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LITERATURE REVIEW

Immature Teratoma and Mature Cystic Teratoma

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Abstract

***Introduction** :* Germ cell tumors arise from primordial germ cells and account for about 30% of all ovarian tumors. More than 95% of this group are benign dermoid cysts (mature cystic teratoma) and the remaining 5% are malignant. Ovarian teratomas represent 15% to 20% of ovarian germ cell tumors. Teratomas are classified as mature or immature and often consist of several embryological layers. While the mature type is benign, the immature type is more aggressive.

***Objective** :* Based on the above, this article will review about immature teratoma and mature cystic teratoma of the ovary.

***Material and methods** :* The method of writing this scientific paper is a literature review. The data used are sourced from relevant literature and in accordance with the topics discussed.

Result : Teratomas are a common form of germ cell tumors. Teratomas are histologically defined as tumors containing tissue derived from all germ cell layers: ectoderm, mesoderm, and endoderm. Teratomas are classified as immature teratoma, mature teratoma and monodermal teratoma. ***Conclusion** :* Teratomas are usually asymptomatic and if there are symptoms, they tend to be non-specific. In patients with no residual tumor after surgery, the survival rate is 90-100%.

Keywords: *Teratoma, Immature Teratoma, Mature Cystic Teratoma*

BACKGROUNDS

Germ cell tumors are the second largest group of ovarian neoplasms after ovarian surface epithelial tumors and account for about 30% of all ovarian neoplasms. Mature cystic teratoma is the most common type (95%) with the majority occurring in adults and the remaining 5% being malignant.[1,2] Malignant germ cell tumor (MGCT) represents about 3% of all ovarian cancers in Western countries and about 20% in Asian and African populations, where epithelial cancer is less common.[3]

Malignant ovarian germ cell neoplasms account for less than 5% of ovarian cancers. However, because these tumors mainly involve women during the reproductive years, treatment with fertility preservation is an important issue. Germ cell neoplasms are interesting because several processes are involved in their origin that are associated with early embryonic development, reproduction, and sex determination. There are various types of histologic types, including: dysgerminoma, immature teratoma, yolk sac tumor, choriocarcinoma, polyembryoma, and mixed MOGCT. This group differs from ovarian

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epithelial cancer, in two aspects, namely a younger age and good prognosis, due to the higher number of diagnoses in the early stages and high chemosensitivity.[4,5]

Ovarian teratomas represent 15% to 20% of ovarian germ cell tumors. Teratomas are classified as mature or immature and often consist of several embryological layers. While the mature type is benign, the immature type is more aggressive. Mature cystic teratoma is the most common type, 8-15% bilateral, but some cases are reported to be bilateral and multiple.[6]

The origin of ovarian teratomas has been the subject of speculation and dispute for centuries. The parthenogenetic theory, which states the origin of primordial germ cells, is now more widely accepted than the theory of teratoma originating from blastomeres separated at an early stage of embryonic development, or the theory of teratoma originating from rest embryos.[4,5]

Based on the above and the number of cases found in daily practice, this article will review this ovarian teratoma more deeply.

IMMATURE TERATOMA

Immature teratoma is a tumor consisting of tissue derived from three layers of embryonic germ cells, ectoderm, mesoderm, and endoderm. In contrast to mature teratomas, immature teratomas contain immature components (usually primitive/neuroectodermal embryonic tissue) including in their most primitive form, embryoid bodies.[7,8]

Immature teratomas are the third most common germ cell tumor, accounting for 15-20% of all primitive germ cell tumors and 3% of all ovarian teratomas. These tumors can occur at any age, but are more common in the first two decades of life.[9] The origin of teratomas has been a matter of interest, speculation, and debate for centuries. The parthenogenic theory, which suggests the origin of primordial germ cells, is now the most widely accepted.[2]

Immature teratomas usually present as a pelvic mass, increased abdominal circumference, and vaginal bleeding. Isosexual precocity is rare, but serum markers, particularly AFP and hCG, are generally elevated. Ultrasound usually distinguishes these tumors from benign cystic teratomas, although some solid components such as goiter may cause confusion.[8]

On ultrasound examination, the appearance of an immature teratoma is nonspecific, although the tumor is usually heterogeneous, the lesion is partially solid, usually with scattered calcifications. On CT and MRI imaging, immature teratomas usually have a large, irregular solid component with calcifications. Small foci of fat help identify these tumors (figure 1).[10]

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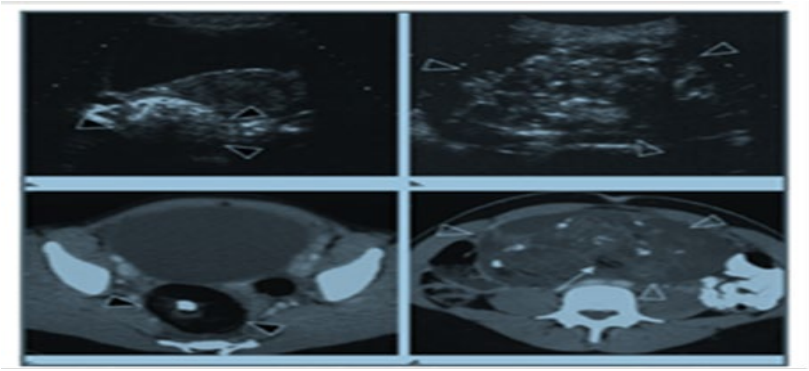

Figure 1. Ultrasound and CT scan of immature teratoma[10]

These tumors are usually unilateral, large, predominantly solid, fleshy, gray in color and may contain cysts, hemorrhages and necrosis. These tumors are usually unilateral, but may coexist with a mature cystic teratoma, as seen in at least 10-15% of cases. Immature teratoma size is usually larger than mature teratoma, with a reported range of 9 to 28 cm. It may be a round, oval, or lobulated solid mass, soft or hard, which often contains a cystic structure with solid areas within the cyst wall (Figure 2).[2]

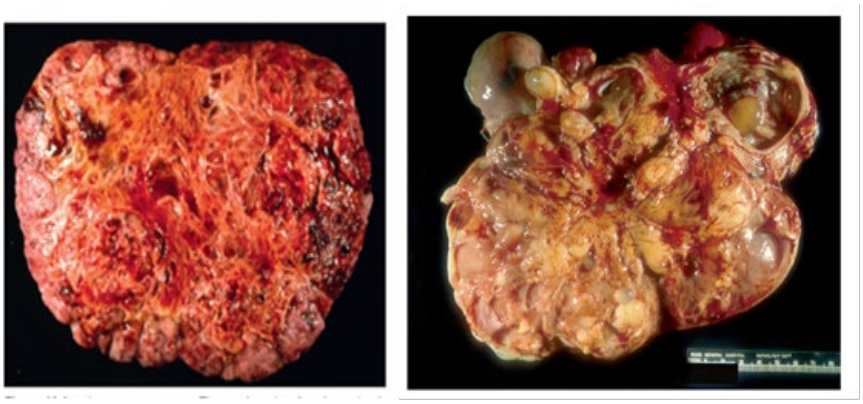

Figure 2. Macroscopic immature teratoma[3]

Microscopically, immature teratomas are found to be immature embryonic variables, mostly in the form of neuroectodermal tubules and rosettes, but occasionally with mitotically active cellular components (glia), mixed with ectodermal elements and endodermal, with varying degrees of maturation. The tubules are lined by overlapping, hyperchromatic cells with multiple mitoses. Immature cartilage, adipose tissue, bone and skeletal muscle are often found. The most primitive component of immature teratoma is in the form of embryoid bodies formed from yolk sac epithelium whose epithelium resembles embryonal carcinoma (dominant tumors composed of embryoids, which die are called polyembryoma). Extensive proliferation of reactive blood vessels can be seen in immature teratomas. (figure 3).[3,5,7]

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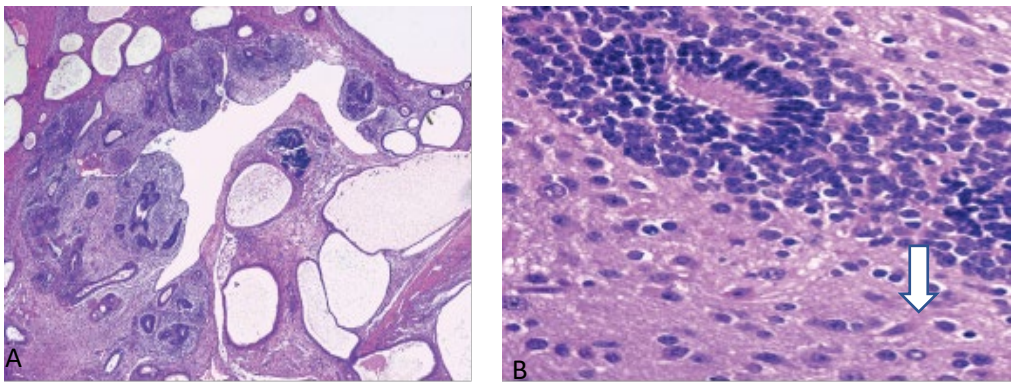

Figure 3. Microscopy of immature teratomas. a). Immature neuroepithelial and mesenchymal elements, b). glial tissue with neuroepithelial tubules[3,5]

O'Connor and Norris proposed that immature teratomas should be divided into two classes, namely those with less immature grades (grade 1; low grade), those not treated with combination chemotherapy, and those with more pronounced immaturity (grades 2 and 3; high grade). (Table 1).[2,7]

Table 1. Grading immature teratoma

Grade	Histological criteria
Grade 1	Tumours with rare foci of immature neuroepithelial tissue that copy <1 low power field (40x) in any slide (kk
Grade 2	Tumours with similar elements, occupying 1-3 low power fieds (40x) in any slide (highr grade)
Grade 3	Tumour with large amount of immature neuroepithelial tissue ocupying >3 low power fields (40x) in any slide (high grade)

Various types of immunohistochemical examination can be performed on this immature teratoma, including SALL4 positive in intestinal and nervous tissue (figure 1.4a). SOX2 identifies more specific areas of immature nerves, and is useful for grading immature teratomas (figure 1.4b). Glypican-3 may also exhibit unequal neuroepithelial immunoreactivity.[3,7]

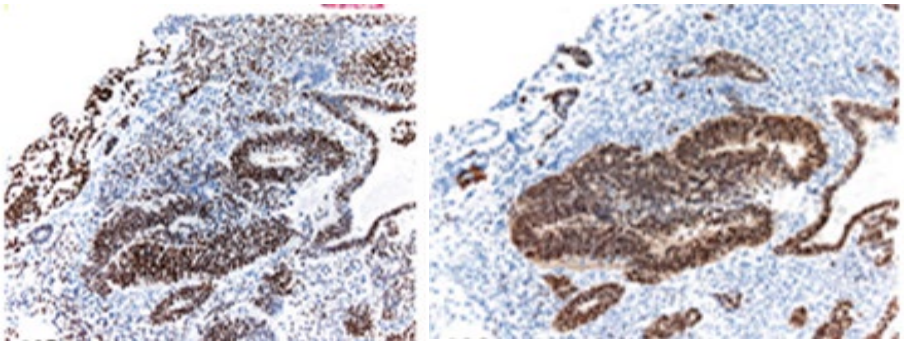

Figure 4. Immunohistochemistry. a) Tubules expressing SALL4, b) Neuroepithelial tubules with strong SOX2 expression[3,7]

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Management of immature teratoma, among others, in a young patient whose tumor appears to be localized to one ovary (stage IA), unilateral and surgical salpingo-oophorectomy should be performed. If fertility is not a problem, or the contralateral ovary or uterus is involved, total abdominal hysterectomy and bilateral salpingo-oophorectomy should be performed. Patients with stage IA, grade 1 tumors or who have exclusively mature glial implants (grade 0) have an excellent prognosis and are treated with surgery alone. Patients with grade 2 or 3, stage IA, or with immature implants should undergo combination chemotherapy. VAC regimens have been replaced by platinum-containing regimens such as cisplatin, etoposide, and bleomycin (BEP).[11,12]

In patients with no residual tumor after surgery, the survival rate is 90-100%. The prognosis is less favorable for patients with residual tumor or recurrent immature teratomas. After chemotherapy, the implant is usually lost, or replaced by mature, necrotic, or fibrotic tissue.[3]

MATURE CYSTIC TERATOMA

Tumors consisting of mature tissue originate from two or three germ layers (ectoderm, mesoderm and endoderm). Tumors are usually cystic (mature cystic teratoma), but rarely solid (mature solid teratoma).[7]

Mature teratomas occur over a wide age range, from infancy to lifelong, even in the ninth decade, although with the greatest incidence during the reproductive years, (80% or more). Mature teratoma is an ovarian neoplasm that most often occurs in children under 15 years of age. Mature cystic teratoma is the only ovarian germ cell neoplasm that occurs in the first year of childhood.[5,7]

Mature cystic teratomas are diploid, have a normal 46XX karyotype, and are ascribed to germ cells after the first meiotic division. Mature ovarian teratoma differs from mature postpubertal testicular teratoma which is malignant, aneuploid, having complex cytogenetic abnormalities including 12p amplification. Ovarian cystic mature teratoma and testicular prepubertal mature teratoma are similar in that they are both diploid, have normal and benign karyotypes.[4,13]

Teratomas are usually asymptomatic and if there are symptoms, they tend to be non-specific. Symptoms present in patients include abdominal pain, abdominal mass, most tumors are incidental findings on imaging studies or at the time of surgery. Ten percent are bilateral. Abdominal pain is the most common symptom, followed by abnormal uterine bleeding. Complications include torsion, acute or subacute rupture (more common during pregnancy), infection, idiopathic autoimmune hemolytic anemia, virilization.[4,13]

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Ultrasonography most often shows a cystic lesion of a dense echogenic tubercle (Rokitansky nodule) protruding into the lumen. The presence of bone confirms the diagnosis. The second manifestation is a diffuse or partial echogenic mass with localized echogenicity usually showing sebaceous material and hairs, whereas the third manifestation consists of several thin echogenic bands caused by hairs in the cyst cavity. On CT scan, mature cystic teratoma is seen as a complex mass with septal division, variable attenuation, calcification and presence of fat. If the tumor contains fat, it can also be differentiated by MRI (figure 5).[2,13]

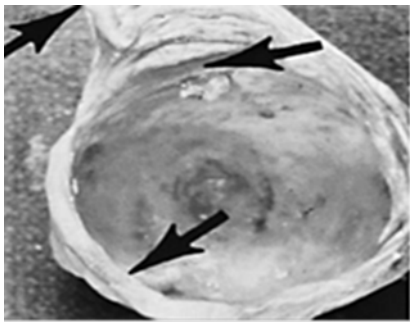

Figure 5. CT scan of mature cystic teratoma, spherical cystic mass with capsule[2]

Mature teratomas are almost always bilateral cystic tumors in about 15% of cases. They range in size from 0.5 to 4cm (average 15cm), but are often <10 cm long, and have a smooth, grayish-white surface. The cross section is a unilocular cyst or a multilocular cyst covered with skin containing sebaceous material and hair. Dense nodules are composed of fatty tissue. with teeth or bone usually protrudes into the lumen of the cyst (Rokitansky bulge). Dermoid cysts can contain a variety of mature somatic tissue that can be seen with the naked eye, such as brain tissue, bone, cartilage, adipose tissue, mucus cysts, and thyroid (Figure 6).[2,9]

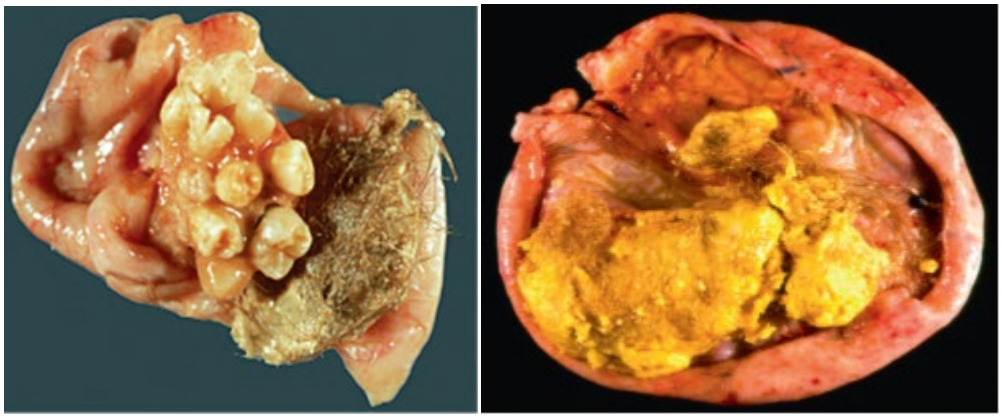

Figure 6. Macroscopic mature cystic teratoma. Cyst containing bone, teeth and hair[2,9]

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Microscopically, mature cystic teratoma found tissue originating from the three germ layers. The ectodermal tissue is represented by squamous epithelium and other skin adnexa, usually the most abundant. Brain tissue, glia, nervous tissue, retina, choroid plexus, and ganglia may also be encountered. Mesodermal tissue is represented by bone, cartilage, smooth muscle, fibrous tissue and fat. Endodermal tissue is represented by gastrointestinal, bronchial, glandular, thyroid, and salivary gland tissues. In a study of 100 cases, ectodermal structures were found in 100%, mesodermal in 93%, and endodermal in 71% of cases. Rare tissues, such as the prostate, have been found (Figure 7).[9,16,17,18]

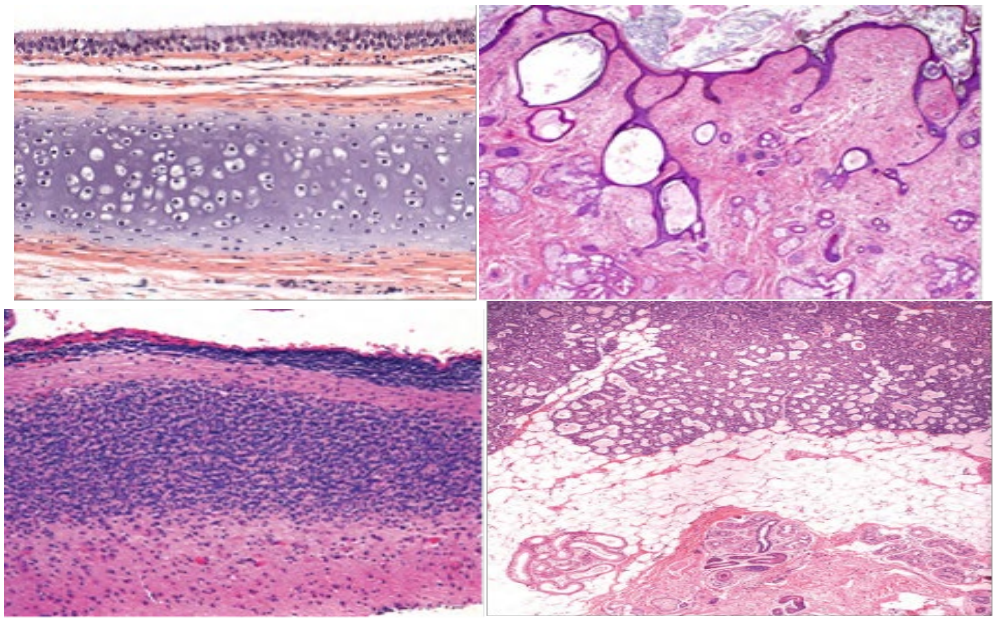

Figure 7. Microscopy mature cystic teratoma, a). respiratory epithelial tissue and cartilage, b) squamous epithelium and skin adnexa, c) brain tissue, d). salivary glands [2,3,5]

Immunohistochemical examination of mature cystic teratoma, namely GFAP and Nestin.[14] Mature cystic teratomas (dermoid cysts) are treated conservatively, especially in children and adolescent girls. Ovarian cystectomy is the treatment of choice. This tumor is a benign tumor and most patients are young at the time of diagnosis, conservative surgery is recommended, with complete resection of the cyst to avoid recurrence. Management should include examination of the opposite ovary to determine involvement.[3,15,16,17]

These mature cystic teratomas are benign, unless malignant transformation occurs. Overall about 4% of adult cystic teratomas recur, according to one study. Tumors that are bilateral, involving women under 30 years of age, and those greater than 8 cm in diameter are more likely to recur.[5,7,19,20]

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CONCLUSION

Histologically, immature teratomas are graded according to WHO and AFIP. Immature teratomas have 3 components with immature tissue, in contrast to mature teratomas which have 3 components (ectoderm, mesoderm, endoderm) without immature tissue. Mature cystic teratomas are benign, unless malignant transformation occurs whereas immature teratomas are more aggressive.

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