STUDY OF HISTOMORPHOLOGICAL CHANGES OF TERATOMAS IN TERTIARY CARE HOSPITAL.

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ABSTRACT: Teratomas are the germ cell tumors composed of multiple cell types derived from one or more of the three germ layers.Teratomas range from benign well differentiated [mature] cystic lesions to those that are solid and malignant [immature].Additionally, teratomas may be monodermal and highly specialized. Rarely, within some mature teratomas, certain elements like squamous component undergo malignant transformation.Teratomas are known to occur at birth and are derived from pleuripotent germ cells and embryonic cells. Teratomas of embryonic origin are congenital and are seen in the midline of the body – skull, neck, mediastinum, retroperitoneum, and coccyx.Teratomas derived from the germ cells are seen in testis in men and ovaries in women. **AIMS:** This prospective and retrospective study was conducted to determine the frequency of the teratomas occurring in various sites along with their histomorphological presentations. **MATERIALS AND METHODS**: The study was conducted at Rajarajeswari Medical College and Hospital between January 2010 to December 2012 in the Department of Pathology. Morphological and histopathological features of teratomas were studied. **RESULTS:** Teratomas were more common in females between 25-35yrs.Most of the teratomas were seen in ovaries followed by retroperitoneum and sacrococcygeal region.87% of teratomas diagnosed were of mature cystic teratoma with histologic grading 0 and remaining 13% showed malignant transformation. **CONCLUSION:** Mature teratomas are typically benign and found more frequently in women and there is risk of malignant transformation.
KEY WORDS: Teratomas, histopathological study, malignant transformation.

INTRODUCTION: Teratomas are the germ cell tumors composed of tissue elements foreign to the organ or anatomic site of origin[1] .The word teratoma is derived from the Greek, teratos means “deformity” or“monster” and –oma which means “tumor”, coined by Virchow in 1863[2]. A more recent elaborate definition , perhaps more appropriate is an encapsulated tumor with tissue or organ components that can be traced to derivatives of the three primordial germ layers; ectoderm, mesoderm, and endoderm.Teratomas display varying degree of

differentiation ranging from primitive somatic elements to highly organized axial and metameric structures meriting in one extreme, the designation of fetus in fetu to highly mature elements [1]. Macroscopically teratomas can appear as a conglomeration of tissue with different colors and textures some of which may be recognizable as gross anatomical structures such as hair, teeth, and limbs[3]. They can affect individuals of all ages. The common locations of teratomas in childhood are the sacrococcygeal, mediastinal, retroperitoneal and the gonadal organs. Teratomas occurring in childhood are of special interest, since their biological behavior is strongly related to age at diagnosis and anatomic site of origin[1]. Here we review the clinical and pathological features of various teratomas seen in the department of pathology, Rajarajeswari medical college, Bangalore.

MATERIALS AND METHODS: This was a prospective work up done in the Department of Pathology, Rajarajeswari medical college over a period of 3 years [Jan 2010 to Dec 2012], which evaluated for the specimens diagnosed as teratomas. The data was collected from medical records in each of these cases. Each case was evaluated for the age of the patient, clinical features, family history, drug history, menstrual history and other significant symptoms. The various morphological and histopathological features of all the cases were examined. The inclusion criteria included all the cases of clinically diagnosed teratomas and those specimens sent for histopathological examination to the department of pathology. Inadequately fixed specimens were excluded from the study. A total of 16 specimens were studied. All the specimens were fixed in 10% formalin solution and assessed with respect to the age, site, gross description and histopathology. Conventional H&E stained microsections were available in all the 16 cases.

RESULTS: All the cases of teratomas were aged between 27 weeks of gestation to 60 years with a female preponderance.The most common mode of presentation was mass lesion with signs and symptoms ascribable to specific location and consequent impingement upon or compression of adjacent organs or tissues. Site wise,most tumors occurred in ovary,followed by retroperitoneum and saccrococcygeal region.One case of ovarian teratoma had associated mucinous cystadenoma (Table1).The clinical features and gross pathology of these distinctive teratomas are considered separately.

OVARIAN TERATOMAS: Ovary is the most common site for the appearance of teratomas.In our setup, the age group of the cases ranged from 23 to 46 years. The mean age at diagnosis was 35 years with malignant transformation in one of the cases (age group of 38 years). The patients typically presented with an intraabdominal adnexal mass and a palpable tumor apparent on physical examination. Majority of the ovarian teratomas were right sided. Imaging studies showed variegated appearance in all of these lesions. One of the tumors showed solid and cystic areas consistent

with malignant transformation, with the mean diameter of 10cm (Table 2).All the specimens examined in theatre, showed contents of teeth, hair, cartilage, bone and brown fluid Fig 1(a,b,c).

SACROCOCCYGEAL TERATOMAS: Our case of sacrococcygeal teratomas (SCT) was diagnosed inutero but due to fetal hydrops and high output failure, the baby was stillborn with features of midaxial, exophytic mass in the buttock area with overlying skin showing dark discoloration Fig 2 (a) .

RETROPERITONEAL TERATOMAS: Of the two cases reported, one of the retroperitoneal lesion was seen in a 27 day, male baby presented by the mother with the distention of abdomen, since birth. The antenatal scan showed a retroperitoneal mass on the right side. Postnatal ultrasound and computed tomography revealed a retroperitoneal mass pushing the right kidney to pelvis which was suspended by a peduncle. The excised tissue consisted of a solitary mass with solid and cystic component along with rudimentary limb or bowel like structures filled with inspissated material consistent with teratoma Fig 2(b &c).

The other case was a 60year old female presented with mass per abdomen. USG and CT scan of the abdomen revealed a heterogeneous cystic mass of size of 18x17.0x8.0cm arising from the mesocolon of sigmoid region. Excised specimen showed multiloculated cyst of variable consistency filled with pultaceous material with a foci of solid component.Squamous cell carcinoma with mature cystic teratoma arising from mesocolon (sigmoid colon) was made on histological examination.Fig2(d)

Fourteen (87%) of 16 cases were benign mature cystic tumors (grade 0) and two cases(13%) had malignant component (grade3). They were classified according to Gonzalez-Crussi grading system. Two or more embryonic germ layer derivatives were apparent in each of the tumors, and all three were represented in 90% or more of the cases. Bone and cartilage was seen in two cases. Respiratory epithelium, intestinal mucosa was seen in three cases**.**Glial tissue, pigmented epithelium and choroid plexus was seen only in one case Fig 3(a,b,c). One of our cases was composed predominantly of thyroid tissue and diagnosed as struma ovarii Fig 4(a). None of our reported cases had immature component .Two of our cases showed malignant component of squamous epithelial tissue, one of which arising from ovarian teratoma and other was from mesocolonic tissue occupying the retroperitonium (Fig 7, 8, 9, 10). Therapeutically, all the patients of teratoma had surgical intervention .Excision of the mass was done in both retoperitoneal cases .One case of retroperitoneal teratoma arising from the mesocolon Fig 4(b,c) of sigmoid region was referred to higher centres for neoadjuvent therapy.

DISSCUSION: Teratomas belong to a class of tumors known as germ cell tumors. The origin of teratomas in earlier days was believed to be due to ingestion of teeth and hair, as well as curses from witches, nightmares or even adultery with the devil. The parthenogenic theory, which suggests an origin from the primordial germ cells, is now the most widely accepted. This theory is bolstered by the anatomic distribution of the tumors ,along lines of migration of the primordial germ cells from the yolk sac to the primitive gonads[3]. The sequestered midline embryonic cell rests explains the location of teratoma in midline of the body – skull, neck, mediastinum, retroperitoneum, and coccyx. Teratomas derived from the germ cells are seen in testis in men and ovaries in women[2].

Of the 16 cases reported, the orders of frequency of teratoma localization were ovarian, retroperitoneal and sacrococcygeal teratoma was least of all.

Our case of SCT was diagnosed at 20weeks during antenatal screening. The patient was followed up with fortnightly USG to monitor the tumor size, foetal growth and signs of foetal hydrops. The patient underwent three inutero foetal blood transfusions.In view of foetal hydrops and anemia, a baby girl was delivered by Caesarean section at 28 weeks. Despite maximal resuscitative efforts, the neonate died 30 minutes after birth due to large friable SCT with massive hemorrhage of Type I variety[2]. This case illustrates the importance of prenatal diagnosis, management and clinical intervention. Early prenatal diagnosis influences clinical decision and antenatal management, which in turn optimizes the outcome. Development of

polyhydramnios increases the risk of premature delivery .Volume reduction by amniocentesis, tocolysis to prevent preterm labour and corticosteroids for foetal lung maturity may be required.

Mature cystic teratomas of the ovaries are often discovered as incidental findings on physical examination, during radiographic studies or during abdominal surgeries performed for other indications with the reported rate of 6-65% in various series[2]. Plain radiograph of abdomen showed a soft tissue opacity containing calcification and teeth. Ultrasonographic waves were interrupted by a calcified lesion. CT scan of abdomen showed a large bilobed cystic lesion with fat-fluid level and solid calcified structure (teeth) protruding into the cyst cavity [Rokitansky protuberance]. The lesion was displacing the contrast filled bowel loops in most of the cases[5, 6].

Struma ovarii is a teratoma composed totally or mainly of thyroid tissue.It accounts for 1-3% of benign teratomas of ovary.Our case was a 41 year old woman with non specific symptoms and palpable mass per abdomen.Histopathology showed predominantly features of benign mature thyroid tissue along with other germ cell derivatives.

The mature cystic teratomas (MCT)/dermoid cyst are always benign. Complications of ovarian teratomas include torsion, rupture, infection, and hemolytic anemias and malignant degeneration[2]. Malignant transformation of a benign cystic teratoma is rare complication with an incidence of 1-2% seen especially in perimenopausal and older women. The most common form of malignant transformation of the MCT is squamous cell carcinoma (75% of cases). Other tumors arising in MCT include basal cell carcinoma, sebaceous tumor, malignant melanoma, adenocarcinoma, sarcoma, and neuroectodermal tumor. The low incidence of secondary malignant transformation of mature cystic teratoma explains why a few reports have been published. It has been thought that squamous cell carcinoma in mature cystic teratoma arises from metaplastic squamous epithelium. Most of the mature cystic teratomas are detected 15–20 years before they undergo secondary malignant transformation. Cytogenetic abnormalities might precede histological changes and prolonged exposure to various carcinogens in the pelvic cavity might cause the malignant changes in mature tissue. Risk factors for malignancy in MCT include patient age,tumor size and imaging characteristics.Tumor size greater than 10cm should raise the suspicion of malignancy.In our case,the tumor diameter was 15 cm,which corresponds to literature.It is postulated that the larger size of ovarian mass indicates long standing disease process and likelihood of any of the components becoming malignant is higher[5,6].

Retroperitoneal teratomas posed a significant problem in the differential diagnosis of an intraabdominal mass due to the young age of the patient . As with teratomas of other sites ,the presence of calcifications or bony structures on plain radiographs was a useful diagnostic aid. Fetus in fetu(FIF) and fetiform teratomas are rare forms of retroperitoneal mature teratomas that include one or more component resembling a malformed fetus[7] . According to Willis (1935) presence of axial skeleton with vertebral axis goes more in favor of fetus in fetu as it indicates abortive attempt after the stage of primitive streak formation[8]. Incidence of FIF is said to be about 1 in 500000 births and about 90% cases are identified before 18 months of age ,as was our case[7]. Differentiation of FIF from a mature or well organized teratoma is controversial.Spencer suggested that FIF and many teratomas are an aberration of monozygotic twinning.Depending on the degree of malformation and timing of the embryologic insult,interruptions of monozygotic twinning can lead to any of these entities.FIF is thought to occur at a very early stage of development,before ventral fusion of the lateral body walls.It has also been suggested that there is a continuum between FIF and teratomas.Supporting this

hypothesis are the observations that FIF and teratomas are increased in families with a history of twinning, FIF may contain multiple fetuses, FIF and teratomas can coexist and FIF and teratomas are found in locations that are involved embryologically in conjoined twinning.WHO also has suggested that the fetus in fetu mass represents a well differentiated, highly organized teratoma[7]. The fetus in fetu is usually suspended by a peduncle within a capsule containing a little fluid as was in our case. Intraabdominal fetus is usually contained in a complete sac, complete excision of the mass with surrounding membrane should ensure definitive cure[9].

The other case of retroperitoneal teratoma was noted in the mesocolon of sigmoid region in a 60year female with features of mature cystic teratoma and malignant transformation into squamous cell differentiation. Generally,teratomas of gastrointestinal tract are rare.Six to ten previous reports of mesenteric teratomas have been located in the English literature [10].Incidence varying from 1 in 1,00,000 to 2,50,000 admissions[11]. The differential diagnosis include mesenteric or omental cyst (lympangioma, enteric duplication cyst, enteric cyst and non-parasitic pseudocyst), cystic spindle cell tumors and cystic mesothelioma. If a tumor contains teeth and bone as opposed to calcification then that is almost pathognomonic of a teratoma[10].Only after surgery and complete histopathological evaluation,malignant change can be predicted. Our case was the rarest case reported by us about the mature cystic teratoma with malignant differentiation to squamous cell carcinoma arising from mesocolon of sigmoid region with only one case reported in 2007 with malignant teratoma arising from mesentry of descending colon as per the MEDLINE Database [12].

Treatment includes complete excision of the mass. An important aspect is to keep the patient in long term follow up along with markers like alpha fetoproteins so that recurrences with malignancies can be diagnosed at an early stage.

CONCLUSION: The opportunity to examine large series of teratomas treated at a single institution over a period of 3 years has allowed us to place into perspective and comparatively analyze their clinical and pathologic features. The differential diagnosis, treatment and prognosis is strongly influenced by anatomic location of primary tumor and age of the patient. The clinical stage or extent of the disease and histologic grade of immaturity are significant features in immature ovarian teratoma.The prognosis in patients with malignant transformation of mature cystic ovarian teratoma is poor but worse in those with metastasis.

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Comparison of teratomas by site of origin, age at diagnosis, sex distribution and mean tumor diameter.

Anatomic site	No[%]	Age at diagnosis	Sex distribution	Tumor diameter
Sacrococcygeal	1	27 weeks gestation	Female	9cm
Ovary	13	38 yrs[mean]	Females	5cm-15cm
Retroperitoneum	2	27 days, 60yrs	1Male 1Female	7cm 18cm

Table2–Comparison of Ovarian Teratoma by age, Location, Tumor dimension, Histopathological diagnosis and Histological Grade.

Case No	Age in Years	Location	Tumor Diameter[cm]	Diagnosis	Histologic Grade
1	34	Right	5	MCT*	0
2	23	Right	10	MCT	0
3	32	Left	10	MCT	0
4	35	Right	9	MCT	0
5	46	Right	7	MCTwith MCA†	0
6	37	Right	6	MCT	0
7	38	Left	15	MCT with SCC$^{\mp}$	3
8	41	Left	7	Struma Ovarii	0
9	32	Left	10	MCT	0
10	40	Right	11	MCT	0
11	40	Right	10	MCT	0
12	25	Right	6	MCT	0
13	24	Left	7	MCT	0

* Mature cystic Teratoma ┼ Mucinous cystadenoma ǂ Squamous cell carcinoma

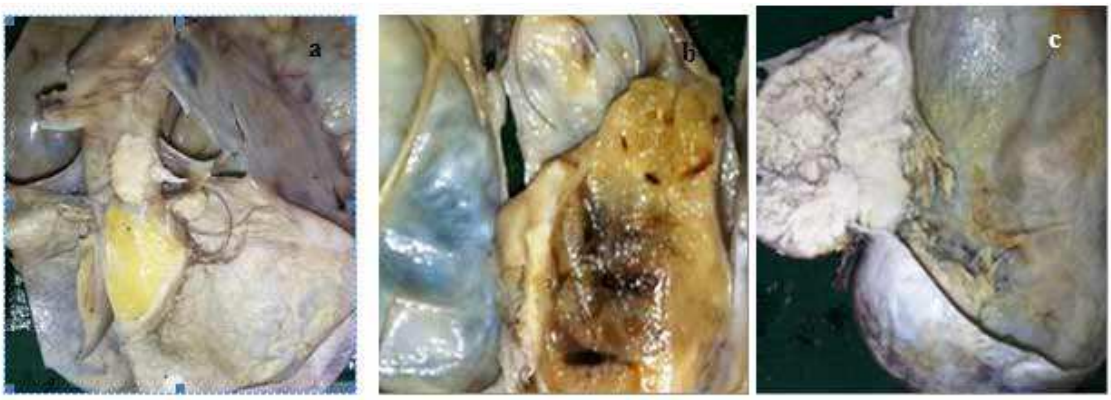

Fig1: *S*urgical specimen of ovarian teratoma with structures of **(a)** teeth, hair & Rokitansky nodule (b) brown translucent thyroid tissue (c) solid component.

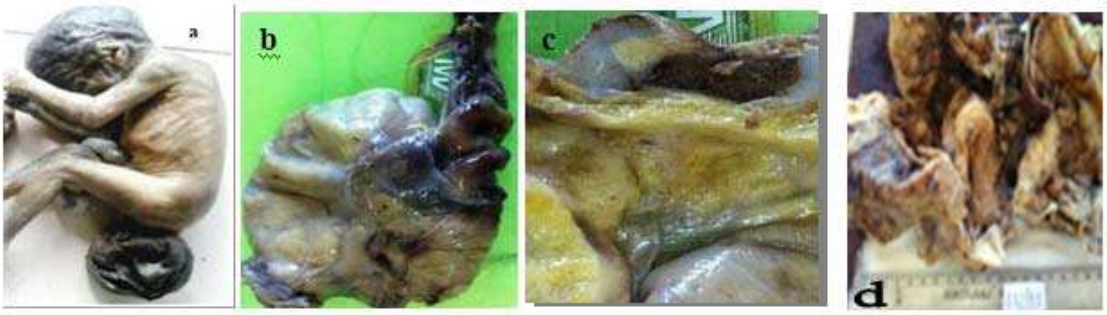

Fig 2: (a) Sacrococcygeal teratoma with exophytic mass. (b) Retroperitoneal teratoma with limb bud like structures(fetus in fetu). (c) Sectioned surface showing areas of bone with cartilage (d) retroperitoneal teratoma arising from the mesocolon with solid component.

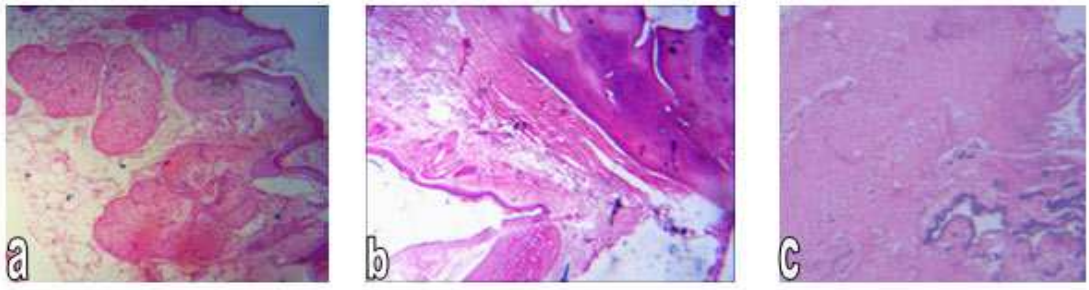

Fig3 (a)Teratoma with mature components of germ cell derivatives(a)skin and adnexal structures(b)cartilage and bony tissue(c)pigmented epithelium along with glial tissue.

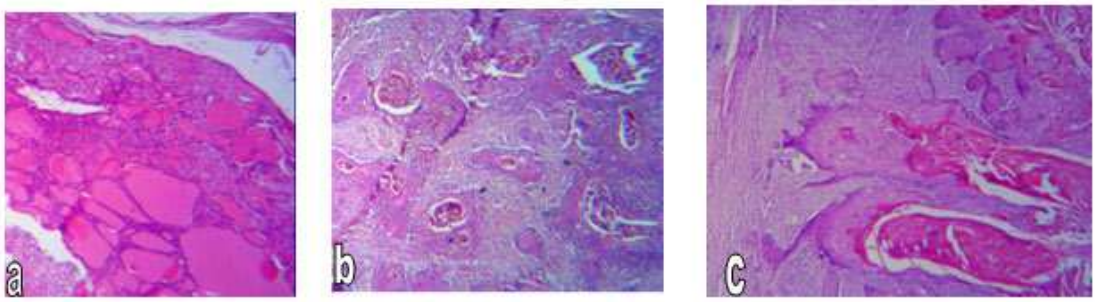

Fig 4: (a) Teratoma with predominant mature thyroid tissue component.(b & c) Mature cystic teratoma with malignant squamoid component.