis with secondary lesions in the liver 4 months after chemotherapy in a young woman.

Case report

A 38-year-old premenopausal woman presented to the Acharya Tulsi Regional Cancer Treatment and Research Institute, Bikaner, Rajasthan, India, with complaints of weakness, distension of the abdomen, loss of appetite and vague abdominal discomfort of 2 months' duration. The menstrual cycle was regular and without associated complaints. Ultrasonography of the abdomen and pelvis revealed a left-sided solid-cum-cystic adnexal mass with mild ascites. A tentative diagnosis of ovarian malignancy was entertained. No hereditary or other risk factor for ovarian cancer was found in the family history. Total abdominal hysterectomy, bilateral salpingo-oophorectomy and omentectomy were performed. Histopathological examination of the specimen revealed mucinous papillary cystic adenocarcinoma in the left ovary. The uterus, cervix and fallopian tube were free and omental deposits were negative for malignancy. The patient was categorised as stage Ic as per International Federation of Obstetricians and Gynecologists staging.

Taxol and platinum-based adjuvant chemotherapy were prescribed. Four months after completion of six cycles of chemotherapy, she developed a mass in the right hypochondrium with backache. There was no evidence of pallor, icterus or lymphadenopathy. Examination of the abdomen showed presence of free fluid with hepatomegaly. Vaginal examination revealed no abnormalities. A contrast-enhanced computed tomography scan of the abdomen and pelvis showed multiple space-occupying lesions in the liver suggestive of metastases and mild ascites with no residual disease, along with postoperative changes (Fig. 1). The CA-125 level was raised (1 012 U/mL). A radiograph of the lumbar spine was not conclusive, so magnetic resonance imaging (MRI) of the

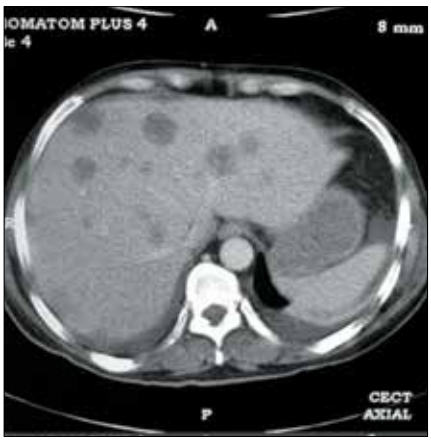

Fig. 1. Contrast-enhanced computed tomography scan showing multiple space-occupying lesions in the liver.

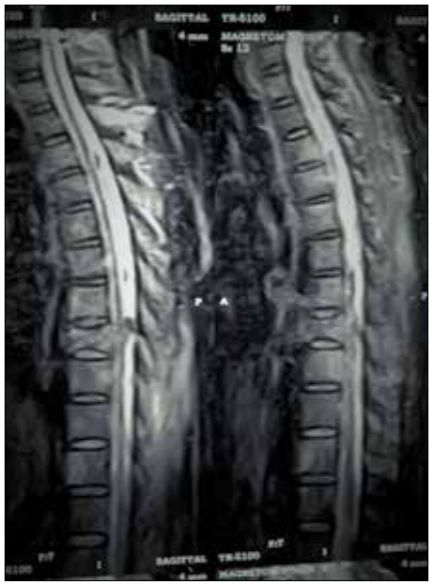

Fig. 2. Magnetic resonance image showing solitary metastasis at D12 vertebra.

spine was done. This revealed collapse of the D12 vertebra (Fig. 2). Biopsy of the lesion confirmed bone metastasis. The patient was hospitalised for further management, and palliative radiotherapy (800 cGy, single fraction) was given to the involved vertebra along with monthly intravenous injections of zoledronate 4 mg. Gemcitabine-based chemotherapy was given with appropriate premedications. The CA-125 level came down to 29 U/mL at the end of six cycles of chemotherapy, and the patient was symptom-free at 6 months of follow-up.

Discussion

The course of ovarian cancer is highly variable, and the standard clinical predictors for metastasis and poor prognosis have met with limited success.[8] Development of distant metastases in the liver, brain, and other sites is uncommon in carcinoma of the ovary.[9,11] A number of authors have evaluated traditional clinical parameters such as histological features, grade, stage and ascites as predictors for prognosis in patients with ovarian cancer.[10-12] Exposure to multiple chemotherapeutic agents and disruption of the blood-brain barrier by these agents may be the cause of distant spread. Carcinoma of the ovary has significant potential for distant metastasis, but bony metastases are rare. The mode of bony spread appears to be haematogenous, although no definite route of spread has been documented in the literature. Dauplat *et al.*[4] analysed 336 patients with distant metastases from ovarian cancer in his autopsy series. Of these, four had bone metastases, two thoracic vertebra involvement, and one each clavicular and bone marrow involvement. According to the authors, bony metastasis is rare and the median time to development ranged from 13 to 49 months. In the present case report, bone involvement also appeared to be a part of haematogenous spread, since both liver and bone were involved. In an autopsy series, Rose *et al.*[6] studied the metastatic pattern in 428 ovarian cancers and correlated different histologies with sites of metastasis. The incidence of bony metastasis was 0.06 - 0.19% with epithelial histology. This reflects the rarity of bony metastasis in this malignancy. There was no difference in the pattern of spread with different histological subtypes.[5] Abdul Karim *et al.*[8] did a clinicopathological audit of bone metastasis from different gynaecological malignancies. They analysed a total of 305 patients, of whom 113 had ovarian cancers. Bony metastasis was seen in seven patients only. Skeletal metastasis was seen in high-grade tumours. Rose *et al.*[6] had observed that presence of lymph nodes in the abdominal cavity was associated with an increased incidence of bone metastasis. Advancing age is the most significant risk factor for the development of ovarian cancer. Marchetti *et al.*[13] showed that out of 545 patients with epithelial ovarian cancer, 49 were under 35 years of age, with most of them having histopathological features of borderline tumour. Advancing age could therefore be an important prognostic factor. However, mucinous cyst adenocarcinoma in an 11-year-old girl has been reported by authors from the same institution, suggesting that no age is immune to the disease.[14]

In the present case, a young woman without lymphadenopathy developed bony metastasis 4 months after treatment. The authors conclude that bony metastasis should be considered in the differential diagnosis of backache in patients with ovarian cancer, even in an early stage and in middle-aged women.

1. Ferlay J, Soerjomataram I, Ervik M, et al. GLOBOCAN 2012 v1.0, Estimated Cancer Incidence, Mortality and Prevalence Worldwide: IARC CancerBase No. 11. Lyon: International Agency for Research on Cancer, 2013. www.iarc.fr (accessed 6 October 2014).
2. Kohn EC, Liotta LA. Molecular insights into cancer invasion: Strategies for prevention and intervention. Cancer Res 1995;55(9):1856-1862.
3. MacDonald NJ, Steeg PS. Molecular basis of tumour metastasis. Cancer Surv 1993;16:175-199.
4. Dauplat J, Hacker NF, Nieberg RK, Berek SJ, Rose PT, Sagae S. Distant metastasis in epithelial ovarian carcinoma. Cancer 1987;60(7):1561-1566.
5. Dvoretsky PM, Richards KA, Bonfiglio TA. The pathology and biologic behavior of ovarian cancer: An autopsy review. Pathol Ann 1989;24:1-24.
6. Rose PG, Piver SM, Tsukada Y, Lau TS. Metastatic patterns in histologic variants of ovarian cancer: An autopsy study. Cancer 1989;64(7):1508-1513.
7. Julian CG, Goss J, Blanchard K, Woodruff JD. Biologic behavior of primary ovarian malignancy. Obstet Gynecol 1974;44(6):873-884.
8. Abdul-Karim FW, Kida M, Wentz WB, et al. Bone metastasis from gynecologic carcinomas: A clinicopathologic study. Gynecol Oncol 1990;39(2):108-114. [http://dx.doi.org/10.1016/0090-8258(90)90414-g]
9. Geisler JP, Geisler HE. Brain metastases in epithelial ovarian carcinoma. Gynecol Oncol 1995;57(2):246-249.[http://dx.doi.org/10.1006/gyno.1995.1134]
10. Ansell SM, Rapoport BL, Falkson G, Raats JI, Moeken CM. Survival determinants in patients with advanced ovarian cancer. Gynecol Oncol 1993;50(2):215-220. [http://dx.doi.org/10.1006/gyno.1993.1195]
11. Seewaldt VL, Figge DC, Greer BE, Tamimi HK, Brown WS, Cain JM. Primary central nervous system recurrence after paclitaxel therapy for epithelial ovarian malignancy. Gynecol Oncol 1994;55(3):456-458. [http://dx.doi.org/10.1006/gyno.1994.1322]
12. Kastan MB, Onyekwere O, Sidransky D, Vogelstein B, Craig RW. Participation of p53 protein in the cellular response to DNA damage. Cancer Res 1991;51(23):6304-6311.
13. Marchetti M, Chiarelli S, Silvestri P, Peron ML. Epithelial ovarian tumors in young women under 35 years. Eur J Gynaecol Oncol 1995;16(6):488-493. [http://dx.doi.org/10.1097/00006254-199604000-00013]
14. Nangal JK, Narayan S, Kapoor A, Purohit R, Kumar HS. Mucinous cystadenocarcinoma of ovary in preadolescence: An ordinary tumor but at an unexpected age. Clin Cancer Inv J 2014;4(1)(in press).