

Types and Frequency of Neural Elements in Mature Ovarian Teratomas: An 11-Year Study from Rural India

Raj Kumar, Seema Dayal¹, Mani Krishna¹

Departments of Neurosurgery and ¹Pathology, Uttar Pradesh University of Medical Sciences, Etawah, Uttar Pradesh, India

Abstract

Introduction: Teratomas are those tumors which are derived from the totipotent cells. They may manifest at any site. Ovary is the most common site for teratomas. Ovarian teratomas may be immature and mature depending on the elements they harbor. Mature ovarian teratomas may contain ectoderm, endoderm, and mesoderm. Ectoderm mainly comprises the skin and its adnexa, followed by neural tissue, whereas mesodermal elements are blood vessels, adipose tissue, cartilage, and hematopoietic tissue, similarly, endoderm consists of respiratory tissue, thyroid gland, and gastrointestinal tissue. **Materials and Methods:** This study was conducted in the histopathology section from January 2008 to April 2019 and included 54 cases of mature ovarian teratomas. The slides of ovarian tumors were evaluated, and the relationship between clinical and pathological findings was studied with emphasis predominantly on neural elements. **Results:** The most common age group among the women with ovarian teratoma was 21–30 (31.48%) years, the youngest patients been 8 years, and oldest of 60 years. The chief complaints were pain in 37 (68.51%), followed by mass per abdomen 25 (46.29%). On gross examination, most of the tumors were unilateral 53 (98.14%), having tufts of hairs with sebaceous material 34 (61.81%). Microscopic examination confirmed the presence of squamous epithelium and its adnexal structure 52 (94.54%). Neural elements were seen in 14 (25.45%) cases. In every case with neural elements, skin, its adnexa, and adipose tissue were also seen. **Conclusion:** Teratomas have diversity in the age of presentation, gross findings, and microscopy features. Neural elements are commonly found in 25.45% of ovarian teratoma which is mostly found in association with skin and adipose tissue. The combination of neural elements with adipose tissue signifies an association between them because both arise from different dermal elements.

Keywords: Histopathology, mature ovarian teratoma, neural elements

INTRODUCTION

Teratoma is a special type of mixed germ cell tumor which consists of mature and immature elements arising from one or more of the three primordial germ layers. The word teratoma is derived from the Greek word “teras” meaning monster or deformed and “oma” means tumor. Virchow coined the term teratoma in his book on tumors published in 1863.^[1] They occur in gonads and in extragonadal sites, that is., in ovary, testis, lung, mesentery, and omentum. Ovary is the most common site of teratoma. It is further divided into mature and immature depending on the contents they have. Teratomas may occur at any age group, but it is frequent in the young age group, that is., 20–40 years of age. Mature cystic teratomas constitute 10%–20% of all ovarian tumors and also the most frequent germ cell tumor of the ovary.^[2] The presence of ectodermal tissue

is common in mature teratomas, and majority of them have skin and adnexa so that some author still prefer the old term dermoid cyst although nomenclature is inaccurate, because, in addition to that, ectodermal, endodermal, and mesodermal tissue are also seen.^[3] The WHO classification of ovarian tumor has separated epidermoid cyst from dermoid cyst^[4] this is because the epidermoid cyst is considered to arise from squamous metaplasia of epithelium elements without evidence of mesodermal or endodermal tissue. Glial tissue is reported to be a common neural component of mature teratoma,^[5] and the presence of well-organized cerebellum and choroid plexus is also reported. A few number of case reports have been

Address for correspondence: Dr. Seema Dayal,
Department of Pathology, Uttar Pradesh University of Medical Sciences,
Saifai, Etawah, Uttar Pradesh, India.
E-mail: seemadayal77@rediffmail.com

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published on neural elements in mature teratoma, but as per the literature search, no original article had been seen depicting this. Thus, this study was conducted with plan to access the correlation of clinical findings with histopathology of mature ovarian tumors with more emphasis on neural elements, the types of neural elements, and its coexistence if any.

MATERIALS AND METHODS

This is a retrospective study conducted in the Department of Pathology, Uttar Pradesh University of Medical Sciences, Saifai, Etawah (UP), from January 2008 to April 2019 and included 54 cases of mature ovarian teratomas. All the cases were studied with reference to age, size, clinical profile, gross, and microscopy, that is., histopathology and immunohistochemistry as per need. Surgically excised ovarian masses were sent in 10% formal saline to be fixed, grossed, and processed, multiple sections were made at 3–4 μ and stained with H and E, whenever required immunohistochemistry was applied. Slides were screened and reviewed. Ethical clearance on histopathological evaluation of hysterectomies was taken, permission from head of institution was also taken before conducting this study.

RESULTS

A total of 54 cases were studied. The most common age group affected with ovarian teratoma was 21–30 (31.48%) years [Table 1], the youngest being 8 years, and oldest 60 years. The common complaint documented was abdominal pain 37 (68.51%), followed by mass per abdomen in 25 (46.29%) [Table 2]. The smallest tumor size was 1.2 cm \times 0.8 cm \times 0.6 cm, whereas the largest was 16 cm \times 14 cm \times 5 cm with an average size of 6 cm. For gross evaluation, the details were noted from histopathology records duly maintained in the departmental archive. On gross examination, most of the tumors were unilateral 53 (98.14%) mostly these have hairs tufts with sebaceous material seen in 34 (61.81%), followed by putty-like material 32 (58.18%), bony elements with teeth and cartilage 5 (9.09%) [Table 3]. Microscopic examination confirmed the presence of squamous epithelium and its adnexal structure 52 (94.54%) [Table 4]. Neural elements were seen in 14 (25.45%) cases which comprised glial tissue, ganglion cells, melanotic cells, choroid plexus, and cerebellum [Table 5]. In all the cases of mature teratoma with neural tissue, adipose tissue was also found. The other pathologies seen were struma ovarii (11%), yolk sac tumor (1.8%), fibroma (1.8%), and thecoma (1.8%). Microscopically, struma ovarii was diagnosed in six cases of mature teratoma whereas one case was having struma ovarii and neural elements together.

DISCUSSION

Mature ovarian teratomas are germ cell tumors which show differentiation along with embryonic rather than extra embryonic pathways. Willis described teratomas as composed

Table 1: Age group of patients presenting with ovarian teratoma

Age group (years)	Total number of cases, n (%)
Under 20	8 (14.81)
21-30	17 (31.48)
31-40	11 (20.37)
41-50	15 (27.77)
Above 50	3 (5.55)
Total	54 (100)

Table 2: Complaints of patients presenting with mature ovarian teratoma

Clinical presentation	Total number of cases, n (%)
Pain	37 (68.51)
Mass per abdomen	25 (46.29)
Abnormal vaginal bleed	20 (37.03)
Pressure symptoms	18 (33.33)
Infertility	5 (9.2)
Others	3 (5.5)

Table 3: Gross finding of ovarian teratomas

Gross findings	n (%)
Tumor size (cm)	
<5	6 (10.90)
5 and more	27 (49.09)
Putty material	32 (58.18)
Hairs with sebaceous material	34 (61.81)
Bony elements with teeth and cartilage	5 (9.09)
Fatty material	2 (3.6)
Others	5 (9.09)

Table 4: Neural elements with other tissue and pathologies in mature ovarian teratoma

Microscopic elements	n (%)
Neural	14 (25.45)
Skin and its adnexa	52 (94.54)
Bone	4 (7.27)
Cartilage	13 (23.63)
Thyroid	6 (10.90)
Respiratory	8 (14.54)
Adipose tissue	23 (41.81)
GI	12 (21.81)
Others	6 (10.90)

GI: Gastrointestinal

of multiple tissues foreign to the parts, and they may arise in both benign and malignant forms. There are some theories regarding histogenesis, first one is being “gastrulation theory” which states that the teratomas arise from remnants of the primitive streak or primitive node, whereas second theory called “missed theory” which suggest that teratomas originate from totipotent primordial germ cells. These cells develop

Table 5: Different neural elements seen in mature cystic teratoma

Neural elements	n (%)
Glial tissue	11 (78.57)
Choroid plexus	3 (21.42)
Ganglion	3 (21.42)
Melanotic cells	3 (21.42)
Nerve fibers	2 (14.28)
Cerebellum	1 (7.1)

among the endodermal cells of the yolk sac near the origin of the allantois and migrate to the gonadal ridge during 4 and 5 weeks of gestation. A few number of cells miss their target destination and produce teratoma. This theory explains the origin of gonadal teratomas. The third theory is called “incomplete twinning.”^[6]

The site of teratoma presentations is gonads which include ovary, testis, and extragonadal tissue including lung, mesentery, mediastinum, retroperitoneal, nasopharyngeal omentum, and brain. In ovary, there are about 10%–20% ovarian tumors and is the most frequent germ cell tumor of the ovary.^[7] They often occur in individuals of reproductive age group, between the age range of 20–40 years^[8] similar to findings in the present study. Unilateral ovarian teratoma is frequently seen, whereas only 10%–15% of ovarian teratomas are bilateral.^[1] Here, we found unilateral ovarian teratomas in 53 (98.14%) cases. For unknown reasons, they are found more in the right side^[9,10] as is noted by us in the present study.

Abdominal pain may arise because of torsion, hemorrhage, infection, and pressure effects.^[11] Abdominal pain was the most frequent clinical complaint (68.51%), which might happened due to pressure effects of ovarian masses owing to their size and cystic components. The presence of fertility and infertility is difficult to access in ovarian mature teratoma but infertility may result because of recurrent endometriosis.^[12] In the current study, a young female was also diagnosed with mature teratoma ovary during her pregnancy.

Gross examination of mature ovarian teratoma characteristically reveals a thin wall cyst lined with an opaque, gray-white wrinkled apparent epidermis, and from wall hair shafts protrudes along with greasy content which is made up of keratin, sebum, and hair. Teeth and sometimes human body-like structures are seen in mature ovarian teratomas called homunculus.^[3,13] In this study, abovementioned contents are seen.

Histopathology is used as confirmatory diagnostic tool for the diagnosis of mature cystic ovarian teratoma. With the help of histopathology, we can access the ectodermal, mesodermal, and endodermal components. Blackwell and Dockerty found ectodermal derivatives in 100% of the teratomas, mesoderm structures in 93%, and endodermal in 71%.^[14] Skin appendages and neural elements, particularly glial tissue, are extremely common, followed by cartilage,

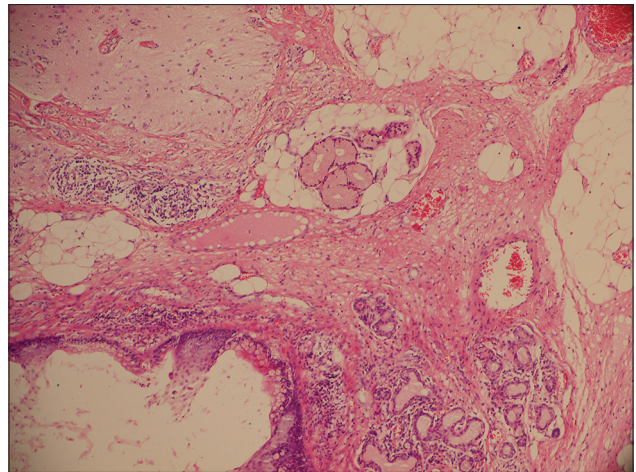


Figure 1: H- and E-stained section of mature cystic teratoma showing adipose tissue, glands, and neural elements

respiratory tissue, and gastrointestinal tract tissue [Figure 1]. In the current study on histopathology examination, skin and adnexa were frequent findings (94.54%), and similarly, neural element was also found common (25.45%). In every case, neural elements were found associated with skin and its adnexa, followed by adipose tissue. In teratoma, different types of neural components are found. Neural elements may be seen in ovarian teratoma as neurogenic cyst which is a monodermal teratoma and predominantly comprises neural tissue.^[15] The other neural elements seen in relationship with ovarian teratoma are gliomatosis peritonei and different neural elements admixed with tissue other than neural such as glial tissue, ganglion, choroid plexus, cerebellum, nerves, and melanotic cells. Gliomatosis peritonei is a rare disease characterized by peritoneal and omental implant with ovarian teratoma found in the majority with immature teratoma.^[3] The Marcial Rojas and Medina reported 22%–47% peripheral nerves, 25%–41% brain tissue, 19%–25% ependymal cells, and 19%–22% ganglionic cells.^[16] We have found neural elements in 14 (25.45%) cases of mature ovarian teratomas out of which glial tissue was also found in (78.57%) cases, choroid plexus in cases (21.42%), ganglion (21.42%), melanotic cells (21.42%), nerve fibers (14.28%), and cerebellum (7.1%) [Figure 2]. GFAP is an intermediate filament protein which is expressed in various cell types of central nervous system (CNS). It is highly expressed in the glial tissue of mature teratoma thus suggesting that the GFAP expression is a indicator of teratoma maturation.^[17] Its expression was also seen in our study [Figure 3]. The another common immunomarker for neural tissue is S100, which was first isolated from the CNS. Its immunoreactivity is seen in glial tissue, that is., astrocytes, oligodendrocytes, ependymal cells, Schwann cells, and melanocytes.^[18] Similar results were found in our study [Figure 4]. The other pathologies seen in our study along with teratomas were yolk sac tumor, fibroma, and thecoma, respectively. Struma ovarii was seen in six cases (11%) and in one case found along with neural elements. Mature cystic teratoma may exist with fibroma

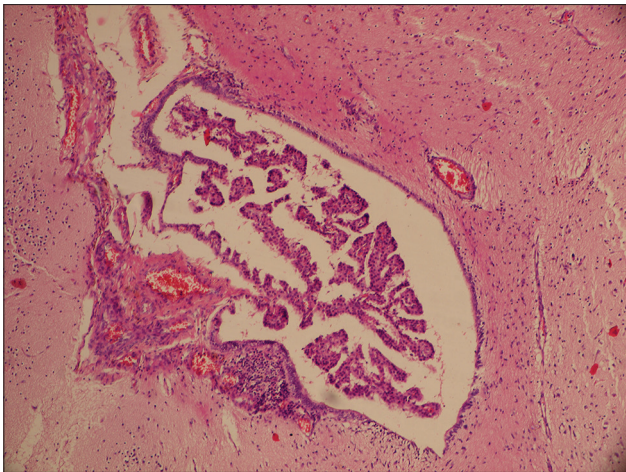


Figure 2: H- and E-stained section of mature cystic teratoma showing choroid plexus with other neural elements

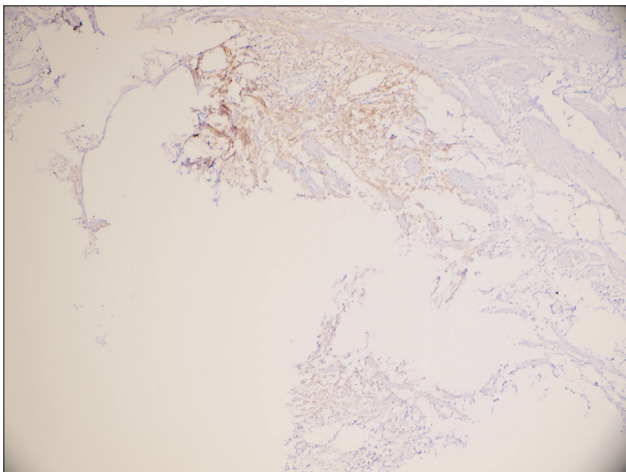


Figure 3: Focal immunopositivity of GFAP in mature cystic teratoma signifying neural tissue

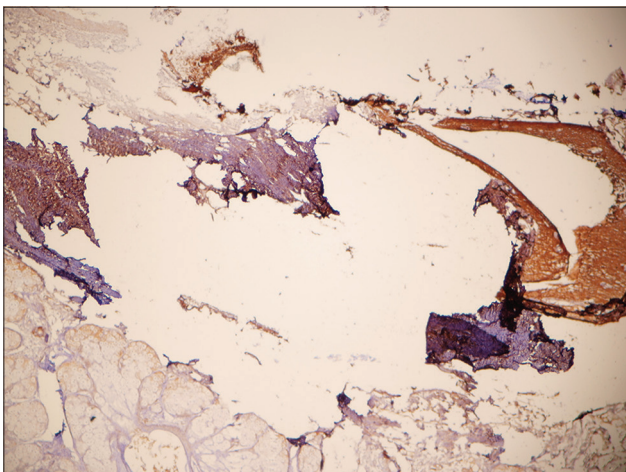


Figure 4: Strong immunopositivity of S-100 in mature cystic teratoma also signifying neural tissue

and thecoma.^[19,20] This was also seen in current research. Yolk sac tumor with ovarian teratoma is rare finding that

we found in our research. Struma ovarii is the variant of monodermal teratoma which shows the expression of the dominant growth of thyroid tissue in teratoma. This was first described in 1889. It comprises <3% of ovarian teratomas.^[21] In the present study, we have found six cases of struma ovarii (11%) among them one case of struma ovarii was also having neural elements. The presence of struma ovarii with neural elements is a rare, but it is also reported in the literature.^[22]

CONCLUSION

Mature ovarian teratoma is the common variant of ovarian tumor. Histopathology examination of ovarian masses is a gold standard diagnostic test and mandatory to diagnose teratomas. Ovarian teratoma contains tissues from different germ layers. Ectodermal components such as skin and its adnexa are commonly seen. The neural elements in teratoma are also found and it was frequent to found neural elements with adipose tissue although both arises from different dermal tissue. Further studies must be carried out with large numbers of cases to fully investigate the significance of neural elements in mature teratomas.

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Conflicts of interest

There are no conflicts of interest.

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