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KRUKENBERG TUMOR
REPORT OF THREE CASES

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ABSTRACT

Krukenberg tumor is an interesting and rare tumor which usually but not always is metastatic. Ovaries more than any other genital pelvic organs are the site of metastasis. Endometrium, gastrointestinal tract and breast are the most common primary sites. The best method of treatment is surgery. Postoperatively, radiotherapy and chemotherapy must be performed.

3 cases of Krukenberg tumor diagnosed during five years are reported from Ghaem Hospital, Mashhad University of Medical Sciences. The patients' age ranged from 30 to 60 years. Clinical, laboratory and surgical follow-up was performed in all cases. Surgical treatment, radiotherapy, and chemotherapy were performed.

Two cases were primary and one was secondary. Two to three years after surgery the patients returned for follow-up. All were in good general health.

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INTRODUCTION

Krukenberg tumor is one of the most interesting ovarian tumors, which usually but not always is metastatic.[1] It's primary location may be distinguished long before its discovery.[2] It was first described by Krukenberg in 1896 who called it "fibrosarcoma mucocellulare carcinomatodes"[8] or "sarcoma ovarii mucocellulare."[1] Several years later it was understood that it is not a sarcoma but an epithelial tumor (Schlagenhaufer, 1902).[9] Finally, in 1960, Novak described this tumor as an infiltrated mucinocarcinoma with peripheral signet ring cells which sometimes will be observed with glandular structures.[4]

Ovaries more than any other genital pelvic organs are the site of metastasis.[3-5] Metastasis usually arises from the upper parts of the gastrointestinal tract (stomach, bilary tract, and pancreas), breast carcinoma and sometimes other organs like kidneys, lungs, thyroid, and endometrium.[3-5] Most of these originate from the stomach, which causes enlargement of ovaries.[6,7]

CASE REPORTS

The first patient was a 30-year old housekeeper living in Mashhad. She returned to the hospital 14 days after her eighth delivery with severe abdominal pain and vomiting, and was admitted to the hospital. After an overall examination a palpable mobile mass separated from uterus was found in the right upper part of the uterus. Ultrasonography revealed enlargement of the uterus, and a large mass of tissue adjacent to the bladder and right part of the uterus, which was reported as echogenic and echo-free. All laboratory tests were normal. In IVP, right kidney showed delayed secretion, and the larger than normal cecum showed a filling-defect on barium enema, and external pressure of an abdominal mass was seen in this area. Laparotomy revealed a 6-week uterus, and left ovary and right and left tubes were normal, but right ovary was larger than normal with a solid and lobulated consistency which after total hysterectomy was found to be a mass of tissue 18×18×10 cm in size and 2240 gr in weight with a lobulated and mixed cystic and solid surface. On microscopic examination ring type epithelial cells were seen with a general view of signet ring that in most areas formed the tumor Krukenberg had talked about, but no origin was found. Postoperative radiotherapy and chemotherapy was performed by the consultant oncologist. After one year when the patient was seen she was in good general health.

The second patient, a 35-year-old housewife from Torbat

Haidarieh city, was referred to the hospital because of acute severe abdominal distention and lower extremity edema in the sixth month of pregnancy (gravida eight). Symptoms appeared to start one week before. The patient had constipation, abdominal pain, and back pain, with no major complaint before that.

On physical examination she had a normal pregnancy but a hard mobile mass with some elasticity was palpated in both sides that was accompanied with ascites.

All laboratory tests except hematocrit (less than 30) were normal, and cytologic examination of the ascites fluid was negative. In laparotomy ovaries were enlarged and multinodular, and in frozen section the right ovary revealed malignancy; so hysterotomy, and then hysterectomy and bilateral salpingoophorectomy was performed. The right ovary was 17×10×10 cm in diameter and 1060 gr in weight and in microscopic examination signet ring cells and frequent atypia was observed. The diagnosisof Krukenberg tumor was made and radiotherapy and chemotherapy was started. Three years after surgery the patient returned for follow-up in good general health. In this patient the primary site of tumor could not be found.

The third patient was a 60-year-old housewife (para 15) living in Shahan city. She was referred to the hospital because of abdominal pain of 3 days' duration. According to her medical history she did not have any major problem before. On examination of the epigastric area a solid nonmobile mass was palpated which extended from right to left. All laboratory tests were normal. Alpha fetoprotein (AFP) was 7.53 IU/ml and CEA 7.00 IU/ ml. In barium enema a mass similar to a neoplastic lesion was observed in the transverse colon. In pelvic ultra-sonography two largemultilocularmasses with irregular echogenicity were observed. The right mass was 81×59 mm and the left 104×89 mm. The uterus was small.

In laparotomy ascites fluid was present in the abdomen and two ovary masses were observed. Oophorectomy and hysterectomy was done to remove the masses. A hard mass was in thecolon. Resection and anastomosis was performed.

In the macroscopic examination of the specimens ovary-like tissue totally weighing 550 gr with lobulated surface and cystic in some parts with a gray surface was observed.

The specimen resected from colon measured 20×30 cm and was gray to cream in color and contained a tumoral mass of 1.5 cm. Microscopically, neoplastic proliferation of the epithelial cells with atypia and mitosis and a glandular pattern in all layers and invasion to lymph nodes was observed. The diagnosis of secondary metastatic Krukenberg tumor[8] of the ovaries arising from colon as the primary source was then made.

Postoperatively, radiotherapy and chemotherapy was instituted. Two years after the surgery when the patient was seen again, she was generally in good health.

DISCUSSION

Krukenberg tumor may be primary or secondary. Novak and Wardruft reported that only 20% are primary. Krukenberg tumor may arise from granulosa, teratomas mucinocyst, or mucoid degeneration in a Brenner tumor.

Metastatic adenocarcinomas may not be differentiated from primary ovarian carcinoma.[1,4] Sometimes, only after a careful GI study the primary neoplasm will be found.[4] Endometrium, gastrointestinal system, and breast are the most common primary sites and in gastrointestinal system. stomach is most commonly affected.[1]

In one study by Holtz and Hart on 27 patients, in 80% of the cases, primary source was stomach and the rest arised from colon, breast, and bladder.[11] The incidence of the tumor varies in different reports. Handly et al. could find only 11 cases of metastatic carcinoma of the ovary in 11200 autopsies, while Stauder, Moyer, and Roddenberg have reported it's incidence to be one percent, two percent, and 0.6 percent of the ovarian tumors, respectively.[12]

Among 125 patients admitted to the Ghaem Hospital during five years, three cases of Krukenberg tumor were found.

The tumor may be small or large and solid or cystic. In most cases the ovary remains elliptical or kidney-shaped and is grey or white in color. Over 50% are bilateral, and often from the secondary type.[4] Microscopically, the Krukenberg tumor is perfectly distinctive, and the diagnosis depends upon the histologic pattern, not on the primary lesion. The acini or small nests of epithelial cells are spread over the fibrous or myxomatous stroma. This distinctive pattern is called "signet ring cells" in which there is collection of mucoid material in the cytoplasm and the nucleus is pushed toward the side of the cell.[1]

Three histologic patterns may be observed in the ovary metastases: (a) spread to lymph vessels, (b) solid alveolar structure, and (c) diffuse infiltration.

In the diffuse infiltration type, signet-ring cells extend diffusely and radially via the lymph vessels, and in the periphery, tumor cells leak from the lymph vessels, infiltrating the stroma.[13] There may be stromal hyperplasia which is a reaction to invasion of signet cells into stroma.[14]

There are different pathways for spread of a tumor to ovaries: lymphatics, blood stream, adjacent organs, and finally from implant of cancerous cells on the surface of ovary, which may be transferred by peritoneal fluid from its primary site. But most pathologists believe that lymphatic or blood stream spread is the cause.[4]

The clinical signs depend upon the place of the primary cancer. Signs of metastasis may present before discovery of the primary base.[2,8]

Age range varies in these patients but most patients are in the reproductive ages.[12] These patients present with pain, loss of appetite, nausea, vomiting, palpable mass,

weight loss, and ascites.[8] Sometimes patients are referred because of torsion of the ovary mass or rupture of the cystic metastasis.

Occasionally, patients with Krukenberg tumor come to the hospital with abnormal uterine bleeding. This is in accordance with the hypothesis that such tumors may be functional.[1,2] In the luteinizing phase stroma of the ovary becomes luteinized and produces hormone. In addition, production of estrogen and likelihood of production of androgen with virilization is suggested.[15] Bullon has reported several cases of virilization in the patients with Krukenberg tumors during their pregnancy.[16-17]

Most endocrine disorders of the Krukenberg tumor are in those metastatic from colon.[4]

Treatment of these patients is surgical. Unilateral or bilateral removal of the ovarian mass and its related tube is mandatory. Also, it is essential to look for the primary tumor. If a tumor is found a suitable decision should be made. If the tumor is imperfectly removed radiotherapy may be needed.

In the secondary Krukenberg tumor the prognosis is worse than the primary type. Since there are lots of metastases from the colon to the ovaries, often bilateral oophorectomy is suggested for postmenopausal patients. But this is still under question whether oophorectomy in menopausal women is useful or not.[17-19]

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