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Case Report

A rare Krukenberg tumor arising from a primary adenocarcinoma of the small intestine

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ABSTRACT

Objective: A Krukenberg tumor is a malignancy in the ovary that metastasizes from a primary site. Here, we report a very rare case of bilateral Krukenberg tumors of the ovaries arising from a primary adenocarcinoma of the small intestine in a 53-year-old Taiwanese woman.
Case report: The patient presented with a 3-month history of abdominal distension and acid regurgitation. Gastroscopy and colonoscopy findings were negative. According to the preoperative image, we highly suspected that the small bowel mass was the primary tumor with metastatic tumors to bilateral ovarian masses. The diagnosis was made immediately after operation. Results from pathology and immunohistochemical report confirmed our diagnosis.
Conclusion: The primary lesion of a Krukenberg tumor is generally too small to be detected. Thus, careful radiographic and endoscopic exploration of the digestive system is necessary to detect the primary tumor. Immunohistochemical evaluation is also useful for determining the primary site of the adenocarcinoma.

Introduction

In 1896, Friedrich Krukenberg, a German gynecologist and pathologist, described what he presumed was a new type of primary ovarian neoplasm. The true metastatic nature of this lesion was established six years later. As first described by Krukenberg, the term “Krukenberg tumor” should be restricted to ovarian metastatic carcinomas that exhibit signet cells and diffuse stromal infiltration [1]. However, the term “Krukenberg” has often been broadly applied to any metastases to the ovaries, irrespective of the site of origin [2]. Krukenberg tumors are uncommon, accounting for 1%–2% of all ovarian tumors [3]. The stomach is the primary site for most (70%) cases of Krukenberg tumors, followed by the colon, appendix, and breasts. Adenocarcinomas of the small bowel are uncommon, with an incidence of 0.23 cases per 100,000 people [4] and Krukenberg tumors arising from adenocarcinomas of the small bowel are even more unusual.

Patients with Krukenberg tumors commonly present with symptoms related to ovarian involvement, the most common of which are abdominal pain and distension (primarily because ovarian masses are usually bilateral and often large) [5]. The remaining patients have nonspecific gastrointestinal symptoms, or are asymptomatic. The patient age range was reported to be 40–50 years [4], and almost all patients with Krukenberg tumors are premenopausal.

Radiologically, Krukenberg tumors usually appear as oval or kidney-shaped ovarian masses on abdominal pelvic sonography and computed tomography (CT) images. Nearly 80% of such cases are bilateral [5] with masses that are usually solid but can also be cystic. Confidently distinguishing between primary and metastatic ovarian cancers is impractical in many cases because of overlapping imaging results; however, masses that are bilateral, sharply delineated, purely solid or predominantly solid lesions with necrosis favor the diagnosis of a metastatic ovarian tumor [5].

The diagnosis of Krukenberg tumors largely depends on the recognition of their characteristic light microscopic features, such as densely fibroblastic and edematous stroma that appears diffusely infiltrated by malignant signet-ring cells arranged singly, in cords, or in nests. Immunohistochemical evaluation is useful for determining the primary site of the adenocarcinoma.

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Case report

A 53-year-old married woman (gravida 2, para 2) presented with a 3-month history of abdominal distension and acid regurgitation. No significant medical history or family history of bowel, breast, or gynecological cancer was noted. Gastroscopy and colonoscopy were performed, and no gastric or colon tumors were observed. Ultrasound examination revealed large well-defined bilateral adnexal masses, consisting of solid and cystic components in the pelvis. The size of the right adnexal mass was 7 ㎝ × 5 ㎝ and the size of the left adnexal mass was 15㎝ × 8 ㎝ with blood flow; both masses showed blood flow and bilateral ovarian metastatic neoplasms were suspected. The ovarian cancer tumor marker antigen 125 (CA -125) was 90.29 U/mL (<35 U/mL).

CT revealed two heterogeneous, space-occupying lesions with lobulated, multicystic masses involving soft tissue components of nearly 7㎝ × 5 ㎝ in the right adnexa and strong enhanced solid components 15㎝ × 8 ㎝ in the left adnexa (Fig. 1). Enlarged small lymph nodes were also observed among the para-aortic lymph nodes. Subsequently, contrast-enhanced CT of the abdomen revealed a segmental thickening of the jejunum, approximately 3 cm in size, which was a suspected primary neoplasm (Fig. 1).The role of tumor markers in the evaluation of a suspected small bowel tumor is unclear [6].

During exploratory laparotomy, both ovaries were observed to be markedly enlarged (R = 7 cm; L = 15 cm). Bilateral salpingo-oophorectomy was performed first and the specimens were submitted for frozen sectioning. The frozen sectioning report showed that a metastatic adenocarcinoma was highly suspected and the microscopic sectioning reports indicated that all the sections had an arrangement similar to that of adenocarcinoma sections. The samples were composed of neoplastic cells arranged in tubular, glandular, cord-like structures infiltrating into the fibrotic stroma. We only suspected that the bilateral ovarian tumors were metastatic adenocarcinomas; however, we could not make a definitive diagnosis during surgery. Based on the no-harm rule to avoid reopening, total hysterectomy and bilateral pelvic lymph node sampling with washing cytology and omentectomy were performed. Gross examination revealed that the ovarian tumors were grayish −white and had a solid smooth external surface (Fig. 2); additionally microcystic and edematous cut surfaces resembled a fibrotic stroma. Immunohistochemically, the tumor cells were diffusely positive for cytokeratins 20 (CK20) (Fig. 2)and caudal type homeobox transcription factor 2

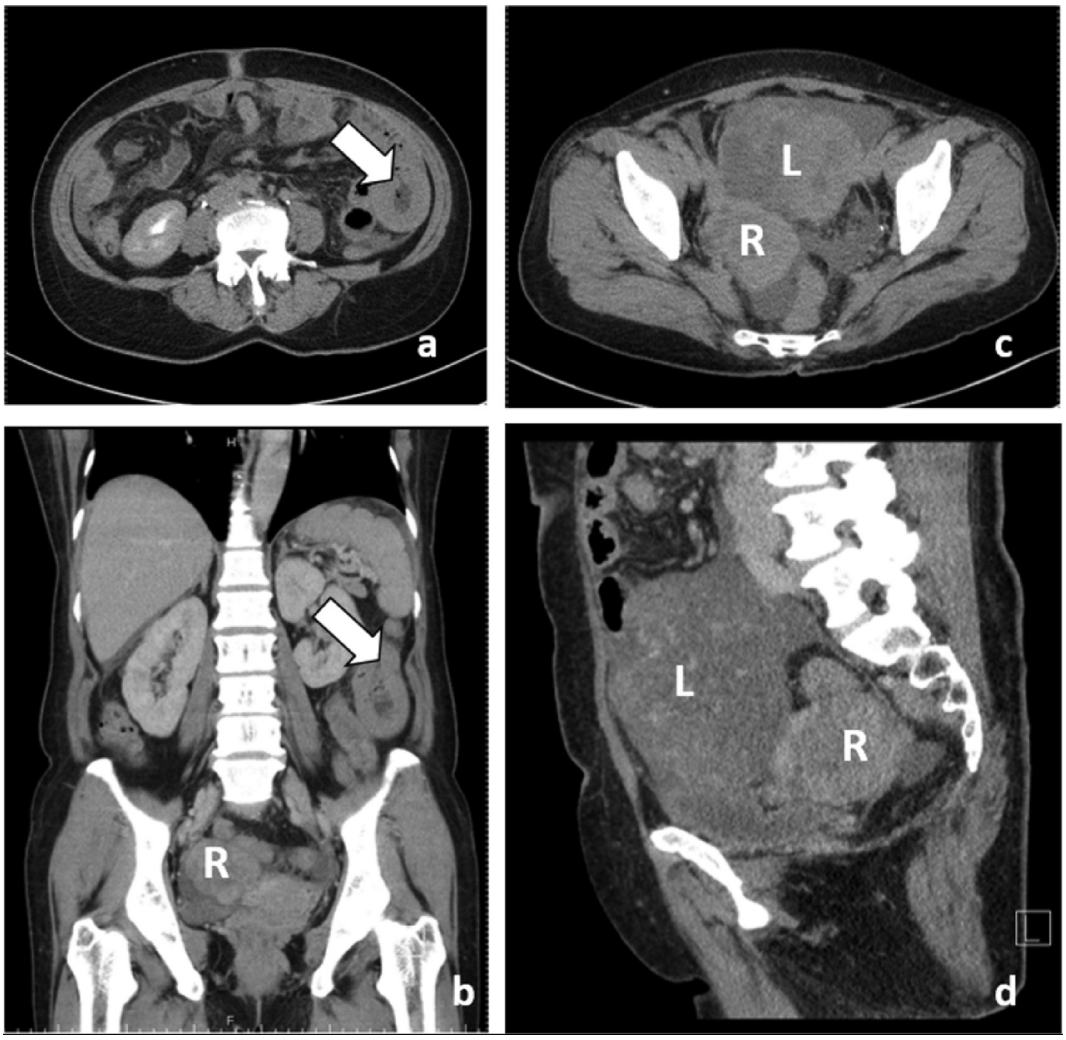

Fig. 1. Computed tomography scan (a) A segmental wall thickening mass of the jejunum, about 3 cm in size (arrow); (b) (coronal view) jejunal mass (arrow) and right pelvic mass (R); (c) bilateral tumors consisting of solid and cystic components, left adnexal mass: 15 cm in size (L) and right adnexal mass: 7 cm in size (R) (d) (sagittal view) left adnexal mass (L) and right adnexal mass (R).

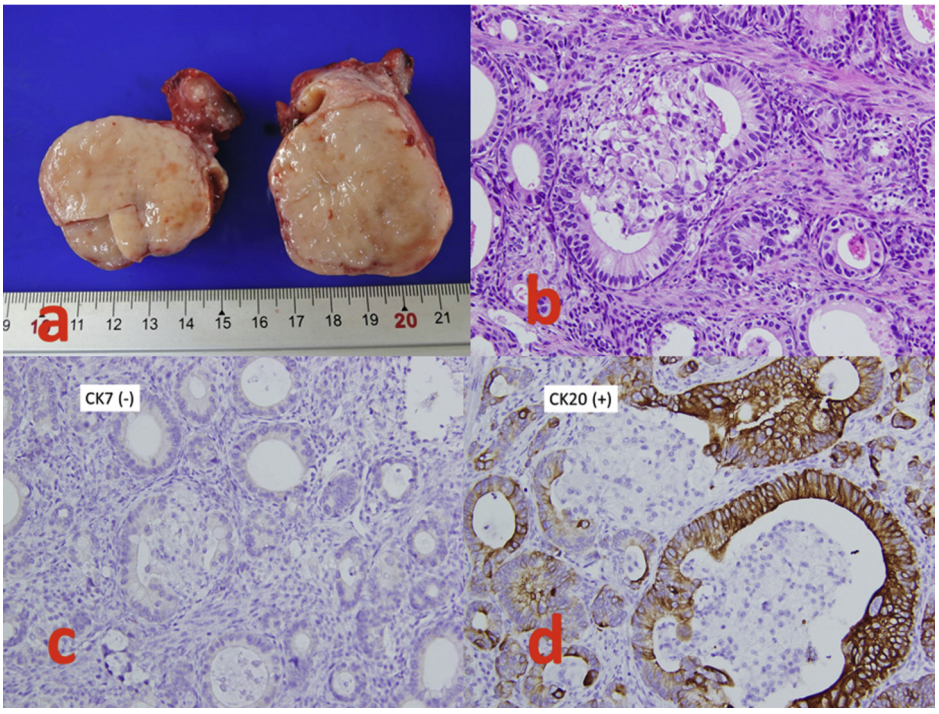

Fig. 2. (a) Resectioned right ovary and right fallopian tube; the tumor is white elastic and firm, and exhibits foci of hemorrhage (b) Hematoxylin-eosin- stained specimens of the ovary. There is extensive infiltration of the fibrous tissue by malignant cells, forming irregular glands, cribriform structures and cords. Immunohistochemical staining: (c) negative for CK7 and (d) positive for CK20.

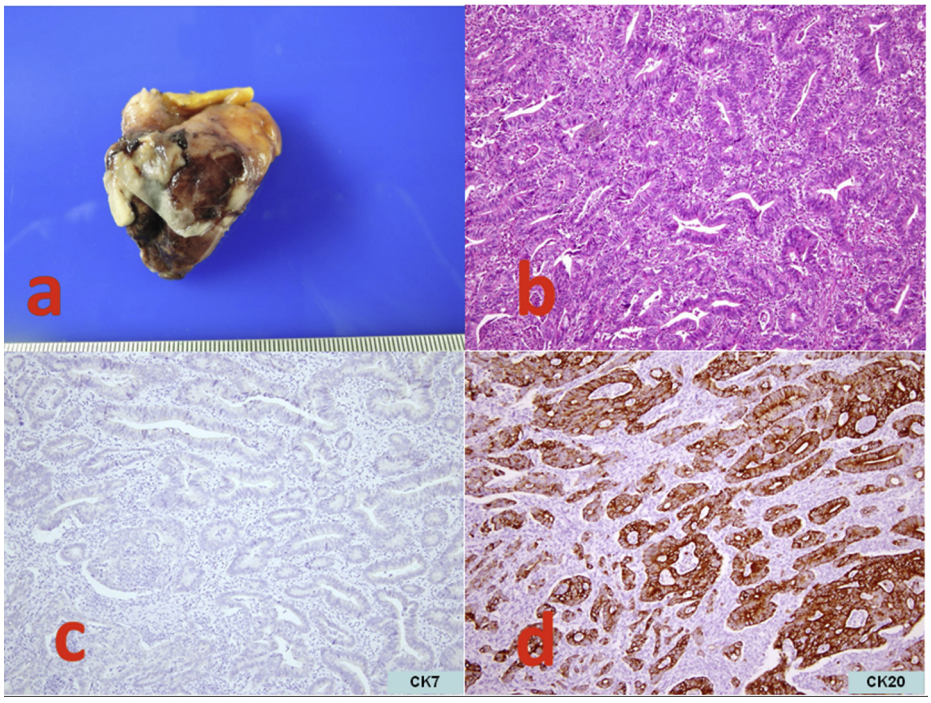

Fig. 3. (a) Segment of the small intestine, measuring 5 cm in length. Grossly, the external surface of the serosa is retracted, red, and granular. Macroscopic tumor perforation was not identified. (b) Microscopically, hematoxylin-eosin- stained specimens reveal adenocarcinoma of the small intestine composed of tumor cells arranged in abortive glands or cell nests infiltrating the mucosa, submucosa, muscle tissue and regional mesenteric fat. Immunohistochemical staining: (c) negative for CK7 and (d) positive for CK20.

(CDX2), but were negative for CK7(Fig. 2) and paired box 8 (PAX-8). According to the immunostaining pattern, the metastatic adenocarcinoma was believed to have originated from the intestinal tract.

A general surgeon was consulted before operation for the resection of the segmental thickening of the jejunum and segmental resection of the small intestine, 20 cm distal to the Treitz ligament, was performed. Microscopically, the resected tumor

resembled an adenocarcinoma of the small intestine that consisted of tumor cells arranged in abortive glands or cell nests infiltrating the mucosa, submucosa, muscle tissue, and regional mesenteric fat (Fig. 3). Immunohistochemical studies revealed that the tumors was positive for CK20 and p53; focally positive for CDX2; and negative for CK7, vimentin, estrogen receptors, progesterone receptors, PAX-8, and WT-1. Thus, this tumor was an adenocarcinoma arising from the gastrointestinal tract, rather than from the ovary; the pathological staging (pTNM) of pT4N0M1 indicated stage IV.

The patient recovered appropriately postoperatively period and the medical oncology department suggested palliative chemotherapy.

Discussion

The diagnosis of a primary tumor can be made either preoperatively, during the operation for ovarian metastasis, or within a few months postoperatively. However, primary tumors are generally too small to be detected. Thus, the diagnosis of Krukenberg tumors warrants careful radiographic and endoscopic exploration of the digestive system for detecting primary tumors. Radiologically, Krukenberg tumors usually appear as bilateral ovarian masses on abdominal pelvic sonography and CT images. The masses are normally solid but can also be cystic [7]. Krukenberg tumors typically appear as oval or kidney-shaped masses on CT images. Confidently distinguishing between primary and metastatic ovarian cancers is not possible in many cases because of overlapping imaging results; nevertheless, masses that are bilateral, sharply delineated, purely solid, or predominantly solid lesions with necrosis favor the diagnosis of a metastatic ovarian tumor [7]. Recently, some studies showed that among patients with undiagnosed pelvic tumors, the CA-125/CEA ratio can be used to preoperatively identify a substantial fraction of patients with nonovarian malignancies [8]. However, most studies have focused on colorectal cancer metastasis in the ovary. No study has focused on small bowel cancer metastasis in the ovary; thus, more research should be conducted on this topic.

The diagnosis of Krukenberg tumors largely depends on the recognition of their characteristic light microscopic features, such as densely fibroblastic and edematous stroma that appears diffusely infiltrated by malignant signet-ring cells arranged singly, in cords, or in nests [5]. Immunohistochemical evaluation is also useful for determining the primary site of adenocarcinomas. The immunophenotypes CK7 and CK20 and CDX2 are specific and sensitive for metastatic intestinal adenocarcinomas [9]. Specifically, the combination of CK7+, CK20−, CDX2− usually indicates an ovarian primary adenocarcinoma [5]. whereas the combinations of CK7−/CK20+ and CK7+/CK20+ (particularly CK20+) strongly suggest a primary gastrointestinal adenocarcinoma [5].

Treatment of ovarian Krukenberg tumors involves total abdominal hysterectomy with bilateral salpingo-oophorectomy. Gastric and intestinal tumors should also be resected according to their staging and some patients may benefit from ovarian metastasectomy [10]. Moreover, because of the rarity of Krukenberg tumors, a national registry should be created to collect information from these patients and thus help improve diagnosis and treatment outcomes. In addition to surgical treatment, chemotherapy is a therapeutic option; palliative radiotherapy may also be applied for unresectable or distant metastatic Krukenberg tumors [11]. To improve survival, establishing the optimal management strategy of Krukenberg tumors is necessary.

Currently, the prognosis of patients with Krukenberg tumors is extremely poor, with average survival times ranging between 3 and 10 months; Only 10% of such patients survive for >2years after diagnosis [12].

In conclusion, this paper presents a very rare case of bilateral Krukenberg tumors in the ovaries, which developed from a primary adenocarcinoma of the small intestine that was diagnosed immediately after the operation. Radiologically, Krukenberg tumors usually appear as bilateral oval or kidney-shaped ovarian masses and purely or predominantly solid lesions on abdominopelvic sonography and CT scans. Generally, the primary tumor is too small to be detected. Therefore, the diagnosis of Krukenberg tumors warrants careful radiographic and endoscopic exploration of the digestive system for detecting the primary tumor. For a definitive diagnosis, immunohistochemical evaluation is useful for determining the primary site of the adenocarcinoma.

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