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Original Research Article

Clinico-histopathological study of gonadal and extragonadal teratomas in tertiary care centre

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ABSTRACT

Background: Teratomas are quite often seen in the gonadal region. As compared to gonadal teratoma extragonadal teratomas are very rare. They can be mature, immature, malignant or mixed germ cell tumor. Many a times they are missed clinically because of their rare locations that include retroperitoneum, sacrococcygeal, mediastinum, thyroid, eye, ear, and mesentery. In such locations the list of clinical differentials is long and it is difficult for the clinicians to make an accurate clinical diagnosis. Aims of the study were: to identify the different locations of extragonadal teratoma, to know the histological types of teratoma in different location, and to correlate histopathological diagnosis and clinico-radiological diagnosis.
Methods: It is an observational descriptive study of histopathologically proven teratomas over a span of 2 years from July 2021 to July 2023.
Results: Out of total 35 cases of teratomas, we had received 14 cases of extragonadal teratomas. The most common sites being sacrococcygeal region. They were most common in the paediatrics age group and most common sex involvement was of male.
Conclusions: While interpreting the histopathological findings, a high index of suspicion for teratomas needs to be kept even if the site is not a gonadal location. Simple excision is a cure for this condition or else it may transform to malignancy.

Keywords: Teratoma, Extragonadal teratoma, Gonadal teratoma, Sacrococcygeal

INTRODUCTION

The term "teratoma" is derived from the word "Teras" meaning monster first introduced by Rudolph Virchow in 1863. The first case of mature teratoma dates back to 1659 reported by Johannes Scultetus while recording autopsy findings of a young woman who died of ovarian tumor. It was described as "dermoid cyst of the ovary".[1] Teratomas originate from totipotential germ cells that are usually found in the gonads and rarely at other extragonadal sites. The totipotent cells can differentiate into any cell type (ectoderm, endoderm and mesoderm) in the body giving rise to neoplasm containing bone, epithelium, muscle, fat, nerve and other tissues. Teratomas are relatively common tumors among women of reproductive age, mostly of age group 20 to 40 years, but they can occur at any age and can also be seen in males.[2] These tumors are mostly benign but may rarely undergo malignant transformation in 1 to 2% of cases.[3,4] They can coexist with other germ cell tumors as well. Although gonadal teratomas are commonly described in literature, their extra gonadal variants are less commonly represented. Teratomas at extra-gonadal sites are uncommon and they vary in presentation and have unpredictable biological behaviour. They occur as a component of extragonadal germ cell tumors. They usually occur in midline, although other sites are also mentioned.[5] The biological behaviour and prognosis of teratomas is influenced by patient's age, site of the tum or, presence of immature elements and cytogenetic abnormalities.[6] The present study is undertaken to study the clinico-

pathological profile and histological spectrum of teratomas with special emphasis on extragonadal teratomas.

METHODS

This is a retrospective study of all histologically confirmed cases of teratomas (gonadal and extragonadal) over a period of two years (from July 2021 to July 2023). The clinical details of these cases were obtained from the histopathology files of the department of Pathology, Government medical college and hospital Nagpur which is a tertiary health care hospital. The findings noted from the records included all clinical and radiological details like age, sex, size, laterality, gross, morphological features, clinical presentation, radiological diagnosis, other investigations and any other relevant findings. Gross findings of the specimen were also noted. Histopathology sections were reviewed for the presence of various tissue components and all cases were categorized into mature or immature teratoma or presence of any other element like other germ cell tumor. Recent World Health Organization (WHO) classification was used to categorise immature teratoma based on the increasing grade of immaturity predominantly of neuroepithelial element.[7] Gonadal and extragonadal teratomas were studied separately for their clinical profile and histological features. Clinically and radiologically suspected cases of teratomas that were not confirmed on histology were excluded from the study.

RESULTS

Our study included total 35 cases of teratomas over 18-months duration. Of them, 21 (60%) cases were gonadal and 14 (40%) cases were extragonadal teratomas. The distribution of gonadal and extragonadal teratomas is as shown in Figure 1a and b respectively.

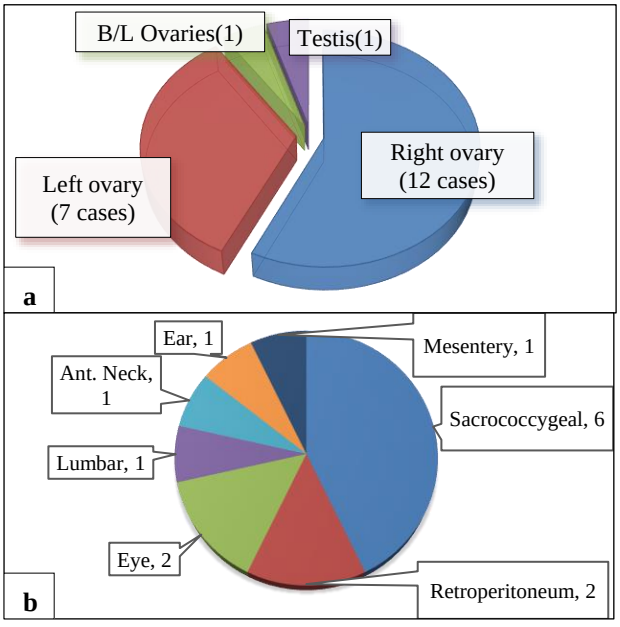

Figure 1: Anatomical distribution of (a) gonadal teratomas, and (b) extragonadal teratomas.

Gonadal teratomas

The size of gonadal teratomas ranged from 3 cm to 20 cm and they are most commonly seen in females (Table 1). Radiologically all of them were diagnosed as teratomas and grossly all were solid cystic in variable proportion (Figure 2). Few cases showed variegated appearance. Solid areas were also seen with presence of various elements like hair, fat, cartilage, bone and myxoid areas (Figure 3). Most common teratoma was mature cystic teratoma which on microscopy showed variable amount of endodermal, ectodermal and mesodermal tissue (Figure 4) followed by struma ovarii then immature teratoma, teratoma with malignant transformation and mixed germ cell tumors with teratoma. (Table 2).

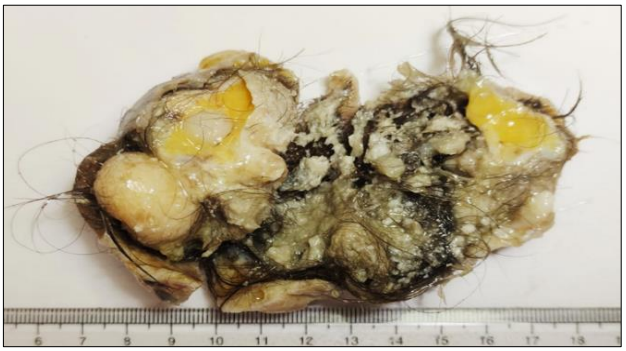

Figure 2: Specimen of ovarian teratoma with cartilaginous areas, sebaceous material and hair tuft.

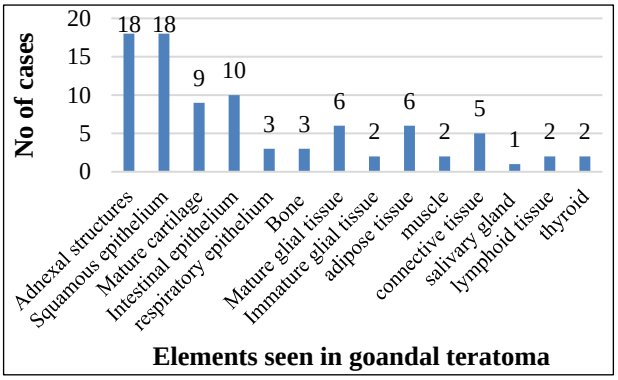

Figure 3: The morphological features in gonadal teratomas.

Extragonadal teratomas

Number of cases of extragonadal teratomas were 14. Out of 14 cases ten were male and four were female. Most common site was sacrococcygeal. In present study, most of the cases (11/14) of extragonadal teratomas were in prepubertal age, while very few cases (3/14) were in postpubertal age group (Table 3). Most common histological type of extragonadal teratoma was also mature cystic teratoma followed by immature and teratoma with mixed germ cell tumor (Table 4). Various components on histology seen in extragonadal teratoma is shown in

(Figure 5). Microscopically mature cystic teratomas showed mature cartilage, fat, and epidermis. Immature teratomas showed immature neuroectodermal tissues alongwith mature ectodermal and mesodermal tissues (Figure 6). Two cases showed foci of yolk sac tumor along with mature component in one case and immature component in other case (Figure 7).

Table 1: Age, sex and anatomical distribution of gonadal teratomas.

Parameter	Age distribution		Sex		Site		Clinical presentation
	Prepubertal	Postpubertal	Females	Males	Ovary	Testis	
No. of cases	1	20	20	1	20	1	Abdominal pain, urge incontinence

Table 2: The histological types of gonadal teratomas.

Site	Mature	Immature	Struma ovarii	Malignant transformation	MGC with teratoma
Right ovary	09	0	02	01	0
Left ovary	06	01	0	0	0
Bilateral ovaries	01	0	0	0	0
Testis	0	0	0	0	01

Table 3: Age, sex and site-wise distribution of all extragonadal cases.

Site	Number of cases	Gender		Age of patients
		Male	Female	
Sacrococcygeal	6	4	2	1 day to 3 years
Retroperitoneal mass	2	1	1	1 month and 42 years
Left eye	2	2	0	3 years and 65 years
Swelling anterior neck	1	1	0	8 years
Mesenteric cyst	1	1	0	21 years
Lumbar region	1	0	1	15 days
Posterior auricular	1	1	0	15 years

Table 4: Histological types of extragonadal teratoma.

Site	Mature teratoma	Immature teratoma	Mixed germ cell tumor with teratoma
Sacrococcygeal	5	0	1 (yolk sac with immature teratoma)
Retroperitoneal	1	1	
Left eye	2	0	
Anterior neck	1	0	
Mesentery	0	0	1 (yolk sac with mature teratoma)
Lumbar region	1	0	
Posterior auricular	1	0	

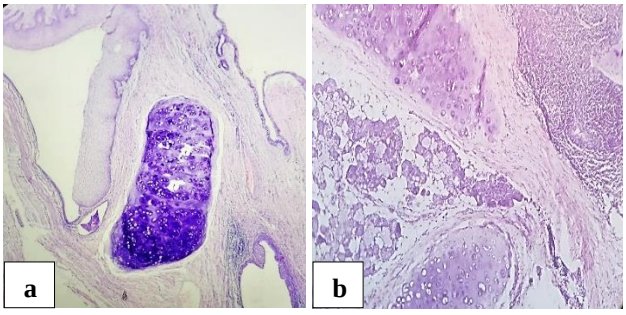

Figure 4: H and E photomicrogram of ovarian Mature cystic teratoma: (a) section shows stratified squamous and cuboidal epithelium with mature cartilaginous tissue, and (b) lymphoid tissue and a focus of salivary gland tissue seen.

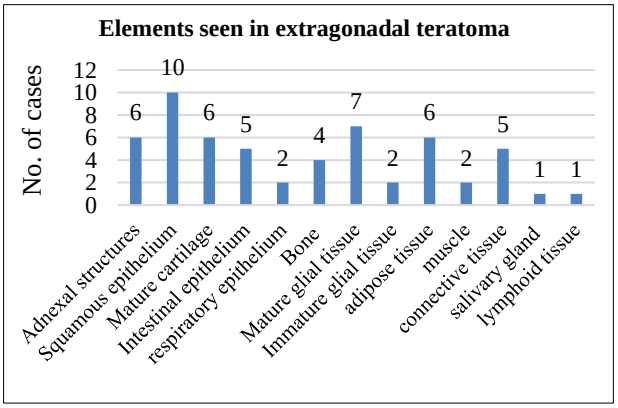

Figure 5: The morphological features in extragonadal teratomas.

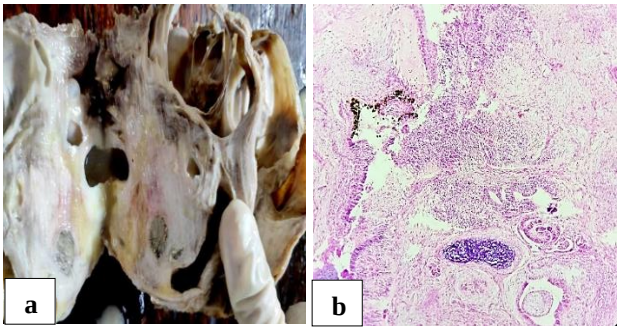

Figure 6: Immature retroperitonel teratoma: (a) gross specimen of retroperitoneal swelling showing solid cystic heterogenous cut surface, and (b) H and E photomicrogram of immature teratoma showing immature neuroepithelium along with mature cartilage and pigmented epithelium.

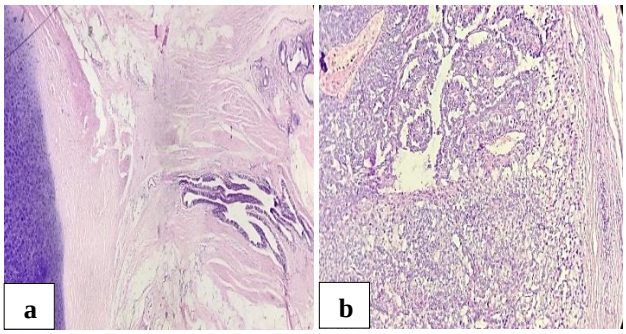

Figure 7: H and E photomicrograph of Mixed germ cell tumor: (a) lower power view having component of immature teratoma showing immature neuroepithelium, mature cartilage and glandular structures, and (b) section shows reticular pattern of yolk sac tumor with presence of Schiller-Duval bodies.

DISCUSSION

Although gonadal teratomas are commonly seen and well-studied, there is paucity of literature on extragonadal teratomas. Since centuries, there has been a dispute, interest and speculation over the origin of teratomas. Origin from primordial germ cells is the most accepted theory which is supported by the anatomical distribution of these tumours along the line of migration of the primordial germ cells.[8] In general, the biological behaviour of teratomas is unpredictable. Morphological features are essential for their histological typing into three main groups: immature teratomas, mature teratomas and monodermal and highly specialized teratomas; but are insufficient to predict their clinical course.[6] There is a difference in the age group, sex distribution and clinical behaviour between gonadal and extragonadal teratomas. As compared to gonadal teratomas, extragonadal teratomas are very rare, equally seen in both sexes and may not be suspected clinically and radiologically.

Present study was undertaken to study the clinicopathological profile and histomorphological spectrum of all teratomas (gonadal and extragonadal) with special emphasis on extragonadal type. This study included total 35 cases of histologically confirmed teratomas, which included 21 cases of gonadal teratomas and 14 cases of extragonadal teratomas. Teratomas exist in distinct mature and immature forms, characterized by their resemblance to either adult or fetal tissues.[9] In a Nigerian study on teratomas, total M: F ratio in all teratomas was 1: 8.3, in our study of the M: F ratio varied widely from 1:20 in gonadal and 10:4 in extragonadal teratomas, overall it was 1:2.2.[10]

Amongst the 21 cases of gonadal teratomas, 20 were ovaries; whereas one single case was seen in testis as a component of mixed germ cell tumour. Most of the cases of ovarian teratomas were seen in reproductive age group 80%, (16/20) with a wide age range from 3 to 59 years. Most of them were of mature cystic type 80% (16/20). In a large study on mature cystic teratomas by Ayhan et al in 2000, median age was 35 years, abdominal or pelvic pain was the most common symptoms and bilaterality rate was 13.2 %, which is similar to our study with median age of 36 years, abdomino-pelvic pain as the most common symptom, and bilaterality rate of 5% (1/20).[11] One patient presented with torsion, 5% (1/20), similar to Ayhan's study (4.9%).[10] Another larger study by Comerci et al on 517 cases of teratomas mentions that 60% of the patients were asymptomatic. In our study, (40%), 8/20 patients were asymptomatic and detected incidentally. They mentioned torsion as the most common complication and also found direct relation between tumour size and rate of torsion.[12] One single case presented with torsion in our study was a cystic tumour of 12 cm diameter. Various other complications mentioned in literature are rupture, infection, hemolytic anaemia and development of malignancy. Malignant transformation is a rare complication of mature cystic teratoma that can be seen in 1 to 3 % of cases.[4] Malignant transformation may occur in the endodermal, mesodermal and ectodermal components of teratomas.[13] The rate of malignant transformation in Comerci's study was 0.17% and in our study was 5% (1/20).[12] Sample size in our study was too small as compared to these studies. All cases were detected on radiology. Most common histological type of malignancy seen in 80% of teratomas is squamous cell carcinoma (SCC), followed by adenocarcinoma, carcinoid tumor, melanoma, and sarcoma.[4]

Immature teratomas form less than 1% of all ovarian teratomas and most of them are seen in first two decades of life either in pure form or as a component of a mixed germ cell tumour.[14] In our study, we found 1/20 (5%) cases of immature teratoma. Patient's age was 22 years and its size was 19 cm. She had abdominal pain as main symptom. Grossly it showed variegated appearance with solid cystic areas. The diagnosis was based on the histological presence of varying amounts of immature tissue including neural differentiation. Bilaterality is less common in immature teratomas as compared to mature cystic teratomas. Such tumours may be sometimes composed of

mature elements predominantly, hence careful examination and thorough sampling of these tumours is strongly recommended.[8] Other case seen in our study was a component of mixed germ cell tumour. This patient was 46 years old. The combination of immature teratoma with another germ cell tumour is also known. In cases of mixed germ cell tumor, proportion of each component should be mentioned in final pathological report, as tumour prognosis in such cases will be on par with the predominant component.[15] Treatment options for immature teratomas depend significantly on the histologic grade and the patient's fertility desires.[16]

Two cases of struma ovarii 10% (2/20) were seen in our study. Although thyroid tissue is seen in 5-20% of mature cystic teratomas, the term struma ovarii should be used only for tumours entirely composed of thyroid tissue or predominant part of the tumour.[17] It comprises of about 3% of ovarian teratomas and shows similar age distribution. No specific clinical features are seen. Some cases may be associated with thyroid gland enlargement and development of thyrotoxicosis. In our study, both cases were in reproductive age group (18, 39 years) with 10 and 20 cm tumour size. One case showed only thyroid tissue and squamous epithelium. In second case other components of mature cystic teratomas were also noted with predominance of thyroid tissue. Larger tumour with 20 cm size clinically presented as torsion. Radiologically both were diagnosed as mature cystic teratoma. Szyfelbein et al in study on cystic struma ovarii mentioned that if the tumour is cystic, then the thyroid follicles may be overlooked.[18]

A single case of testicular teratoma was observed in our study. It was seen as a 10 cm tumour mass in 40 years male and on histology it was a malignant mixed tumour showing mature cystic teratoma and yolk sac tumour. Similar retrospective study on teratomas by Edegbe et al in 2018 found all cases of mature teratomas. No case of immature teratoma or monodermal teratoma was seen.[10] Although ovarian teratomas are typically cystic, composed of mature elements and almost uniformly benign, post pubertal testicular tumors are considered to nearly always carry a potential for malignant behaviour, even when composed entirely of mature elements. Thus, testicular teratoma need wide and extensive sampling and careful follow up.

Extragonadal teratoma

Our study of teratomas included 14/35 cases of extragonadal teratomas (40%) over a period of 24 months. Teratomas in extra-gonadal sites are uncommon, varied in presentation and show unpredictable biological behaviour.[19] As shown in Table 3, extra gonadal teratomas in our study showed varied sites, most frequent being sacrococcygeal (6/14) followed by retroperitoneum (2/14). Other sites were thyroid, eye, mesenteric cyst, lumbar and postauricular region. They can be seen at any site including retroperitoneum, mediastinum, lungs, stomach, floor of mouth, tongue, kidney, thyroid, liver, heart, fallopian tubes and even placenta.[20] Most of the cases of extragonadal teratomas in our study 11/14 (78%) were prepubertal. Three cases 3/14 were in adults. O'Donovan et al mentioned that these extragonadal teratomas can occur at any age, and their frequency at different sites varies with age. About 40% teratomas occurring in children are seen in abdominopelvic region (sacrococcygeal, retroperitoneum), other sites include typical midline location. They are uncommon in adults and due to their rarity, may not be considered in differential diagnosis or may be confused with other common lesions at that site. Example: retroperitoneal teratomas can be confused with Wilm's tumour or neuroblastoma clinically and radiologically.[5] Gurda et al in their study of 16 sacrococcygeal teratomas, found 11 prepubertal and 5 post pubertal patients. All immature teratomas were prepubertal. They further stated that 80% of sacrococcygeal teratomas in adults represent known recurrences. Sacrococcygeal teratomas are most commonly seen as congenital neoplasms. After correlation of the clinical characteristics like age, tumour markers, imaging, follow up and histology in them, their study concluded that mature sacrococcygeal teratomas have a favourable outcome.[6] Various large case series and meta-analysis have shown that mature teratomas of the anterior mediastinum are usually benign and those with immature elements show a risk of aggressive behaviour putting them in prognostically intermediate group. Further studies are essential for analysing the data of extragonadal teratomas arising in other locations. Rare, unusual sites in our study included mesenteric cyst, anterior midline neck swelling, and lateral canthus of eye. Histological diagnosis in such locations should be finalized only after ruling out other possibilities with overlapping histology in that location. Example, in midline neck swelling, diagnosis of thyroglossal cyst needs to be ruled out. In other superficial locations, possibility of epidermal cyst or a sebaceous cyst should be ruled out. Epidermoid cysts have only squamous epithelial lining whereas dermoid cysts show adnexal structures in addition, like hair follicles and sebaceous glands, the data for remaining sites is lacking especially in adults.[5] The prognostic implications of teratoma primarily depend on anatomic location of the tumour, patient demographics and histological typing of the tumour. The case of mesenteric cyst in our study was a malignant mixed germ cell tumour with yolk sac tumour component in addition to immature teratoma. Preoperative diagnosis of germ cell tumour on imaging and tumour marker status like alpha feto protein levels are very helpful in such cases. Malignant teratomas may cause a rise in serum levels of tumor markers like alpha-fetoprotein and carcinoembryonic antigen.[21]

In our study, there were five cases which were misdiagnosed both clinically and radiologically. Mesentric teratoma was clinically suspected as gastrointestinal stromal tumor, anterior neck swelling was provisionally diagnosed by clinician as thyroglossal cyst. Mass in the lumbar region was diagnosed as neuroblastoma clinico-radiologically and the histopathologically diagnosed

dermoid cyst at eye and ear was clinically presumed as epidermal cyst and on histopathology they all turn out to be different types of teratomas. Overall line of management and patients outcome of these clinically suspected conditions is very different from that of teratomas indicating that the precise histopathological diagnosis is always needed.

Limitations

The study had a brief duration, and there was insufficient follow-up to offer insights into the potential progression to malignancy.

CONCLUSION

Extragonadal teratomas are uncommon and due to their rare sites, they can cause diagnostic confusion. Hence, a high index of suspicion for teratomas at rare sites need to be kept not only by pathologist but also by clinicians and radiologists. Most of the teratomas are cured just by complete surgical excision and hence, accurate histopathological diagnosis is the need of the hour.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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