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Case Report

Pathology Section

An Unusual Presentation of Neuroendocrine Carcinoma in a Young Female Patient

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ABSTRACT

Carcinoid is a type of neuroendocrine tumor originating in the enterochromaffin or Kulchitsky cells, distributed throughout the body. Carcinoid tumors metastatic to the ovary are uncommon, most of which arise in the gastrointestinal tract. We report herein a case of young female presenting with bilateral ovarian metastatic neuroendocrine tumor with synchronous bone metastases.

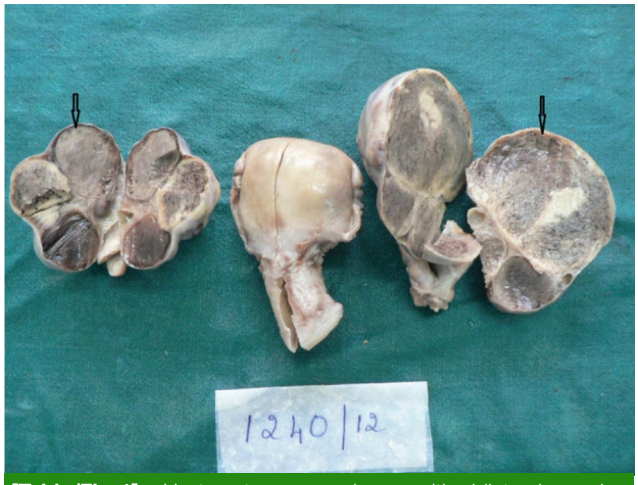
Keywords: Carcinoid, Ovary, Tumor, Well-differentiated

CASE REPORT

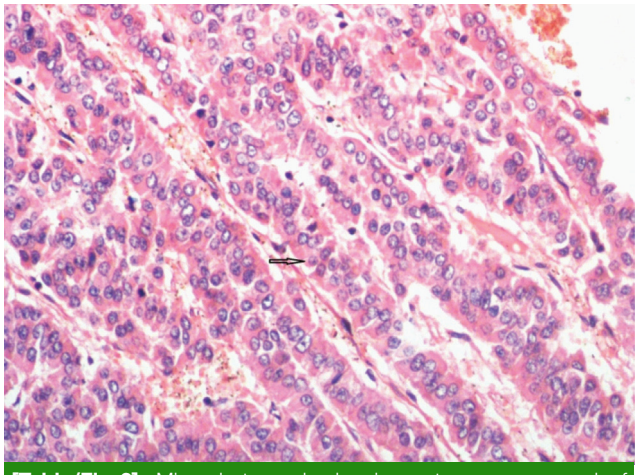
A 31-year-old lady presented to the Department of Obstetrics and Gynecology with pain abdomen, dragging sensation in legs and backache for 6 months associated with loss of weight. She was multiparous with 2 children and tubectomised 6 years earlier. On examination, she had bilateral iliac fossa tenderness. Abdominal ultrasound detected bilateral ovarian masses. Total abdominal hysterectomy with bilateral salpingo-oophorectomy was done after taking informed consent and the specimen was sent to the Department of Pathology for histopathological evaluation.

Uterus with cervix measured 8x5x4 cm. Right and left ovarian masses measured 5x4x3 cm and 8x6x4 cm respectively. Outer surfaces of both the masses were bosselated with intact capsules. Cut section was solid grey brown with focal tiny cysts [Table/Fig-1]. Histopathology of both the ovarian masses revealed a tumor composed of cells arranged in trabecular, glandular patterns and in cords [Table/Fig-2]. Cells showed moderate amount of eosinophilic cytoplasm and oval vesicular nuclei. Mitotic count was 10-12/10 high power fields. Ki-67 labeling index was 10-12% in highest proliferating areas. Angio-invasion was noted with focal areas of necrosis. A differential diagnosis of metastatic neuroendocrine tumor versus sex cord stromal tumor was offered.

On immunohistochemistry, the tumor showed diffuse and strong reactivity for synaptophysin and chromogranin A [Table/Fig-3]. A final diagnosis of bilateral metastatic neuroendocrine tumor of intermediate grade was made. Patient was evaluated for features of cord compression based on her complaints of backache and bilateral lower limb weakness. MRI of spine detected multiple metastases

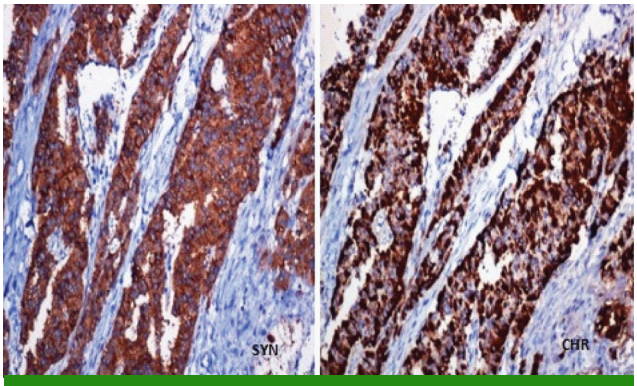


[Table/Fig-1]: Hysterectomy specimen with bilateral ovarian masses. Cut section showing solid grey brown areas (arrows).

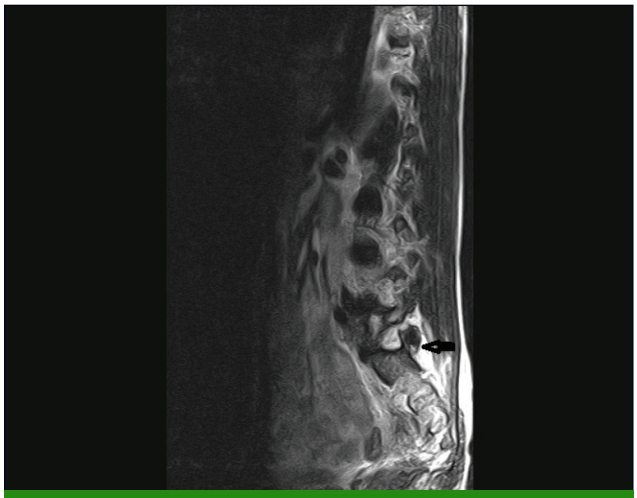


[Table/Fig-2]: Microphotograph showing a tumor composed of cells arranged in trabecular (arrow), glandular patterns and in cords. (H&E,x200).

in the vertebral bodies [Table/Fig-4]. Patient expired during her evaluation for primary.



[Table/Fig-3]: Tumor showing diffuse and strong positivity for synaptophysin and chromogranin A on immunohistochemistry. (x200).



[Table/Fig-4]: MRI of lumbar spine showing multiple lytic lesions (arrow) involving lumbar vertebrae and anterior epidural soft tissue in the spinal canal from L-5 to S-2 level.

DISCUSSION

Carcinoid tumors are rare causes of ovarian malignancy and represent approximately 0.1% of ovarian neoplasms. Metastatic carcinoid tumors to the ovary are even more uncommon [1]. Other sites of metastasis include liver, lung, peritoneum with bone being an unusual site [1-3].

Neuroendocrine tumors are studied extensively where they represent a broad clinicopathologic spectrum with variable morphologic features and biologic characteristics. Gastrointestinal tract (about 65%) is the commonest affected site by carcinoid tumors followed by the bronchopulmonary tract (about 25%). A good number of cases (22%) present with distant metastases, where half of them are reported to have unknown primaries [4]. Primary ovarian carcinoids are unilateral and are localized to the ovary, which arise in the setting of dermoid cysts. Metastatic carcinoids in the ovary are usually bilateral and arise most often from primary ileal carcinoids [1,2].

The median age at the time of diagnosis of ovarian disease is 55 years [1,3]. The present case is unusual for a young age of presentation at 31 years.

The differential diagnosis of primary ovarian carcinoid/ strumal carcinoid was excluded based on the presence of extraovarian metastases, bilaterality, multinodularity, vascular invasion, and absence of teratomatous elements in the present case [2]. Based on the European Neuroendocrine Tumor Society (ENETS) and WHO classification, Gastro-enteropancreatic-Neuroendocrine Tumors (GEP-NETs) are classified into well differentiated (low grade and intermediate grade) and moderately differentiated (high grade) [5].

Grade refers to the inherent biologic behavior of the tumor with a mitotic count of <2, 2-20 and >20 for low, intermediate and high grade tumors respectively. Ki 67 index reflects the proliferative activity of the tumor with <3%, 3-20% and >20% in low, intermediate and high grade tumors respectively [5].

Well differentiated neuroendocrine tumors shows characteristic histopathologic features of relatively uniform tumor cells in nesting, gyriform or trabecular patterns of which show diffuse and intense expression of neuroendocrine markers-Chromogrannin A and Synaptophysin, reflecting the production of abundant neurosecretory granules by them. They have an indolent behavior. Whereas, the poorly differentiated neuroendocrine tumors show diffuse sheets of tumor cells, reduced granularity and significantly reduced expression of neuroendocrine markers with an aggressive clinical course [5].

The tumors are known to cause elevated levels of serotonin in blood and urinary excretion of 5-hydroxy indole acetic acid (5-HIAA), with symptomatic carcinoid syndrome presenting with flushing and/or diarrhea [1,2,4,6]. The present case had no features of carcinoid syndrome.

Neuroendocrine tumors are known to have high propensity for regional and distant metastases. The sites of metastases include regional lymph nodes, peritoneal surfaces (including mesentery and omentum), lung, breast, ovaries, bones and skin [1,3]. The incidence of skeletal metastasis has been reported to be between 10-12% and axial skeleton is the most commonly affected site [4,6].

The prognostic indicators are evidence of invasion, distant metastases and proliferative rate as assessed by mitotic count and Ki 67 index [3,6]. There has been a reported 5-year survival rate for carcinoid tumors regardless of site or stage, ranging from 70%–80% and for patients with distant metastases, it is estimated to be 20-30% [4]. The present case was rare for presentation in a young female with synchronous bone metastases and showed a rapid disease progression though the tumor was well differentiated on histopathology. The case posed a diagnostic challenge where, the initial diagnosis was a primary ovarian tumor, considering the young age at presentation.

CONCLUSION

The present case highlights the importance of considering metastatic neuroendocrine tumor in the differential diagnosis of a young patient presenting with bilateral solid ovarian tumor in addition to primary ovarian tumors in young age group. The diverse presentations of metastatic disease can be diagnosed with the help of neuroendocrine markers chromogranin A and synaptophysin. Prolonged survivals may be achieved with Octreotide therapy and cytoreductive surgery.

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