

Situs Invertus Totalis in a Patient with Bilateral Papillary Serous Cystadenocarcinoma Ovary: Rare Association with Review of Literature

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ABSTRACT

Situs Invertus Totalis (SIT) is a rare congenital anomaly inherited as autosomal recessive disorder. It is characterized by transposition of thoracic and abdominal viscera including dextrocardia. It occurs in 1:8,000 to 1:20,000 of general population. The patient usually remains asymptomatic with normal life expectancy, unless a gastrointestinal or a cardiac anomaly is present.

35 years female resident of Haryana state (India), presented with pain, lump abdomen and secondary amenorrhoea. USG revealed bilateral ovarian mass. On MRI, Situs Invertus Totalis was incidentally discovered with bilateral ovarian mass and ascites. USG guided FNAC was done for bilateral ovarian mass and, it was diagnosed as bilateral ovarian carcinoma (papillary type). Later Total Abdominal Hysterectomy with bilateral salpingo-oophorectomy was done. Diagnosis of papillary serous cystadenocarcinoma was confirmed by histomorphology and immunohistochemistry. Here, we report a case of bilateral papillary serous cystadenocarcinoma of ovary in an incidentally discovered case of Situs Invertus Totalis with review of literature. Although SIT is not considered a premalignant condition

widely but possibility of malignant lesion and its correlation is yet to be ruled out. SIT cases requires a great care due to abnormal anatomy. Further studies on genetics and molecular biology are needed to explore and establish the relation.

Keywords: Situs Solitus, Situs Invertus Totalis (SIT), Papillary Serous Cystadenocarcinoma Ovaries.


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INTRODUCTION

Situs Solitus means normal placement of thoracic and abdominal visceral organs. While, Situs invertus is a condition in which the location of organ is reversed. Situs ambiguous is visceral malposition along with dysmorphism associated with intermediate atrial arrangement. Situs Invertus Totalis is a condition with transposition of thoracic and abdominal viscera along with Dextrocardia.¹ Its incidence accounts for 1:8000 to 1:25000 of normal population.^{2,3}

20-25% of SIT cases coexist with Kartagener's syndrome (Immobility of bronchial cilia, chronic sinusitis, bronchiectasis and male infertility). It is usually associated with cardiac, vascular, renal and intestinal defects.⁴⁻⁶

Incidence of cardiac anomaly in association of SIT documented is 3-5% and 80% of these patients have a right sided aortic arch.^{7,8} Other vascular anomalies are variation of celiac trunk and superior mesenteric artery. Other involvements can be of the gastrointestinal tract include biliary tree atresia, duodenal atresia,

preduodenal portal vein, colonic aganglionosis, malrotation of the intestine, polysplenia/asplenia, annular pancreas, diaphragmatic hernia etc.⁹

On reviewing the literature, rare case reports exist where association of ovarian malignancy with SIT has been reported. One case was reported with involvement of ovaries by embryonal cell carcinoma and other with evidence of mucinous cystadenoma in association with SIT.

SIT was first described by Fabrizio in 1600. The famous patients representing SIT was French Queen Maria of Medici (1573-1642). The association of SIT and neoplasia is a rare coincidence; only sporadic cases have been reported. The first case was published by Maekawa in 1927; it was an autopsy case of gastric carcinoma in a 43-year-old man with SIT.¹⁰⁻¹²

Surgical procedures are considered more difficult in patients with situs invertus than other patients because of different anatomic position of organs, especially in laparoscopic surgery.

CASE PRESENTATION

A 35 years old female resident of Haryana state (India), presented in SMS Medical College & Hospital, Jaipur with complains of pain, lump abdomen and secondary amenorrhoea. A routine USG abdomen was done, which revealed bilateral ovarian mass with ascites. For proper evaluation of ovarian mass and any other metastatic/primary lesion, a MRI abdomen and whole pelvis was done. Finding suggested liver on left and spleen on right suggestive of Situs Invertus. Gall bladder seen on left and appeared normal. Appendix was seen in left iliac fossa. Free fluid in peritoneal cavity and both ovaries showed predominantly solid mass with cystic component measuring approximately 62 X 68 mm on right side and 83 X 87 mm on left side. Chest X ray was done which incidentally showed dextrocardia (Fig.1) and Hence, Situs Invertus Totalis was diagnosed in the case with associated ovarian mass in both ovaries. On MRI, Situs Invertus Totalis was incidentally discovered with bilateral ovarian mass and ascites. (Fig.2,3)

Ultrasonography Guided FNAC of B/L ovarian mass, was done. Smears were prepared as per standard staining protocol for cytological examination. Smears were cellular comprising of clusters, sheets and papiloid arrangement of malignant epithelial cells having discernable eosinophilic cytoplasm. Nuclei had high N:C ratio and pleomorphism. At places nuclei were lobated and multilobated with focal giant cell formation. Chromatin was clumped and intranuclear inclusions were seen focally.

Cytomorphology favoured bilateral ovarian carcinoma papillary type (Fig.4,5). Later, Total Abdominal Hysterectomy with bilateral salphingo-oophorectomy was done.

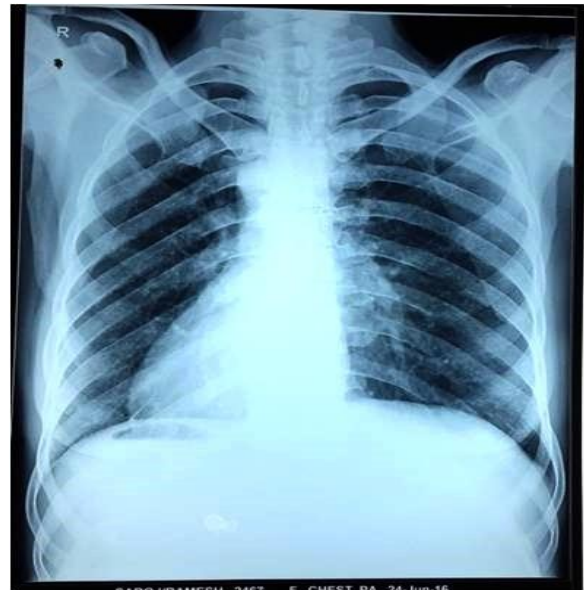


Fig 1: Chest X-Ray – Dextrocardia with fundic shadow on left side.

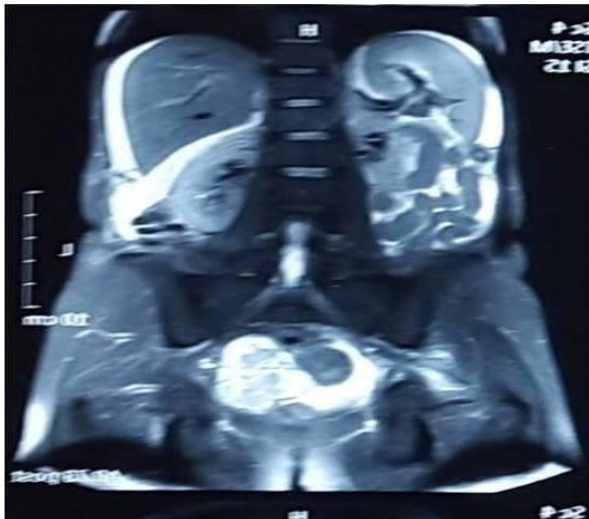


Fig 2: MRI Abdomen and Pelvis – Liver on left and spleen on right . Also, Left kidney lower than right.



Fig 3: MRI Bilateral ovarian mass.

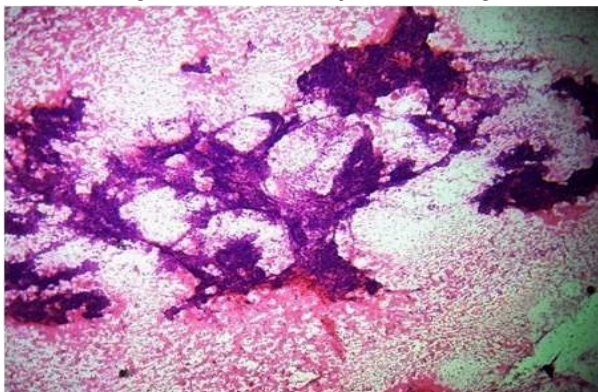


Fig 4: USG Guided FNAC Ovaries– Papillary and syncytial aggregates of columnar cells, at places attempting to form acini - (H & E staining) X 40.

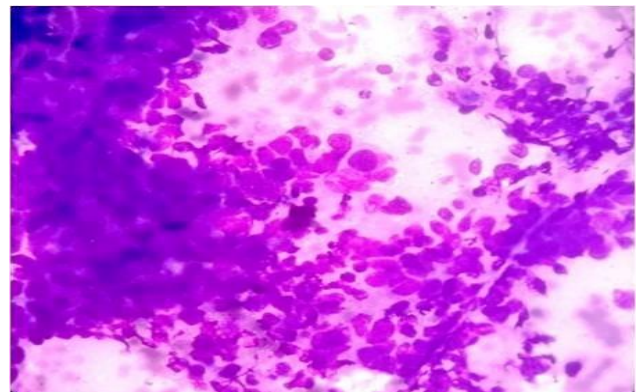


Fig 5: US Guided FNAC Ovaries– Papillary aggregates, at places attempt to form acini, Columnar cells with high N:C ratio, nuclear pleomorphism, prominent nucleoli - MGG X 400.

PATHOLOGY

Gross

On gross examination we found uterus with attached bilateral adnexa. The size of the uterus was normal, 7.2 cm × 4.1 cm × 2.5 cm. On cut-section Uterocervical canal was patent with normal cervix. Endometrial and myometrial thickness was normal. Fallopian tubes were patent with attached ovarian mass both sides. Ovaries measured 6.9 X 7.0 cm on right side and 8.9 X 6.6 cm on left side. External surface of both ovaries showed lobulations. On cut-section mass was partially cystic with focal solid greyish white homogenous areas. Multiple sections were processed from different areas using standard grossing protocol and section examined.

Microscopically

On examining Hematoxylin – Eosin stained sections, histomorphology revealed branching papillary fronds, slit like fenestrations, attempt to form glands like structures with stratification of cells seen at places. Moderate to marked nuclear atypia and pleomorphism. Prominent nucleoli, frequent mitosis. Stromal invasion and lymphovascular invasion was seen. Psammoma bodies were also appreciated focally.(Fig.6,7)

Histology and Immunohistochemistry

Immunohistochemical (IHC) examination was performed. On IHC staining tumor cells were positive for WT-1 and CA-125.(Fig.8,9)

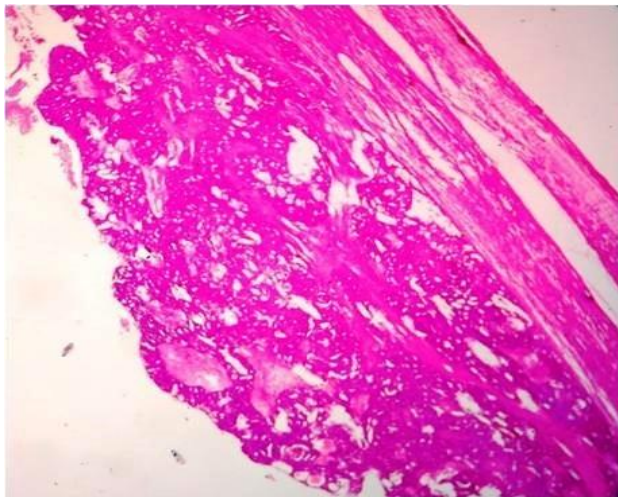


Fig 6: Cyst lining with branching papillary fronds and slit like fenestrations attempt to form glands – HPE- (H&E stained section-X 40).

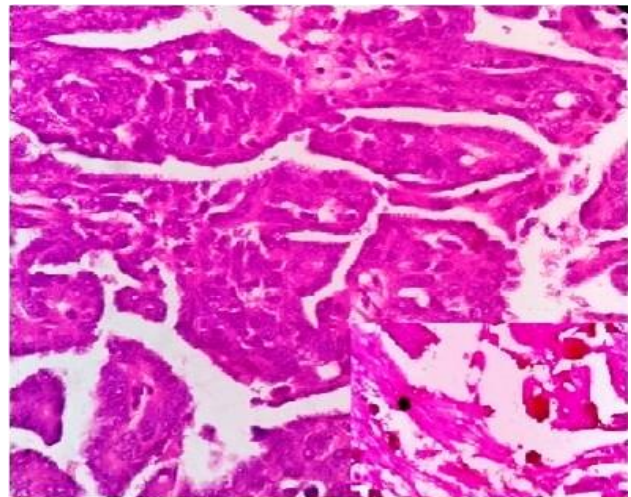


Fig 7: Marked pleomorphism, High N: C ratio, Prominent nucleoli, stratification and frequent mitosis – H & E X 400 (Inset: Psammoma Bodies – H& E X 400).



Fig 8: Nuclear positivity of WT1 – IHC WT1 X 400.

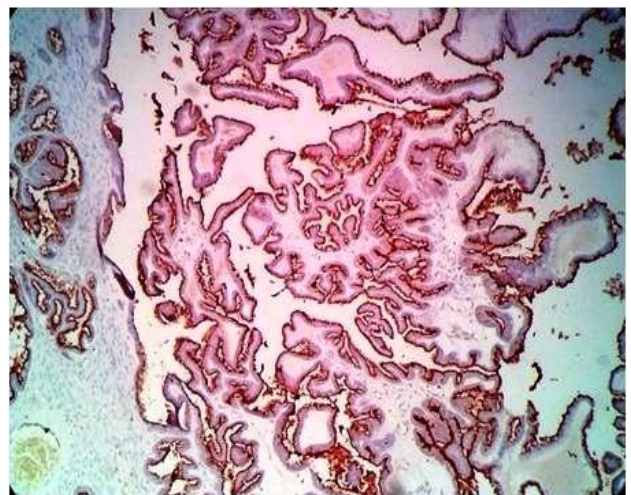


Fig 9: Membranous positivity of CA-125 – IHC CA-125 X 40.

RESULTS

Bilateral papillary serous cystadenocarcinoma was diagnosed on the basis of above finding. The patient received surgical resection followed by chemotherapy. She is now disease free after 6 months of post-surgical follow up.

DISCUSSION WITH REVIEW OF LITERATURE

SIT is a rare autosomal recessive disorder; it is probably associated with X chromosome defect and its possible familial occurrence with varying expression.¹³⁻¹⁵ Incidence given by majority of authors in their study is 1:8000 to 1:20000 of births.¹⁶⁻¹⁸

Ciliary motility disorder leads to improper extra embryonic fluid flow and false heart tube rotation during embryogenesis, which probably results in SIT. This genetically driven process possibly triggered by some external factors.¹⁹⁻²¹ However, the issue seems even more complicated, as ciliary dyskinesia syndrome without situs inversus, and SIT cases without ciliary dyskinesia has been described.

A correlation between SIT and carcinoma or multiple neoplasms is suspected.^{22,23} Ciliary dyskinesia is observed in intracellular

protein pump KIF3 dysfunction which is involved in proper structure and functioning of cilia. KIF3 dysfunction blocks N-cadherin/beta-catenin system, which is important in cellular adhesion and proliferation control. Adhesion and proliferation play a key role in the development and progression of neoplasms. A hypothesis has been set that KIF3 dysfunction might be common

for SIT and neoplasms.²⁴⁻²⁸ There are many papers describing neoplasms concomitant with SIT, however, the correlation of SIT and neoplasm is not yet widely accepted and demands further clinical and epidemiologic investigations.²⁹⁻³⁰ Situs Invertus Totalis shows frequent association with neoplastic lesions, however not established as premalignant condition. (Table 1)

Table 1: Rare associations with SIT reported in literature

S.No.	Cases in literature reported with SIT	Number of each reported
1.	Left sided acute appendicitis	63
2.	Cholecystitis	26
3.	Lung cancer	21
4.	Gastric cancer	14
5.	Colorectal cancer	14
6.	Bile duct carcinoma	4
7.	Renal Cell Carcinoma	2
8.	Adenocarcinoma transverse colon and Gastrointestinal fistula	1
9.	Embryonal cell carcinoma ovaries	1
10.	PEComa uterus	1
11.	Endometrial carcinoma	1

More frequent incidences of SIT are reported from Japan and Eastern Europe probably could be explained by demographic reasons.³¹⁻³⁵

Upto best of knowledge, bilateral papillary serous cystadenocarcinoma of ovary with situs invertus will be the first case to be reported.

On reviewing the literature, until now there are only 3 cases that have been reported in which SIT involved ovaries. Rao PG et al (1977) reported first case of SIT with cholecystitis and mucinous cystadenoma of ovaries.³⁶ Ibrahim E.M. et al (March 1984) reported second case of embryonal cell carcinoma in SIT patient.³⁷ Third case was reported in October 1984 was Liver metastasis from embryonal carcinoma of ovaries with SIT.³⁸

Left sided acute appendicitis has been reported with SIT. Diagnosis is rather challenging due to altered anatomy and abnormal pain localization. Although viscera are transposed, central nervous system may not share reverse transposition leading to confusing symptoms and signs in the patients. Thus, pain and rebound tenderness is reported to be in right iliac fossa in patients with situs invertus totalis.³⁹⁻⁴⁴ In present case appendix was found on left side. Prophylactic resection was done to avoid further complications.

In Twenty one cases of SIT, association with lung carcinoma was found. First case to be described in 1952. 13 cases came from Japan, 4 from Eastern Europe, 2 from Western Europe, 1 from Australia and USA each.⁴⁵⁻⁵²

Fourteen cases of Gastric malignancy upto now has been reported with SIT.⁵³⁻⁵⁹ Fourteen cases of colorectal cancer and SIT have been reported.⁶⁰⁻⁶⁶

In the setting of SIT, only four cases have been reported of cholangiocarcinoma.⁶⁷⁻⁶⁹ Only two cases of renal cell carcinoma has been reported in SIT patient.

Single case of each endometrial carcinoma and PEComa uterus has been reported with co-existence of situs invertus totalis.

CONCLUSION

We report a rare presentation and association of bilateral papillary serous cystadenocarcinoma ovary with an incidentally diagnosed situs invertus totalis patient and reviewed the all available literature to see the possible reported associations of SIT. The present association is extremely rare and first to be reported, upto best of our knowledge. Till now there is no evidence available to prove that SIT predisposes the development of bilateral papillary serous cystadenocarcinoma ovary. Hence further studies regarding manifestation of SIT and its genetic and molecular associations are needed.

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