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Review Article

A review of Radiological Imaging Features to ameliorate radiologists' knowledge of Krukenberg Tumor (KT).

Diana Donatello
Radiologist, Independent Researcher, Costa Contina Street 19, Vasto (CH), Italy.

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***Corresponding author:** Diana Donatello, Radiologist, Independent Researcher, Costa Contina Street 19, Vasto (CH), Italy.

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Abstract:

Object: Aim is to delineate the major radiological findings with US, CT and MR of the Krukenberg Tumor.
Method: Revision of the literature.
Introduction:
A Krukenberg Tumor refers tipically to a gastrointestinal cancer that metastasizes to the ovaries; this tumor was named after Krukenberg, who originally described this pathologic condition of the ovaries in 1896. The prognosis of this tumor is uniformly poor.[1]
Discussion: Krukenburg tumor (KT)is a metastatic malignancy of the ovary characterized by mucin-rich signet-ring adenocarcinoma that primarily arises from a gastrointestinal site in most cases and less commonly from other sites. Often these tumors are bilateral (over 80%), given their metastatic nature. The images of a Krukenberg Tumor highlight that the masses are mostly: bilateral, lobulated, solid/mixed solid and cystic.
Conclusion: On imaging, Krukenberg Tumor should be suspected when bilateral solid, mixed solid and cystic, or predominantly cystic ovarian masses are seen in the presence of a known or suspected gastrointestinal primary malignancy. Krukenberg Tumors should also be considered when a ovarian mass shows the so-called "lead vessel sign"[1-12-15].

Introduction

Krukenburg tumor is a metastatic malignancy of the ovary characterized by mucin-rich signet-ring adenocarcinoma that primarily arises from a gastrointestinal site in most cases and less commonly from other sites. This tumor is named after Friedrich Ernst Krukenberg (1871-1946), who reported a new type of ovarian malignancy in 1896.[2-3-4]. Nearly 80% of Krukenberg Tumors are bilateral and the prognosis of this tumor is uniformly poor [1-2-3]. The most common origin of KT is from gastric cancer (in up to 70% of cases), especially the poorly cohesive/signet ring-cell type [6]. Even though KT are probably the best-known secondary tumors of the ovary, they account for only about 30–40% of all secondary ovarian tumors [7]. Metastases from other sites that do not comply with the histopathological definition of KT are frequently found in ovaries, including colon, breast, small intestine, and pancreatic cancer, malignant melanoma, and others [5]. It is vitally important for radiologists to recognize a metastatic tumor to direct future therapies.

Discussion:

In most cases, the stomach has been attributed to be the primary site, with studies showing this in about 70% of cases. Recent sources note an increasing prevalence of colorectal tumors.[4] Gastric and colorectal cancers collectively account for almost 90% of the primary site for this tumor. Other less common primary sites described in the literature are the breast, appendix, small

intestine, gallbladder, urinary bladder, biliary tract, pancreas, ampulla of Vater, or uterine cervix.[5][6][7] Recurrences can occur years after the primary has been treated. Krukenberg Tumors are further defined as either "synchronous metastasis," where the metastasis is discovered within three months of the primary tumor's diagnosis, or "metachronous metastasis," where the metastasis is found after three months, frequently after the completion of initial curative therapy.[8] The presence of pregnancy, concurrent with a KT, complicates the diagnosis.[8][9] As the tumor increases in size, it compounds an already increasing abdominal girth from the uterus. Sex hormones can augment gastric cancer dissemination. Placental growth factor levels are elevated in gastric cancer and associated with serosal invasion and lymph node metastases. Surgery appears to be the only treatment advocated for this situation - the role of the other modalities is questionable [4].Compared with primary ovarian cancers, Krukenberg Tumors more often occur in younger women, possibly because the functioning ovary is prone to metastatic disease as a result of the normal rich ovarian blood supply. The average age of diagnosis is 35 to 45 years. However, it can be seen in all age groups. The incidence is higher in Asian countries like Korea, Japan, and China, where these tumors make up about 20% of all ovarian cancers. It is felt that the high prevalence of gastric cancer in these areas accounts for its predominance.[10] Krukenberg Tumors are metastatic tumors to the ovary that contain well-defined histological characteristics (mucin-secreting “signet ring” cells) and usually originate in the gastrointestinal. The exact mechanism of primary tumor metastasize to the ovaries is unclear. However, several mechanisms have been proposed, such as through lymphatic channels, blood vessels, and peritoneal cavity. The time from diagnosis of the primary neoplasm to the development of ovarian metastasis is variable and can range from several months to >10 years. Cytologic examination often reveals mucoid degeneration and many large cells shaped like signet rings. They can originate from: stomach cancer (signet ring cells): most common, colorectal carcinoma: second most common breast cancer, lung cancer, contralateral ovarian carcinoma, pancreatic carcinoma, cholangiocarcinoma / gallbladder carcinoma Grossly, the ovaries are asymmetrically enlarged with a bosselated (protuberance-laden) contour. They are usually solid but can occasionally be cystic. The capsular surface is mostly free of any tumor infiltrates, adhesions, implants, or deposits which can be deceptive and appear as a primary ovarian tumor. The characteristic finding of this tumor is the presence of mucin-laden signet-ring cells, which are present in at least 10% of the cases. The diagnostic criteria of WHO based on Serov and Scully's description are for making the diagnosis states:

The presence of stromal involvement,the ovarian stromal sarcomatoid proliferation and the presence of mucin-producing signet-ring cells[20].

Histochemically, the intracytoplasmic mucins of the signet-ring are neutral and acidic and stained with Mayer mucicarmine, periodic acid-Schiff with diastase digestion, and Alcian blue stain. The signet ring cells have eccentric hyperchromatic nuclei, often presenting as nests, cords, tubules, or acini.[10] They diffusely infiltrate the mesenchymal stroma. The patients may have elevated CEA or CA125 level. Patients commonly present with abdominal or pelvic pain, bloating, dyspareunia, irregular vaginal bleeding due to the ovarian metastases, or a combination of these symptoms. Quite often, the primary tumor does not cause the presenting symptoms. Ascites, typically a late feature of peritoneal metastases, can occur alongside intestinal obstruction and cachexia and heralds a sharp decline in the patient's quality of life. Krukenberg Tumors with benign ascites and right hydrothorax that contain no malignant cells are known as Pseudo-Meig syndrome.[11] These tumors can move about, leading to ovarian torsion and abdominal pain. Patients can manifest pain during sexual intercourse.[1] (Fig. 1)

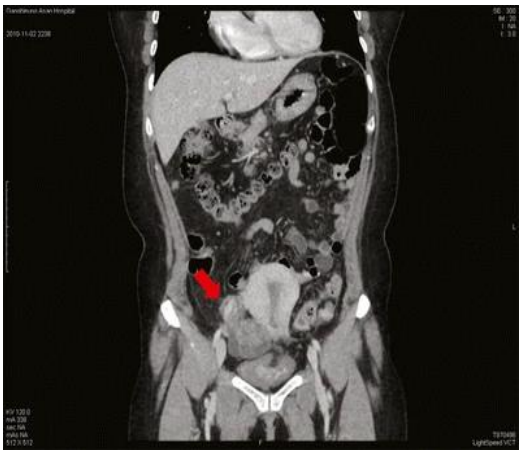


Fig. 1[1]
Incidental diagnosis of torsion of a KT originating from sigmoid colon cancer in a 46 old woman.
The coronal section of abdominopelvic CT showed a right ovarian mass with torsion (arrow).

Radiological findings:

Ultrasound can be the first instrument for try to find a suspected ovarian mass, but the clinical presentation of KT it could be vague with mostly abdominal symptoms, and CT may be the primary imaging test performed. On US, Krukenberg metastases, accordingly to Crasta et al [12], can be solid (stomach or breast primary tumor), mixed solid and cystic (colon, rectum, appendix, or biliary tract primary tumor), or less commonly, predominantly cystic masses (colon or appendix primary tumor) with clear well-defined margins. These metastases move freely when pressure is exerted on them by the vaginal probe. Sometimes hypoechoic irregular areas within the solid mass change their homogeneously solid echostructure; this feature probably reflects necrosis, moreovere moth-eaten–like cyst formation is considered a characteristic feature (Fig.2).

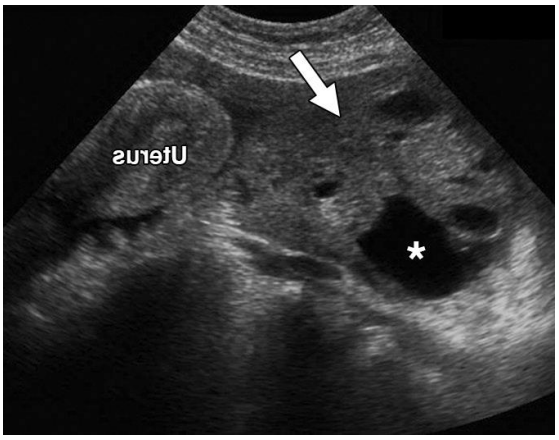


Fig. 2[2]
37 old woman with KT.
Transabdominal pelvic ultrasound image shows a solid mass in the right ovary (arrow) with some cystic areas (asterisk).

Doppler shows randomly spread out tumor vessels with low-impedance flow [13]. Low impedance might assist the radiologist in making differential diagnoses between primary ovarian carcinoma and Krukenberg Tumors. Some studies have suggested a possibility of KT in the presence of prominent vascular signal along the wall of the well-demarcated intratumoral cysts [13-14]. Testa et al. [15] depicted the presence of a main peripheral vessel in solid ovarian metastases, seen in a tree-shaped configuration and traversing into the central part of a solid ovarian mass, which is known as the lead vessel sign (Fig. 3).

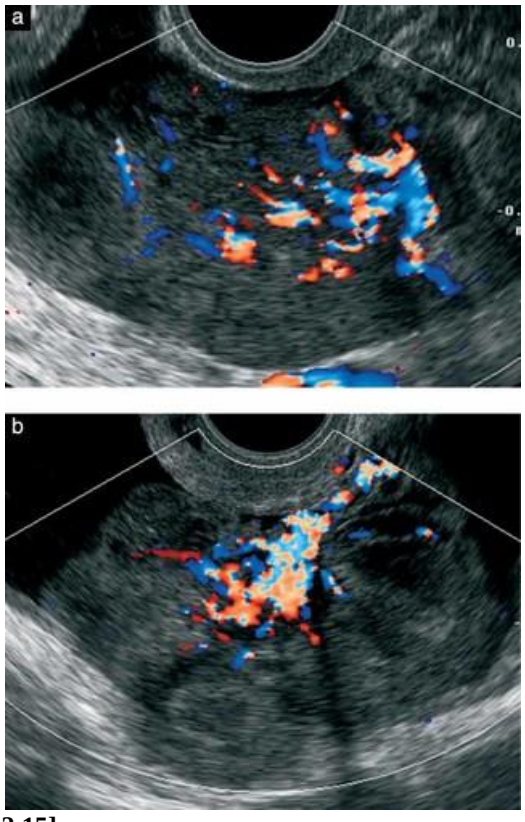


Fig. 3 [12,15]
US shows the sonographic appearance of the lead vessel, a major vessel penetrating from the periphery into the central part of the ovarian mass with a tree-shaped morphology. Color Doppler images from KT shows main vessel exhibiting a tree-shaped morphology, and penetrating from the periphery into the central part of the ovarian mass.

On CT the ovaries appears like bilateral masses that may be solid, mixed solid and cystic, and sporadic they can be mostly cystic. The use of CT is absolutely helpul for recognizing the extent of extra-ovarian involvement, particularly the engagement of bowel, ureter, urinary bladder, or other organs. Moreover on CT study, the stomach, colon, appendix, pancreas, and biliary tract should be scrutinized for a mass, and when such a mass is identified, a KT should be strongly suspected (Fig. 4). On contrast-enhanced CT scans, ovarian metastatic lesions from stomach cancer appear more solid than, more frequently have dense enhancement of the solid portion, and are smaller than ovarian metastatic lesions from other neoplasm.

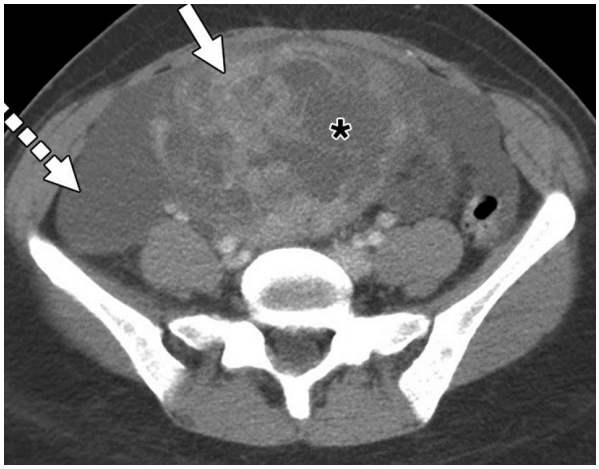
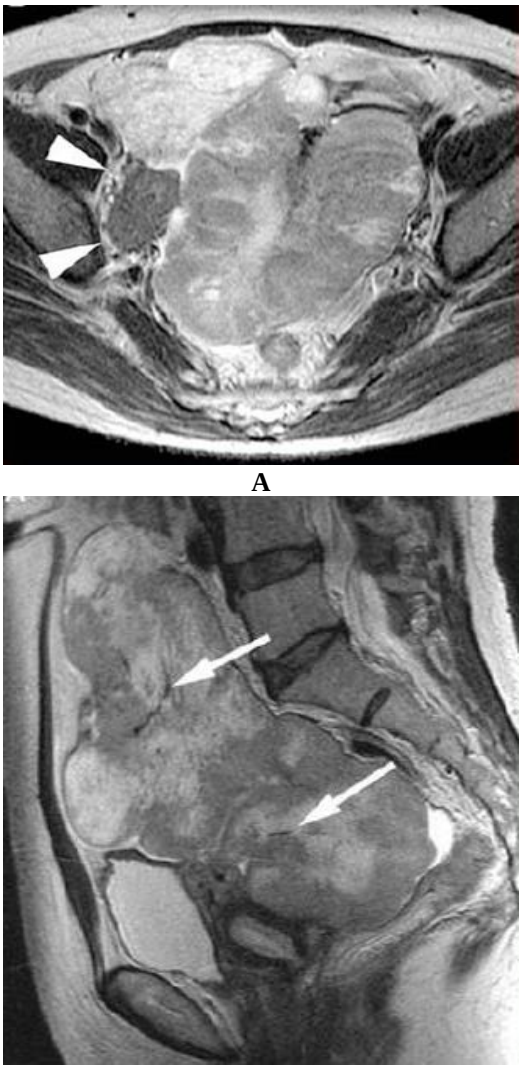


FIG.4 [2]
Same patient of Fig 2, axial CT images of abdomen and pelvis with IV contrast medium show a pelvic mass with enhancing solid components (solid arrow) and areas of cystic change (asterisk) with associated ascites (dashed arrow).

On the T1 and T2 sequences of the MRI, the solid components appear to be hypointense because of dense stromal reaction, and they show a restriction of diffusion and enhancement on contrast-enhanced sequences. In the cystic areas could be see a T2 hyperintensity that reproduce mucin that does not enhance. Identification of hypointense solid components within an ovarian mass on T2-weighted MR images is a characteristic, although not specific, finding for Krukenberg's Tumors, especially when the tumors are bilateral, have sharp margins, and have an oval configuration [16, 17](Fig 5 A,B).A great enhancement is observed in the solid components of these tumors after contrast administration, where there is an initial time period of relative rapid contrast uptake by the tumor, followed by decreased enhancement toward the second part of the examination (washout) [18].



A

B

Fig.5 [19]
A: Axial T2 MRI image demonstrates bilateral ovarian tumor. The lesion present in the right ovary demonstrates a predominant decrease in intensity (arrowheads)
B: Sagittal T2 fast spin-echo MRI image demonstrates the presence of a solid and lobulated mass, with heterogeneously high-intermediate signal intensity, with empty flows within the mass (arrows).

Treatment:

Arró Ortiz et al, reported a case of a 34-year-old female patient with a history of Hartmann's operation for occlusive acute abdomen three years previously. The pathological examination confirmed a sigmoid colon, well-differentiated panmural adenocarcinoma, without vasculolymphatic invasion and with perineural permeation (High-risk stage II-pT4b N0 Mx). The patient received eight cycles of chemotherapy treatment with Capecitabine and Oxaliplatin for six months. One month after the adjuvant; thorax, abdomen and pelvis CT scan detected a cystic image in the right ovary. In successive controls, laboratory results revealed elevated levels of serum CEA of 28.2 ng/ml. Magnetic resonance (MR) detected adenopathy in aortoiliac bifurcation, 18 × 8 mm of undetermined origin, and a lesion in the right adnexal, 36-mm witch could correspond to aneoplasia process linked to endometrioma. PET-CT scan informed adenopathy in aortoiliac bifurcation (SUV 7.3) and an image in the right adnexa with a mixedcomponent (SUV 23). Laparotomy surgery was performed. Right salpingooophorectomy and adenopathy resection were performed. The histopathologic confirmed a KT of the ovary and immune profile favored a metastatic gastrointestinal carcinoma. The postoperative outcome was uneventful. Thepatient completes the chemotherapy treatment: eightcycles with Capecitabine and Oxaliplatin. Currently, three years after the initial diagnosis, she is in clinical follow-up with a favorable outcome, and no evidence of recurrence. [21] In the early 1990's Sugarbaker et al. introduced cytoreductive surgery (CRS) and hyperthermicintraperitoneal chemotherapy (HIPEC) as a new innovative therapy option for selected patients withperitoneal carcinomatosis. Nowadays, there is no established treatment for patients with KT with peritoneal metasasis. There is a need for the future high-quality randomized multicenter trials to make a strong recommendation.[22]

Conclusion:

KT, also known as carcinoma mucocellulare, refers to the "signet ring" subtype of metastatic tumor to the ovary. The stomach followed by colon are the two most common primary tumors to result in ovarian metastases, followed by breast, lung, and contralateral ovarian primary tumors. Most imaging features are non-specific, consisting of predominantly solid components or a mixture of cystic and solid areas. It is often difficult to differentiate from other ovarian neoplasms. US: These tumors are typically seen sonographically as: bilateral, solid and sometimes cystic ovarian masses, with clear well-defined margins an irregular hyper-echoic solid pattern and moth-eaten-like cyst formation are also considered characteristic features [23].CT: Appearances can be indistinguishable from primary ovarian carcinoma 2. Features will favor towards a KT if a concurrent gastric or colic mural lesion is seen. There is some evidence that tumors originating from the stomach may be denser on contrast-enhanced CT than those originating from the colon.[24] MRI: Signet ring cells disperse in the ovarian stroma ,have abundant collagen or marked edema, so Krukenberg Tumors can occasionally show low or high signal intensity on T2-weighted images[25].Krukenberg Tumors may show typical characteristics on MRI, such as: bilateral complex masses with hypointense solid components (dense stromal reaction); internal hyperintensity (mucin) on T1 and T2 weighted MR images; strong contrast enhancement is usually seen in the solid component or the wall of the intratumoral cyst.[24-26]

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