



KRUKENBERG TUMOR OF OVARY WITH EXTENSIVE STROMAL PROLIFERATION: A DIAGNOSTIC DILEMMA

Pathology

Dr Kirti Panwar

Senior Resident, Department of Pathology Vardhaman Mahavir Medical College & Safdarjung Hospital Delhi

Dr Charanjeet Ahluwalia*

Professor, Department of Pathology Vardhaman Mahavir Medical College & Safdarjung Hospital Delhi *Corresponding Author

ABSTRACT

Krukenberg Tumor is the malignancy of ovaries which is metastatic from a primary site. The primary carcinoma is usually in the stomach. Signet ring carcinoma of the breast, gall bladder and colon can also metastasize to ovaries. In 80% of cases, it presents as bilateral ovarian carcinoma. We report a case of 25 year old female with bilateral ovarian masses diagnosed as Krukenberg tumor. A detailed clinical work up and with pathological examination helped to locate the site of primary tumor.

KEYWORDS

Krukenberg tumor, metastasis, immunohistochemistry

INTRODUCTION

Krukenberg tumor is an uncommon ovarian tumor, accounting for 1% to 2% of all ovarian tumors. The primary carcinoma is usually in the stomach, but signet ring carcinomas of the breast, gall bladder and colon can also metastasize to bilateral ovaries.¹ In 80% of cases it presents as bilateral ovarian carcinoma.² Friedrich Krukenberg (German Gynaecologist and Pathologist) in 1896 believed it to be a primary neoplasm of ovary. After six years the ovarian neoplasm was termed as "Krukenberg tumor" and its metastatic nature was established.³ It generally occurs in females of less than 40 years of age.⁴ The tumor generally metastasizes by lymphatic route.⁵ We report a case of a 25 year old female with bilateral ovarian mass diagnosed histologically as Krukenberg tumor of the ovary with primary in the stomach

CASE REPORT

A 25 year old female P₁L₀A₂ presented to gynecology department with amenorrhea since 1 year. The patient complained of pelvic pain and abdominal discomfort. She gave past history of a single episode of hemoptysis an year back. There was history of loss of appetite. Bowel and bladder habits were normal. Family history was insignificant. General physical examination was within normal limits. Per abdomen examination revealed a 15X10 cm firm non tender mass in the lower abdomen. On per vaginum examination a firm non tender freely mobile mass measuring 15 X 14 cm was present in right and anterior fornix. Cervix was deviated to left. Mild tenderness was present in right fornix. However left fornix was free.

Laboratory results revealed elevated carcino embryonic antigen (CEA) levels of 6.2ng/ml. Serum cancer antigen 125 (CA 125) and cancer antigen 19-9 levels were within normal range being 5.5U/ml and 5.6 U/ml respectively. Follicle Stimulating Hormone level was also within normal range being 2.2mIU/ml.

Abdominal ultrasonography was done thrice with variable impression each time. Initially USG abdomen showed a large midline mass in pelvis anterior to uterus measuring 9.1X6.5cm. Internal echoes were seen within mass. Another small mass was seen adjacent to the mass measuring 4.5X4.1 cm. Increased vascularity of both masses was seen. Ovaries were not seen separately. Free fluid was present and differential diagnosis suggested were endometriosis and inflammatory mass.

An ascitic tap was done. Cytological examination of ascitic fluid revealed signet ring cells lying singly and in clusters. (Figure 1)

She underwent staging laparotomy with right salpingo-oophorectomy with left ovarian cystectomy with infracolicomentectomy. Intraoperative findings revealed bilateral ovarian tumors and 1500 ml of straw coloured peritoneal fluid drained out.

We received right and left ovarian mass. The right ovarian mass measured 18X11X8 cm and the left ovarian mass measured 10 X 6 X 4 cm. External surface of both the ovaries was bosselated in appearance. On cut the bilateral ovarian mass were firm grey brown in appearance

without any cystic and haemorrhagic areas. (Figure 2,3,4,5)

Haematoxylin and eosin stained slides of right and left ovarian mass were prepared. Sections examined showed extensive stromal proliferation with stromal cells arranged in intersecting fascicles showing mild to moderate atypia and increased mitosis. (Figure 6 and Figure 7) Seen infiltrating in between the stromal cells were atypical epithelial cells arranged in nests, cords and were lying singly. These cells showed moderate to abundant amount of eosinophilic to vacuolated cytoplasm, vesicular nuclei with coarse chromatin and marked pleomorphism. At places these cells were forming gland like structure. Many atypical mitotic figures were seen. On close examination, signet ring cells with cytoplasmic mucin and peripherally pushed nuclei were also seen infiltrating the stroma singly and in clusters. (Figure 8 and Figure 9)

An IHC panel of EMA, MUC-1, CA-125, Vimentin, Inhibin and Calretinin was done. On immunohistochemistry epithelial cells were positive for EMA (Figure 10) and MUC1 (Figure 11). Stromal cells were positive for Vimentin and negative for Inhibin and Calretinin. Based on the above morphology a diagnosis of Signet ring cell adenocarcinoma, bilateral ovaries with possibility of Krukenberg tumor was suggested.

A secondary IHC panel including CK7 and CK20 was done so as to look for primary site. Tumor cells were positive for both CK 20 and CK 7. (Figure 12 and 13) Therefore a possibility of metastatic tumor from GIT was suggested. The patient was further investigated for locating the primary tumor. An upper GI endoscopy was performed which showed a growth in stomach. A biopsy specimen was sent from the growth in stomach which showed signet ring cell adenocarcinoma and hence confirmed the primary site as stomach. (Figure 14 and 15)

DISCUSSION

Krukenberg tumor is an uncommon ovarian tumor, accounting for 1% to 2% of all ovarian tumors. The primary carcinoma is usually in the stomach, but signet ring carcinomas of the breast, gall bladder and colon can give rise to metastasis of this type.¹ In 80% of cases it presents as bilateral ovarian carcinoma.² Friedrich Krukenberg (German Gynaecologist and Pathologist) in 1896 believed it to be a primary neoplasm of ovary. After six years the ovarian neoplasm was termed as "Krukenberg tumor" and its metastatic nature was established.³ It generally occurs in females of less than 40 years of age.⁴ The tumor is known to metastasize by lymphatic route and are diagnosed histologically.⁵

The patients complain of abdominal pain, palpable mass, irregular menstrual cycles, amenorrhoea, loss of appetite and weight loss. Our patient was a 25 years old female with history of amenorrhoea, pelvic pain and abdominal discomfort. Ascites is seen in half of the cases and was present in our case also. Few patients may present with virilization, which occurs when the ovarian stroma becomes luteinized, thereby producing estrogen and androgen hormones.

Mostly the imaging features are not specific as in our case, consisting of majorly solid components or cystic and solid areas. Krukenberg tumors can demonstrate few distinctive findings on MRI like bilateral complex masses with hypo-intense solid components (dense stromal reaction)⁶⁻⁷ and internal hyperintensity (mucin) on T1 and T2 weighted MR images.⁶

The gross pathological features of bilateral (14 X 9 X 6 cm) and asymmetrically enlarged ovaries with a bosselated surface is classical feature of Krukenberg tumor. The capsular surface is smooth. In our case, both the ovaries were markedly enlarged and solid with no areas of cystic change. The microscopic features show both stromal and epithelial components. Mucinladen signet ring cells with eccentric hyperchromatic nuclei seen in cords, nests, acini or tubules infiltrate the stromal component.^{8,9} Sometimes the stromal proliferation is extensive and obscures the signet ring pattern which leads to difficulty in diagnosis and can be confused with possibility of stromal tumor as it was in our case.¹⁰

Immunohistochemistry plays an important role in differentiating primary ovarian tumors from metastatic tumors. Immunostain profile of CK 20 and MUC1 positive goes in favour of metastatic gastrointestinal carcinoma. Tumors showing positivity for CK 7/20 includes stomach carcinoma, small intestine adenocarcinoma, cholangiocarcinoma, pancreatic adenocarcinoma.^{11,12} Therefore a possibility of metastasis from gastrointestinal tract was suggested in our case and endoscopic biopsy of stomach revealed the primary site.

The metastasis to the ovaries is mainly through lymphatic spread as the gastrointestinal tract mucosa and submucosa have lymphatic plexus and lie close to retroperitoneal lymph nodes.¹³

CONCLUSION

Krukenberg tumors are rare metastatic bilateral ovarian tumors presenting with vague symptoms. Microscopically these tumors may rarely show extensive stromal proliferation which may obscure the signet ring cells, giving false impression of a stromal tumor. Therefore a careful look for signet ring cells is warranted as in our case. Histological features along with immunohistochemistry help to clinch the diagnosis. Prognosis of Krukenberg tumor is poor. But early diagnosis and identifying the primary site can prolong the survival.

CONFLICTS OF INTEREST

There are no conflicts of interest.

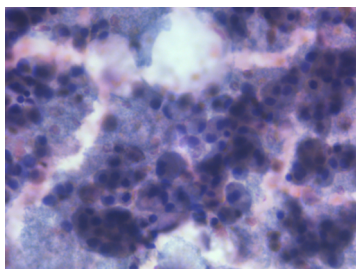


Figure 1 40X Ascentic fluid smear shows clusters of mesothelial cells along with a few signet ring type of cells having abundant cytoplasm and eccentrically placed nuclei.



Figure 2 : Right ovarian mass shows a bosselated external surface

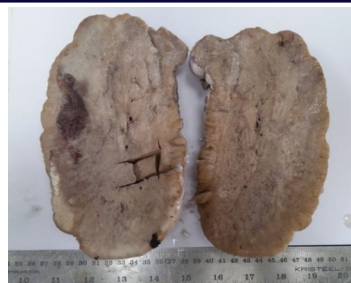


Figure 3 Right Ovarian mass :Cut section shows homogenous firm grey brown area.



Figure 4 Left Ovarian Mass shows a bosselated external surface



Figure 5 :Left ovarian mass on cut section shows homogenous firm grey brown area

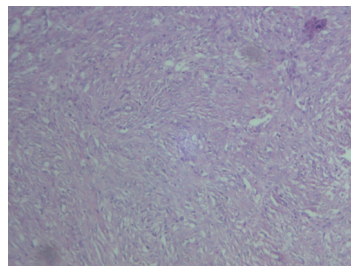


Figure 6 10 X Right Ovarian Mass. Section shows extensive stromal proliferation along with stromal cells arranged in intersecting fascicles showing mild to moderate atypia and mitosis

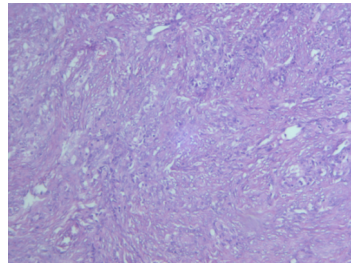


Figure 7 10 X Left Ovarian Mass. Section shows dense stromal proliferation along with atypical epithelial cells arranged in nests,

cords and lying singly.

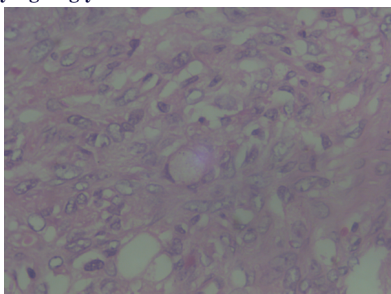


Figure 8 : 40X Right ovarian mass. The tumor cells show moderate to abundant amount of eosinophilic to vacuolated cytoplasm, vesicular nuclei with coarse chromatin and marked pleomorphism .Also seen are signet ring cells with cytoplasmic mucin and peripherally pushed nuclei

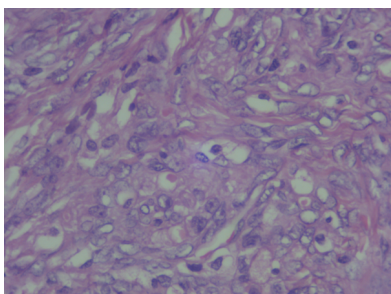


Figure 9.40X Left Ovarian Mass . The tumor cells show moderate to abundant amount of eosinophilic to vacuolated cytoplasm, vesicular nuclei with coarse chromatin and marked pleomorphism .Also seen are signet ring cells with cytoplasmic mucin and peripherally pushed nuclei

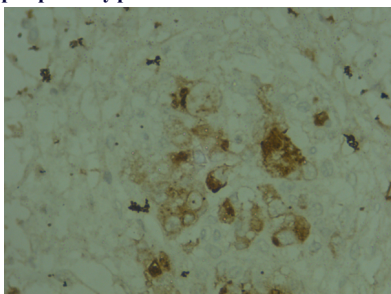


Figure 10 . 40 X EMA Positive

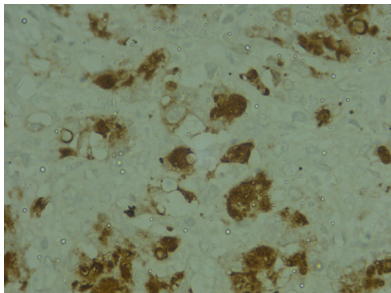


Figure 11 : MUC1 positive

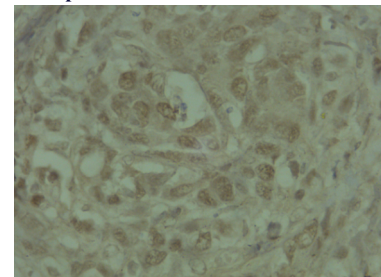


Figure 12. 40 X : CK7 Positive

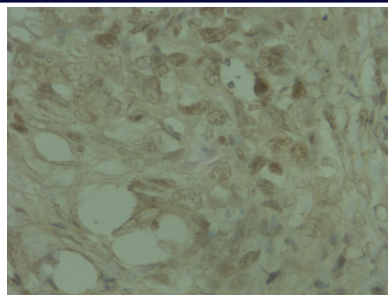


Figure 13. CK 20 Positive

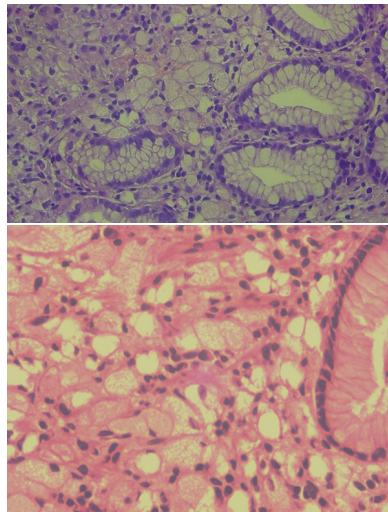


Figure 14 and Figure 15. 40 X Stomach biopsy showing Signet Ring Adenocarcinoma

REFERENCES

1. Christopher D.M. Fletcher. Diagnostic Histopathology Of Tumors. Fourth Edition. Philadelphia. Elsevier Saunders
2. Osama M. Al-Agha, MD and Anthony D. Nicastrì, MD. From the Department of Pathology, State University of New York, Brooklyn Reprints: Osama M. Al-Agha, MD, Department of Pathology, State University of New York Downstat Medical Center, 450 Clarkson Ave, Box 25, Brooklyn, NY 11203 (osama.al-aghah@downstate.edu or osamaalaghah@yahoo.com)
3. Asian J Androl. 2015 Jan-Feb; 17(1): 171–172. Right cryptorchid testicular metastasis from descending colon carcinoma: a case report of “Krukenberg tumor” in male Qi Xu Xiao-Lei Li, Ya-Wei Yu, Lai-Rong Dong, Jian-Guo Shen and Lin-Bo Wang
4. Young RH. From Krukenberg to today: The ever present problems posed by metastatic tumors in the ovary: Part I. Historical perspective, general principles, mucinostom tumors including the Krukenberg tumor. Adv Anat Pathol 2006; 13:205-27.
5. Fujimoto D, Hirano Y, Goi T, Yamaguchi A. Sigmoid colonic metastasis by lymphatic spread occurring with unilateral Krukenberg tumor considered to be caused by stage IA early gastric cancer: A case report. Oncol Lett. 2016 Jan; 11(1):668-672.
6. Jung SE, Lee JM, Rha SE et al. CT and MR imaging of ovarian tumors with emphasis on differential diagnosis. Radiographics. 22 (6): 1305-25. doi:10.1148/rg.226025033
7. Ha HK, Baek SY, Kim SH et al. Krukenberg's tumor of the ovary: MR imaging features. AJR Am J Roentgenol. 1995; 164 (6): 1435-9. AJR Am J Roentgenol (abstract) - Pubmed citation
8. Kiyokawa T, Young RH, Scully RE. Krukenberg tumors of the ovary: A clinicopathologic analysis of 120 cases with emphasis on their variable pathologic manifestations. Am J Surg Pathol 2006; 30:277-99.
9. Shiono S, Saito T, Fujii H, Arakawa A, Nakamura T, Yao T. A case of Krukenberg carcinoma metastasized from colon cancer resembling mucinous cystadenocarcinoma of the ovary. Int J Clin Exp Pathol 2014; 7:394-401.
10. Osama M, Al-aghah and Anthony D .Nicastrì. An in depth look at Krukenberg tumor: An Overview. Archives of Pathology and Laboratory Medicine: November 2006, Vol 130, No 11, pp1725-1730
11. Ormsby AH et al. The utility of cytokeratin subsets in distinguishing Barrett's related esophageal adenocarcinoma from gastric adenocarcinoma. Histopathology 2001; 38:307-311
12. Kende, A.I, Carr et al. Expression of cytokeratin 7 and 20 in carcinomas of gastrointestinal tract. Histopathology 2003; 42:137-40
13. Das S, Sahu D, Wani M, Reddy PK. A curious discourse of Krukenberg tumor: A case report. J Gastrointest Oncol 2014; 5:E117-20.