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PRIMARY MALIGNANT MIXED MULLERIAN TUMOR OF MESENTRY - A RARE CASE REPORT WITH REVIEW OF LITERATURE

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Abstract : Extragenital malignant mixed mullerian tumors are very rare neoplasms occurring in postmenopausal women from the so called secondary mullerian system. This tumor is composed of both malignant epithelial and mesenchymal components. So far only 49 cases have been identified in English literature1. Here, we present a case of primary malignant mixed mullerian tumor of mesentery in a 64 year old female with a brief literature review.

Keyword: Carcinosarcoma, Extragenital malignant mixed mullerian tumor, Mesenteric MMMT.

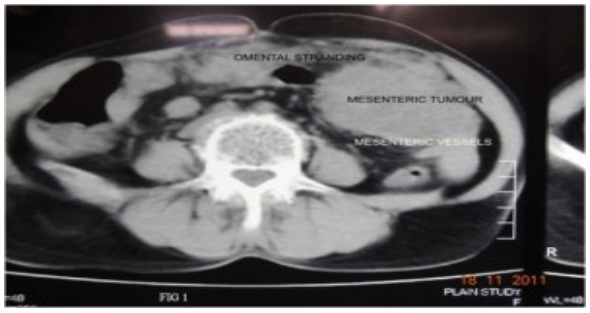
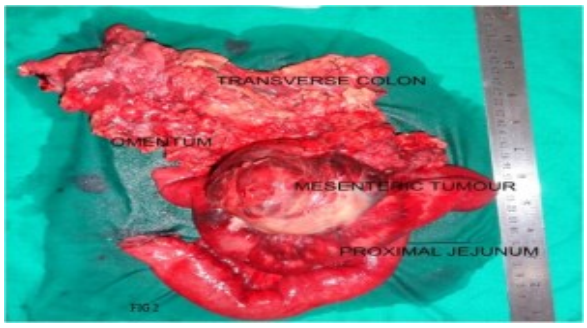


fig 1



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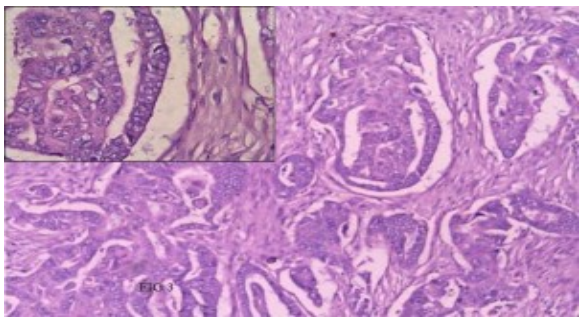

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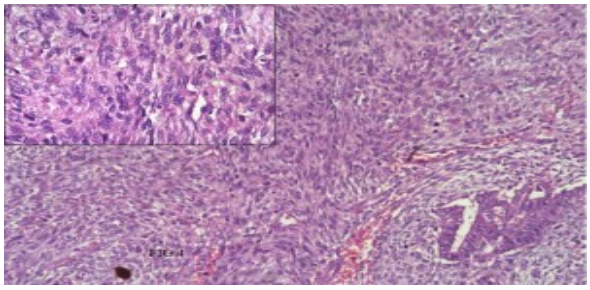

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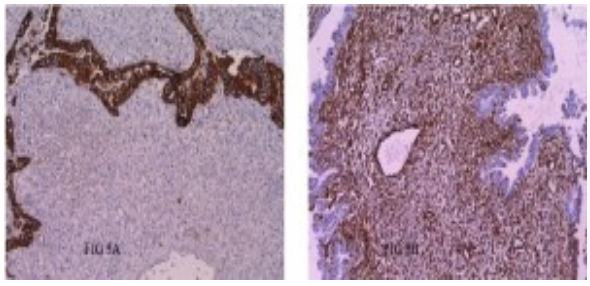

fig 5

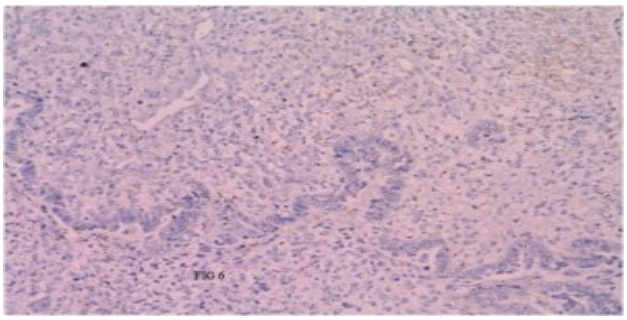

fig 6

Introduction:

Mixed mullerian tumor is a biphasic tumor composed of both pithelial and mesenchymal components. . Incidence of this tumor is less than 1%[2].This may be benign or malignant and is more common in organs of mullerian origin such as ovary, uterus, cervix and vagina. Rarely they do arise in secondary mullerian system such as abdominal and pelvic peritoneum. The biphasic nature can be discerned by immunohistochemistry to epithelial and mesenchymal markers.

Case report: A 64 year old post menopausal woman, known type II diabetic on treatment, came to our surgery department with complaints of vague abdominal pain that aggravated on food intake. She had history of loss of appetite and loss of weight. On examination, she was thin built and pale. Her abdominal examination revealed a soft 9x8 cm mass in left iliac fossa with well defined borders and extending up to midline with limited mobility. Her other systems and biochemical investigations were within normal limits. USG abdomen showed a 6.8x10.0x6.3 cms mixed echogenic lesion with septations in? left adnexa. CT abdomen had revealed necrotic solid soft tissue mass in the small bowel mesentery with omental thickening(fig 1). With a working clinical diagnosis of mesenteric cyst an exploratory laparotomy was done which revealed a 10 x10 cm necrotic hemorrhagic mass in the proximal jejunal mesentery, 2 I/2 feet from the duodenojejunal junction. The mass could not be separated from the jejunum and transverse colon. Omentum was densely adherent to the gallbladder. Apart from the main mass, numerous small 3mm nodules were seen in the pelvic and anterior abdominal wall peritoneum. Uterus, both ovaries and tubes were normal with no ascites or liver metastases. Enbloc resection of mass with jejunum, transverse colon and gallbladder was done along with the biopsy from peritoneal nodule and intra opspecimen was sent for histopathological examination (fig 2).

Pathological findings: We received a loop of jejunum measuring 52.0 cm in length with attached mesentry, segment of large intestine measuring 22.0 cm with adherent gallbladder measuring 7.0x2.5x1.4 cm.

Gross: The mesentry appeared dark brown and thickened with a large nodular mass measuring 10.0x9.0 cm, focally adherent to jejunum. External surface was focally haemorrhagic and partly encapsulated with a variegated tan brown cut surface showing cystic areas. The surrounding area showed multiple nodular projections. The jejunal loop appeared congested with no remarkable changes in the mucosa. The colon and gallbladder appeared unremarkable grossly.

Light microscopy: Sections from the mass showed an infiltrating neoplasm composed of neoplastic epithelial and mesenchymal elements. The epithelial component is composed of cells arranged in tubular, papillary and focal cribriforming pattern(fig 3). These cells showed stratification, nuclear enlargement, hyperchromasia and vesicular nuclei with prominent nucleoli. Increased mitotic activity and focal squamous differentiation were observed. The intervening stroma was composed of pleomorphic spindle shaped cells in bundles arranged mostly in haphazardous pattern with focal interlacing fascicles(fig 4). Scattered bizarre cells, increased mitotic activity, areas of necrosis, numerous psammoma bodies and foci of fat necrosis with collections of foamy macrophages were also observed. There was no evidence of endometriosis in the multiple sections examined. Sections from other peritoneal nodules showed tumor of similar morphology. Jejunum and colon were free of tumor and gall bladder showed tumor deposit in the periserosal adipose tissue.

Immunohistochemistry: The neoplastic epithelial component expressed strong cytoplasmic positivity for Cytokeratin 7 and EMA(fig 5a). The malignant mesenchymal component expressed vimentin(fig 5b) and CD10. SMA, desmin, cakretinin, CK20(fig 6) and S100 were negative.

Discussion: Malignant mixed mullerian tumors of extragenital location is very rare and the first case was reported by Ober and Black [3] where the tumor arised from rectovaginal peritoneum. Traditionally, these tumors occur in the genital system of elderly postmenopausal women and comprise of both carcinoma and sarcoma components, hence also named as carcinosarcomas. The sarcomatous component may be homologous or heterologous. Homologous elements are those that are indigenous to the site and heterologous elements are those containing tissues alien to the site such as skeletal muscle and cartilage[2]. The term malignant mixed mullerian tumor is derived from the observations of the embryogenesis of female genital tract. The body of the uterus, along with the fallopian tubes, the cervix, and the upper part of the vagina, develop from the müllerian ducts, which in turn are derived from the mesenchyme of the urogenital ridge and the celomic lining epithelium. This mullerian epithelium gives rise to all the elements of female genital tract like myometrial smooth muscle, endometrial glands and stroma and cervical and tubal epithelium. Thus smooth muscle tumors of the uterus, the endometrial stromal tumors and endometrial carcinomas are all müllerian in origin. The term 'mixed müllerian tumor' is applied to the group of tumors composed of both mesenchymal and epithelial elements and all the components of which are of müllerian origin. Malignant mixed mullerian tumors are rare tumors mostly arising in the endometrium, ovaries, fallopian tubes, cervix and vagina[3].

The extragenital locations of these tumors are pelvic peritoneum, the serosal surface of the colon, retroperitoneum, antero-lateral abdominal peritoneum, mesentery and omentum.[4] Primary extragenital mixed mullerian tumor arises from secondary mullerian system, a term coined by Lauchlan in 1972[5], derived from invagination of coelomic epithelium during embryogenesis. These tumors may also arise from mullerian duct remnants, malignant transformation of peritoneal endometriosis, endosalpingiosis or endocervicosis and directly from the mesothelium by metaplasia[5].

The various theories behind the biphasic nature of these tumors include [6]: 1] Collision theory states that the carcinoma and sarcoma are two different neoplasms and collided to give the impression of a single mixed tumor. 2] Combination theory suggests that both the elements are derived from a single germ cell which can undergo divergent differentiation in course of their evolution. 3] Conversion theory suggests that the sarcomatous elements are derived from the carcinomatous component. 4] Composition theory

states that the spindle cell component is just a stromal reaction to the carcinomatous element. The conversion theory is currently widely accepted. Various cytogenetic and immunohistochemical studies on cultured cell lines from MMMT have proved that most of malignant mixed mullerian tumors are monoclonal supporting the conversion theory[7]. Extragenital location origin is extremely rare. So far 49 cases of extragenital malignant mixed mullerian tumors have been reported in literature. Of these 22 cases were of peritoneal origin and majority of the patients were in the postmenopausal age group. Sixteen out of these 49 cases of extragenital malignant mixed mullerian tumors were associated with synchronous or metachronous gynaecologic malignancy or colonic malignancy and primary peritoneal carcinoma. Hence a detailed examination of the genital tract should be made before and during surgery[1]. In our case detailed examination did not reveal any other mass lesion. The uterus, cervix and bilateral adnexal structures were unremarkable. Mac CJ and his colleagues reported a malignant mixed mullerian tumor of mesentery associated with synchronous ovarian cancer and they enumerated the risk factors to be obesity, nulliparity, exogenous estrogen and long term tamoxifen use[8]. A similar case of primary malignant mixed mullerian tumor arising from the mesorectum with a synchronous ovarian cancer was reported by Chuang- Chi Huang and his collegues[1].

The clinical presentation may be non-specific and it depends on the tumor site. Most of the uterine neoplasms present with vaginal bleeding . Extragenital malignant mixed mullerian tumors usually present with vague symptoms such as abdominal pain or discomfort and palpable abdominal mass[2] . Grossly, these tumors are solid and fleshy with variegated cut surface. Cystic degenerations are common. If cartilage or bone is present then the tumor may be hard. Microscopically, both genital and extra-genital MMMT show similar findings. One would see both epithelial and mesenchymal elements. These two elements may be intermittently mixed or may be seen as two distinct components. Malignant epithelial component is mostly glandular with endometrioid, clear cell or papillary serous type. Papillary serous type is the commonest. Presence of other histological subtypes likes squamous cell carcinoma, basaloid carcinoma, adenobasal carcinoma, adenoid cystic carcinoma and undifferentiated carcinomas have also been reported. The malignant mesenchymal component may be homologous or heterologous. The homologous components include undifferentiated sarcoma or Leiomyosarcoma. The heterologous component has malignant cartilage, skeletal muscle or liposarcoma. Other unusual features include melanocytic and neuroendocrine differentiation.[2] K. Cokelaere and his collegues have reported a case of primary mesenteric malignant mixed mullerian tumor with neuroendocrine differentiation[4]. The confirmation is by immunohistochemistry. The epithelial elements are immunoreactive for cytokeratin and sarcomatous components are positive to vimentin. Other markers like desmin, myogenin, S100 and SMA are positive based on their differentiation. In our case both the carcinomatous and sarcomatous components were intermittently mixed. The malignant epithelial components expressed strong cytoplasmic positivity for CK7 and EMA. The malignant mesenchymal elements were vimentin and CD 10 positive and were negative for S100, desmin and SMA. CK 20 and calretinin were negative in both carcinomatous and sarcomatous areas. Negative reaction for CK20 and calretinin suggested that the tumor was of mullerian origin[1].

The treatment of choice is cytoreductive surgery followed by chemotherapy. Naniwadekar et al reported the first case of MMMT of primary peritoneal origin where the patient died inspite of treatment with cisplatin and ifosfamide 2 months postoperatively. The tumor has a very aggressive behavior and poor prognosis [5]. Recently in 2011, Fisnik kurshumlui and his men reported a similar case as ours. It was in a 72 year old woman presented as pelvic mass with no uterus or adnexal involvement. Inspite of treatment with carboplatin the patient died in 12 months [9]. Garamvoelgi et al in their review article reports that most patients passed away within one year with median postoperative survival time being 14 months[10]. Our case was lost for follow-up after surgery. In summary, we report a case of primary mesenteric malignant mixed mullaerian tumor in a 64 year old woman. There was no evidence of any synchronous or metachronous gynecologic tumors.

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