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Krukenberg Tumour with Skin Metastasis: A Rare Calamitous Disease

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ABSTRACT

Krukenberg tumour with cutaneous metastasis is a rare entity signifying a disseminated disease with poor prognosis. The prevalence of Krukenberg tumour differs among populations. In regions with a high prevalence of gastric carcinoma, such as Japan, these tumours comprise up to 17.8% of all ovarian carcinomas. We report a case of 42-year-old female patient who presented with lower abdomen pain and nodular lesions over the skin after undergoing total gastrectomy for gastric carcinoma eighteen months back. Through a review of relevant literature and case studies, this paper elucidates the clinical significance of cutaneous metastasis in Krukenberg tumors and highlights the importance of multidisciplinary approaches in managing this condition effectively.

Keywords: *poor prognosis, signet ring adenocarcinoma, gastric adenocarcinoma, skin metastasis, krukenberg tumour*

INTRODUCTION

Krukenberg tumours are defined as a type of metastatic ovarian cancer with mucin-producing signet ring cells that are found infiltrating the ovarian stroma. These tumours are uncommon and comprise 1-2% of all ovarian tumours. Asian countries such as Japan, Korea, and China report a higher prevalence of these tumours accounting up to 20% of all ovarian cancers.[1]

In majority of Krukenberg tumour cases (70%) stomach is the primary site. The next commonest primary sites include carcinomas of colon, appendix, and breast (mainly invasive lobular carcinoma).[2] Bilateral ovaries are involved in around 80% cases of Krukenberg tumours. Owing to the rich blood supply of functioning ovaries making them susceptible to metastatic disease, these tumours are more frequent in younger women.[3]

Cutaneous metastasis is seen in about 0.7-9% of patients with internal malignancies. Breast, followed by the lung and colon are the most common sites of primary. Metastasis to skin from Gastric Cancers is very rare with an incidence of approximately 0.8-1.0%. The presence of cutaneous metastasis suggests a systemic spread of disease with poor prognosis and a mean survival of 3-18 months.[4]

Here we describe a female patient who developed concurrent Krukenberg Tumour and skin metastasis after undergoing gastrectomy for gastric carcinoma eighteen months back. While metastasis is a common feature of Krukenberg tumors, cutaneous involvement remains relatively rare yet clinically significant. This paper aims to delve into the intricacies of Krukenberg tumor with cutaneous metastasis, shedding light on its clinical implications and poor outcome.

CASE REPORT

A 42-year-old female presented to the gynaecology outpatient department with the history of pain lower abdomen for the past three months. The patient gave history of undergoing total gastrectomy with esophago-jejunal anastomosis in view of gastric carcinoma eighteen months ago. Following this the patient received eight cycles of chemotherapy, the last cycle being taken one year back. Presently, the general physical examination of the patient was unremarkable. Tumour marker levels (CA-125, CEA & CA 19-9) of the patient were within normal range. On Computed Tomography, left ovary is markedly enlarged with poorly enhancing parenchyma (Figure1). No discrete enhancing lesion was visualised. Radiological impression of Subacute/Chronic Ovarian Ischaemic changes was given.

Patient then underwent laparotomy followed by Transabdominal Hysterectomy with Bilateral Salpingo- oophorectomy & peritoneal biopsy under combined spinal anaesthesia.

We received surgical specimens consisting of uterus, cervix, bilateral fallopian tubes, bilateral ovaries along with peritoneal biopsy. Gross examination revealed markedly enlarged left ovary. Cut section was predominantly solid, grey white to grey brown with few cystic spaces containing mucinous material (Figure2). Rest of the specimen was grossly unremarkable.

On Microscopic examination, left ovarian parenchyma was infiltrated by abundant signet ring cells with intra-cytoplasmic mucin (Figure 3-4). The mucin was highlighted by magenta colour on Periodic Acid Schiff stain (Figure 5). Lympho-vascular Invasion (LVI) was seen (Figure 6). The right ovary though grossly normal was also infiltrated by signet ring cells. In addition, the parenchyma of both ovaries revealed myxoid degeneration. Histopathological diagnosis of Krukenberg Tumour of Bilateral ovaries, consistent with patients known history of gastric primary was given.

On postoperative day seven, two raised nodular lesions on the skin, one each over the abdomen and right axilla were noted (Figure 7). The patient was then referred to Dermatology department. Biopsy from the lesions was taken and sent for histopathological examination. Microscopic examination of skin biopsy revealed presence of signet ring cells in the dermis. A diagnosis of cutaneous metastasis of Signet ring Adenocarcinoma was given.

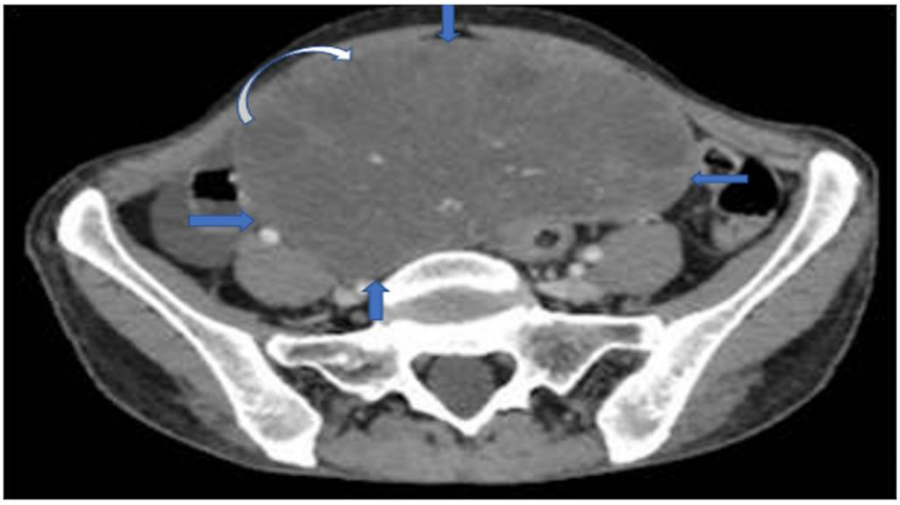

Figure 1: Enlarged Left Ovary (Blue arrows) with peripheralisation of follicles (white arrow). Note poorly enhancing edematous stroma with arborising vessels. No discrete enhancing lesion distorting ovarian architecture is visualized.

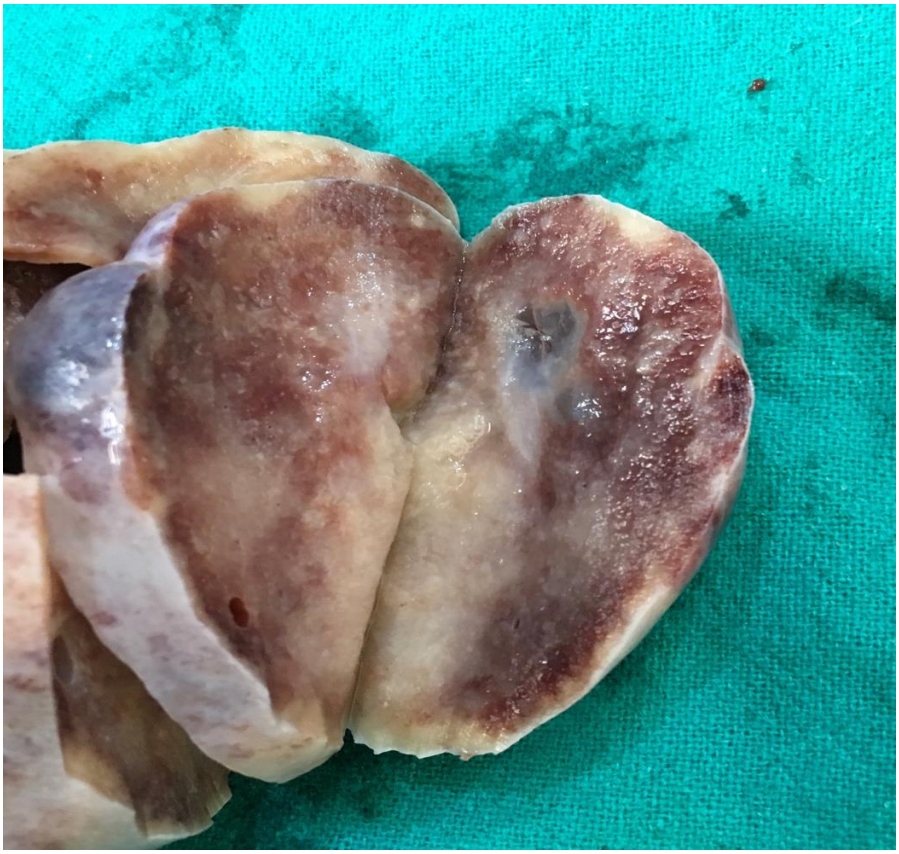

Figure 2: Cut section of left ovary show grey white to grey brown areas with few cystic spaces containing mucinous material.

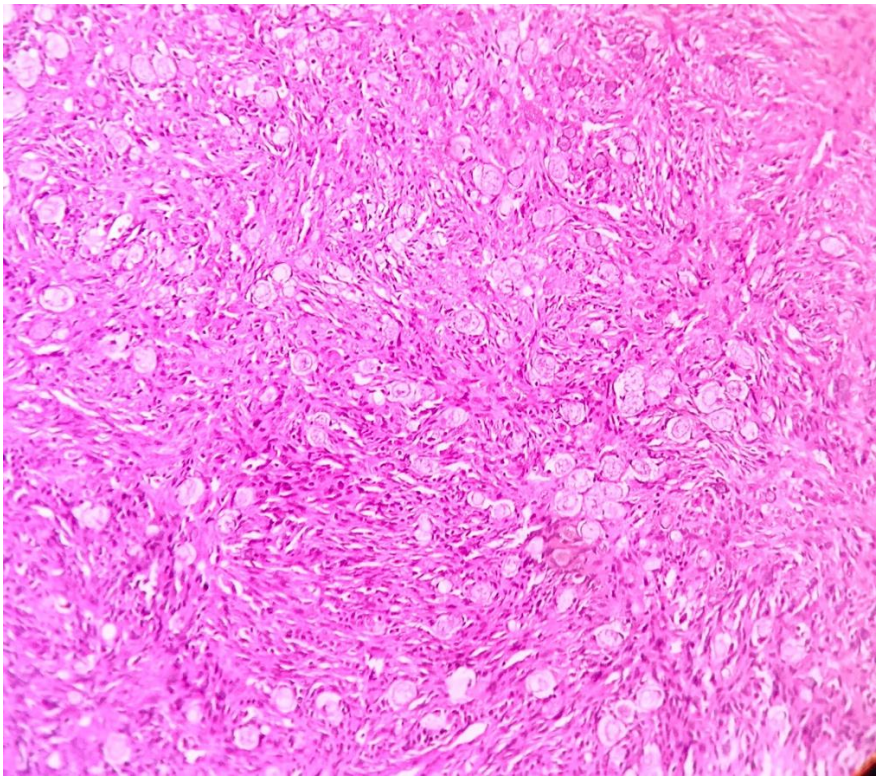

Figure 3– Ovarian parenchyma infiltrated by abundant signet ring cells containing mucin. H&E 10X

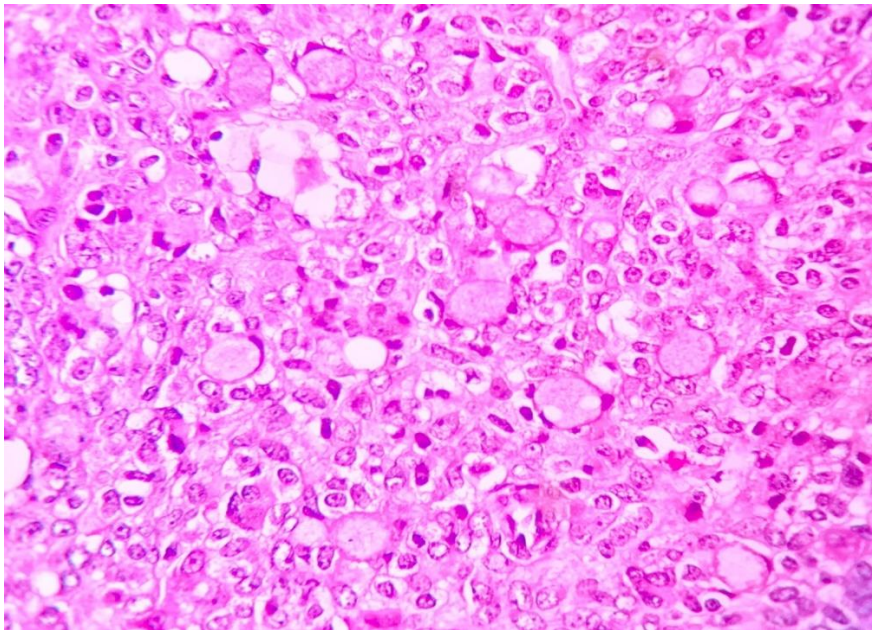

Figure 4: Signet ring cells containing intracytoplasmic mucin. H&E 40X

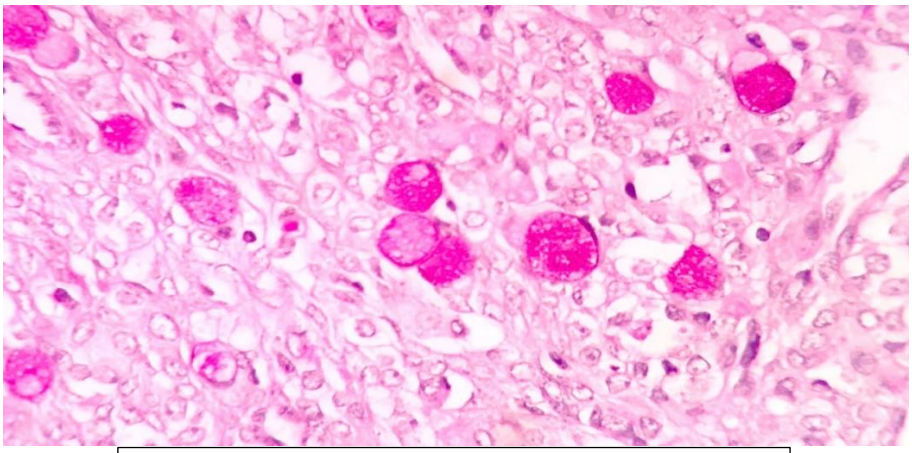

Figure 5: PAS stain highlighting the intracytoplasmic mucin. 40X

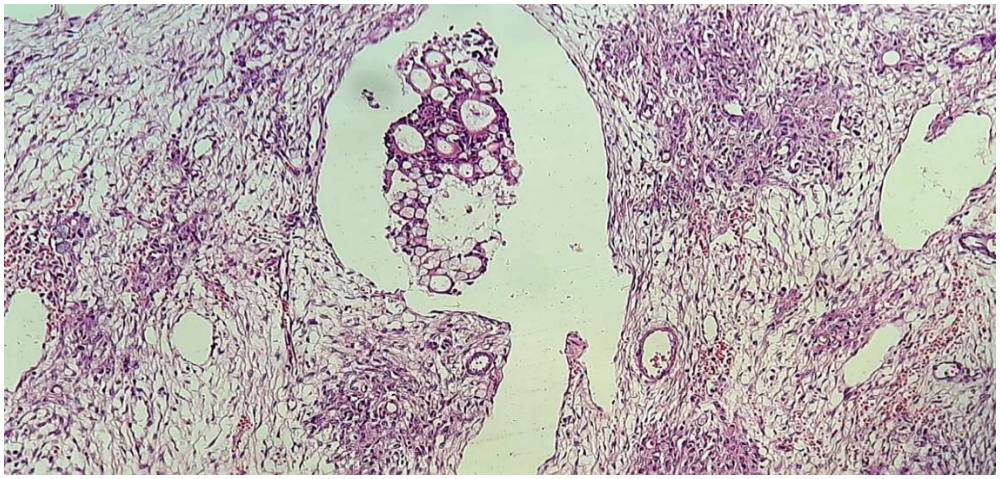

Figure 6: Lymphovascular Invasion (LVI).

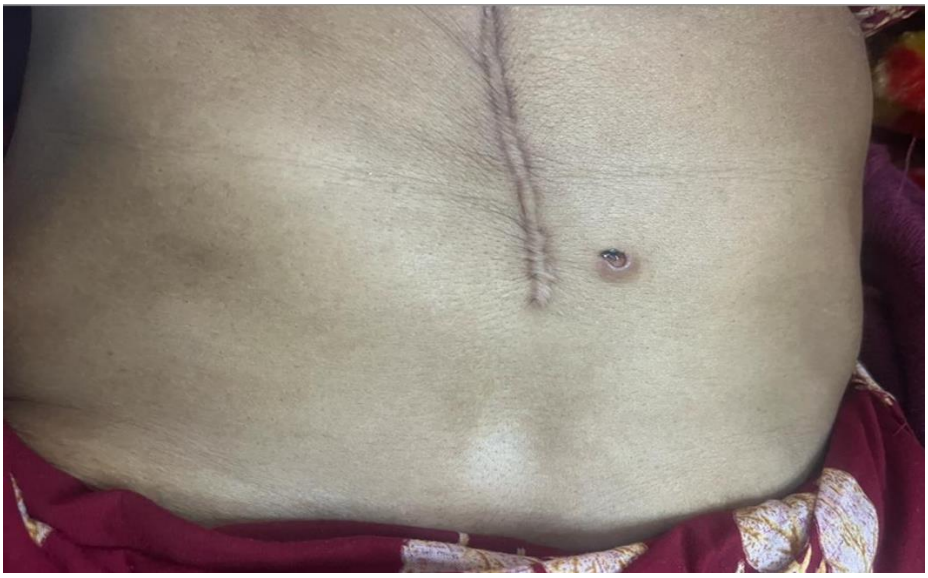

Figure 7: Raised hyperpigmented nodule over the abdominal skin parallel to previous laparotomy scar.

DISCUSSION

It is now widely acknowledged that adenocarcinomas exhibiting signet ring cell morphology from various organs demonstrate a higher propensity to metastasize to the ovaries compared to adenocarcinomas of other histological types. Signet ring cell type gastric adenocarcinoma is frequently encountered in clinical practice. The prevalence of Krukenberg tumors correlates with the incidence of gastric carcinoma within specific populations. For instance, in countries such as Japan, characterized by a high frequency of gastric carcinoma, Krukenberg tumors constitute the majority (17.8%) of all ovarian cancers. These tumors predominantly occur in the fifth decade of life, with a mean age of 45 years, partly due to the elevated occurrence of gastric signet ring cell carcinomas in younger females. Previous studies have indicated a grim prognosis in cases where the primary tumor is identified subsequent to the detection of ovarian metastasis, and the prognosis deteriorates further if the primary tumor remains undisclosed.[2]

While ovarian Krukenberg tumors primarily originate from gastric cancer, according to some sources, there is literature suggesting the reverse, where the colon serves as the primary site followed by the gastrointestinal tract.[3]

A systematic review conducted in 2021, examining 3025 patients with Krukenberg tumors, revealed that the gastrointestinal (GI) tract was the most frequent primary site, accounting for 42.5%, followed by the colon at 26.1%. Additionally, Krukenberg tumors can originate from other common primary carcinomas, including those affecting the breast, appendix, endometrium, uterus, cervix, pancreas, small intestine, gallbladder, and biliary tract.[1]

Cutaneous metastasis, although uncommon, represents a rare presentation of visceral malignancies. Typically, it emerges late in the disease's progression, yet it can also manifest as an initial symptom of underlying tumors.[5] It is most commonly observed in individuals aged between 50 and 70 years. On average, skin metastasis occurs around 33 months after the initial diagnosis of primary malignancy. Following diagnosis, the average survival time is approximately 7.5 months, with roughly 50% of patients succumbing within the first 6 months. The spread of tumor cells to the skin primarily occurs through lymphatic and/or hematogenous routes, although direct extension to the skin or accidental

implantation in surgical wounds and tracts has also been reported.[6]

The mechanisms underlying the propensity of certain internal malignancies to metastasize to the skin remain poorly understood. It's suggested that the skin might offer a conducive environment for the colonization and survival of select types of cancer cells. Furthermore, particular factors likely play a pivotal role in facilitating the migration of metastatic cells to the skin. Recent research has highlighted the involvement of chemokines and their receptors in both tumorigenesis and metastasis. [7]

In gastric cancer, metastases commonly occur in the liver, regional lymph nodes, and peritoneal cavity, while skin involvement is less frequently observed. The abdominal wall is the most commonly reported site for skin metastasis, often referred to as the Sister Mary Joseph nodule. Other less frequently reported sites include the scalp, eyelids, fingertips, neck, and trunk.[8] Only 6% of all skin metastases in males and 1% in females are from gastric origin. [9]

Clinicians should maintain a high index of suspicion for cutaneous metastasis in patients with a history of ovarian carcinoma, especially in the presence of characteristic clinical findings such as umbilical nodules (Sister Mary Joseph's nodule).[10]

Diagnosis of cutaneous metastasis in Krukenberg tumors relies on a combination of clinical evaluation, imaging studies, and histopathological examination. Special stains such as mucicarmine, alcian blue and periodic acid Schiff are very useful tools for the demonstration of intracytoplasmic mucin. Immunohistochemistry (IHC) markers such as CDX2, CK7, CK20, SATB2, carcinoembryonic antigen (CEA), and epithelial membrane antigen (EMA) can be utilised in cases of occult primary.

Prognosis in Krukenberg tumors with cutaneous metastasis remains poor, with a median survival rate ranging from months to a few years. Factors influencing prognosis include the extent of metastatic spread, response to treatment, and underlying histological subtype.

CONCLUSION

In conclusion, Krukenberg tumor with cutaneous metastasis poses diagnostic and therapeutic challenges, necessitating a comprehensive understanding of its pathogenesis, clinical features, and management strategies. Further research is warranted to elucidate the molecular mechanisms driving cutaneous metastasis and to develop targeted therapies aimed at improving outcomes in this subset of patients.

Declaration by Authors

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