Gac Méd Caracas 2022;130(Supl 1):S7-S14
DOI: 10.47307/GMC.2022.130.s1.3

Immature Teratoma Ovarium in Young Women: Two Case Reports and Literature Reviews

Teratoma ovárico inmaduro en mujeres jóvenes: informes de dos casos y revisión de la literatura

Ni Putu Ekawati[1a*], I Wayan Juli Sumadi[2a], Ni Made Mahastuti[a], I Made Wirya Santosa[a]

SUMMARY

Immature teratoma is teratoma that contains several variations of immature tissue, including primitive forms and embryoid bodies. This type of neoplasm is rare, accounting for less than 1 % of all ovarian tumors and 20 % of malignant germ cell tumors in the ovarium. The incidence occurs in young women usually in the first two decades of life and rarely occurs in postmenopausal women. Two cases of immature teratoma were reported in women aged 16 and 25 with abdominal swelling and lower abdominal pain. Macroscopic examination of the first case revealed some solid, some cystic, containing hair, bones, teeth, and dermal plaque. Routine histopathologic examination showed tumors consisting of ectoderm, mesoderm, and endoderm components, as well as an immature neuroectodermal component with a pseudorosette. Macroscopic examination of the first case revealed a solid mass, containing bones and hair. The tumour consists of ectoderm, mesoderm, and endoderm components, in the form of immature cartilage, immature mesenchymal and neuroectodermal cells that form tubular structures, and some rosette-shaped features. The primitive neuroectodermal cells were oval-shaped, narrow cytoplasm with an increased N/C ratio, and the hyperchromatic nucleus was arranged in a stratified way. Based on clinical data and histopathologic examination, those patients were diagnosed as having grade 2 and grade 3 immature teratoma.

Keywords*: Immature teratoma, ovary, young woman.*

RESUMEN

El teratoma inmaduro es un teratoma que contiene varias variaciones de tejido inmaduro, incluidas formas primitivas y cuerpos embrioides. Este tipo de neoplasia es poco frecuente, representa menos del 1 % de todos los tumores de ovario y el 20 % de los tumores malignos de células germinales en el ovario. La incidencia ocurre en mujeres jóvenes generalmente en las primeras dos décadas de vida y rara vez ocurre en mujeres posmenopáusicas. Se informaron dos casos de teratoma inmaduro en mujeres de 16 y 25 años con hinchazón y dolor abdominales bajo. El examen macroscópico del primer caso reveló algo sólido, algo quístico, que contenía cabello, huesos, dientes y placa dérmica. El examen histopatológico de rutina mostró tumores que consistían en componentes de ectodermo, mesodermo y endodermo, así como un componente neuroectodérmico inmaduro con una pseudoroseta. El examen macroscópico del primer caso reveló una masa sólida que contenía huesos y pelo. El tumor consta de componentes de ectodermo, mesodermo y endodermo, en forma de cartílago inmaduro, células mesenquimatosas y neuroectodérmicas inmaduras que forman estructuras tubulares y algunas características en forma de roseta. Las células neuroectodérmicas

DOI: https://doi.org/10.47307/GMC.2022.130.s1.3

ORCID ID: 0000-0001-6607-2259[1]
ORCID ID: 0000-0003-3971-2438[2]

[a]Anatomical Pathology Department, Faculty of Medicine, Udayana University, Sanglah Hospital, Bali, Indonesia

*Corresponding Author: Ni Putu Ekawati
E-mail: niputu.ekawati@yahoo.com

Recibido: 1 de mayo 2022
Aceptado: 3 de mayo 2022

primitivas eran de citoplasma estrecho, de forma ovalada, con una relación N/C aumentada, y el núcleo hipercromático estaba dispuesto de forma estratificada. Según los datos clínicos y el examen histopatológico, a esos pacientes se les diagnosticó teratoma inmaduro de grado 2 y grado 3.

Palabras clave: *Teratoma inmaduro, ovario, mujer joven.*

INTRODUCTION

Immature teratoma (1,2) is teratoma that contains several variations of immature tissue (typically primitive/embryonal neuroectodermal), including primitive forms and embryoid bodies (3). These cases are rare, accounting for less than 1 % of all ovarian tumors and 20 % of malignant germ cell tumors in the ovaries (4,5). Immature teratoma mostly occurs in young women less than 30 years old and is very rare at an older age (6).

The most common symptoms of this ovarian teratoma are complaints due to surrounding pressure, resulting in pelvic pain, as well as irregular bleeding. These symptoms can be found in complications of torsion, rupture, peritonitis, and autoimmune hemolytic anemia (7-10).

Here are two cases of Immature Teratoma that occurred in a 16-year-old and a 25-year-old woman. This case was raised because immature teratoma malignancy cases are very rare compared to benign tumors in cystic mature teratomas (11); the cases also have various types of immature components.

CASE DESCRIPTION

The first case was of a 16-year-old woman who came to the hospital complaining of abdominal enlargement (12) over 2 months. She also suffered from pain during menstruation, which was prolonged and profuse. Physical examination was within normal limits.

Ultrasound examination revealed enlargement of the uterus with a solid cystic mass of 30x30x25 cm, lobulated, ultrasound result concluded there was a solid cystic mass originating from the adnexa consistent with ovarian mass suspected malignancy and a Salfingo-oophorectomy-omentectomy was performed. Ovarian and tubal tissue was sent to the Anatomy Pathology laboratory of Sanglah Hospital for examination and omentum was sent to the Anatomy Pathology Laboratory Center for examination. A macroscopic examination of the tumor was carried out on a piece of ovarium tissue received in a plastic bag containing a piece that had been split into a size of 26x 18x 11 cm with an attached tube 12 cm in size, diameter about 0.3-0.5 cm. The cut section revealed clear liquid, a solid partially cystic mass with a wall thickness of about 0.3 to 1 cm; the tumor also contained hair, bones, and teeth. A dermal plaque was found about 2 cm in diameter (Figure 1).

Macroscopic examination of the omentum preparation showed fat tissue 13x10x3 cm in size within the haemorrhagic area.

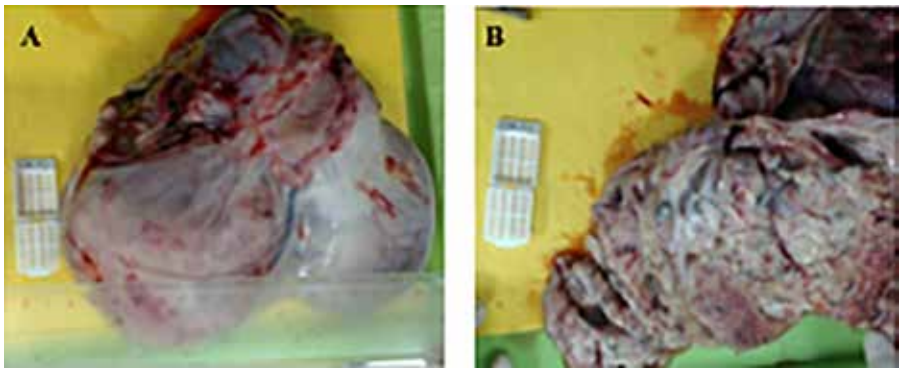

Figure 1. Case 1. Macroscopic (A) solid mass. (B) Solid consistency partly cystic, also visible areas of necrosis and haemorrhagic.

Routine histopathology examination showed the ovarian tissue consisted of ectoderm, mesoderm, and endoderm components. The ectoderm components were skin epithelial and adnexal (epidermis, hair follicles, sebaceous glands) and neural tissues comprising glial cells (Figure 2).

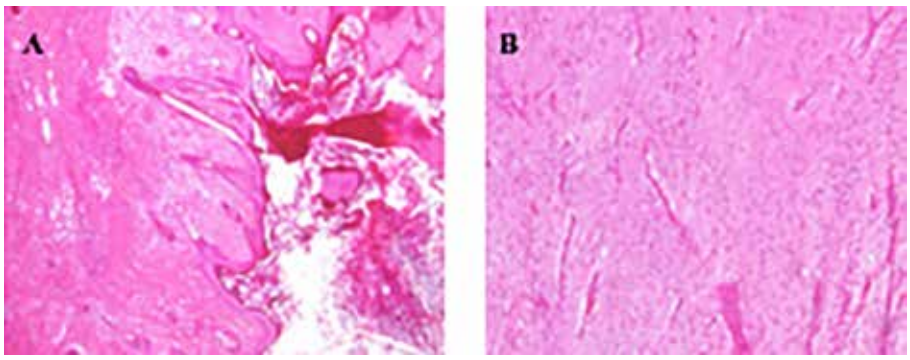

Figure 2. Case 1 Ectodermal component (A) skin epithelial, hair follicle, sebaceous. (B) Neural tissue (glial cells).

The mesoderm components (13) were cartilage and compact bone and mature fat cells (Figures 3A and 3B). The endodermal components were gastrointestinal and respiratory epithelial cells (Figure 3C). At the edge of the tissue, 2 foci of immature neuroectodermal components with pseudorossete form were found. The cells were arranged stratified, columnar, and hyperchromatic (Figure 3D). Tuba fallopii consist of mucosal, muscular, and serous layers. No visible infiltration of malignant cells was found in this preparation. Omentum contained glial tissue proliferation arranged in lobules of various sizes, tissue edges were surrounded by mesothelial cells with some foci which appeared to be proliferative, the surrounding stroma contained inflammatory cells, blood vessels, and haemorrhagic foci (Figures 3E and 3F). Based on a routine histopathology examination above, this case was concluded as a grade 2 immature teratoma.

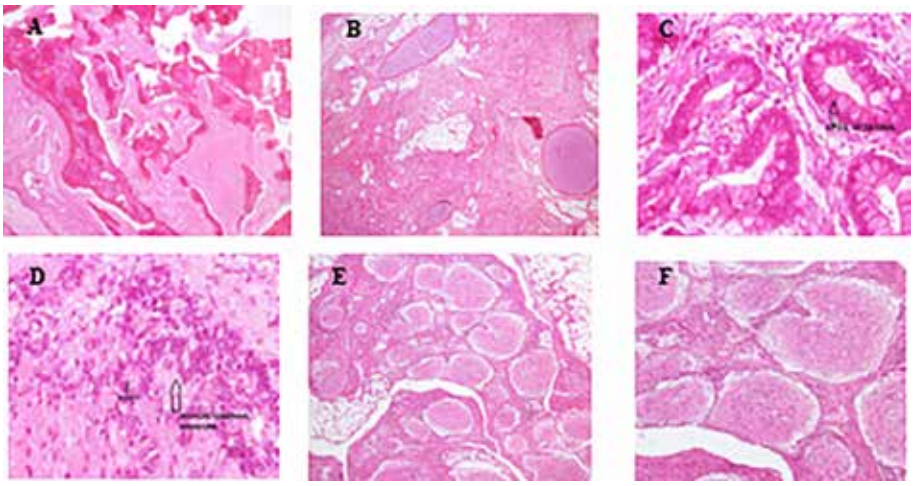

Figure 3. Case 1 Mesodermal Component (A) cartilage tissue, matured fat. (B) compact bone tissue, glial cells. (C) Endoderm Components (Intestinal). (D) Immature neuroectodermal Components. (E) Endoderm component (Gliomatosis peritonii) magnification 4x. (F) Magnification 40x

The second case was of a 25-year-old woman with abdominal enlargement over 4 weeks. She suffered from fever, decreased appetite, and stomach pain. Physical examination was within normal limits. Laboratory examination revealed LDH 817 (240-480 U/L) and AFP 3.711 ng/mL(N≤15). Ultrasonography revealed a normal-sized uterus. The right and left adnexa showed a solid cystic mass from the adnexa to the abdominal cavity, which measured approximately 11x11x14 cm, invisible enlargement of the lymph nodes in the paraorta, free fluid in the abdominal cavity and pelvic cavity were found by an echo. Impression: the cystic solid mass derived from the adnexa was consistent with an ovarian mass suspected malignancy (Figure 4).

Figure 4. Ultrasound abnormal adnexa right; left: a solid cystic mass visible from the adnexa to the abdominal cavity.

Salfingo-oophorectomy was performed and tissue was sent to the laboratory of Anatomy Pathology, Sanglah Hospital for examination. The size of the right ovarian cyst was 20x17x7 cm. The cut section revealed a solid mass, whitish-gray and brittle. Also found was clear yellow liquid, with bone and hair, a cyst wall thickness of about 0.3-1 cm in size (Figure 5).

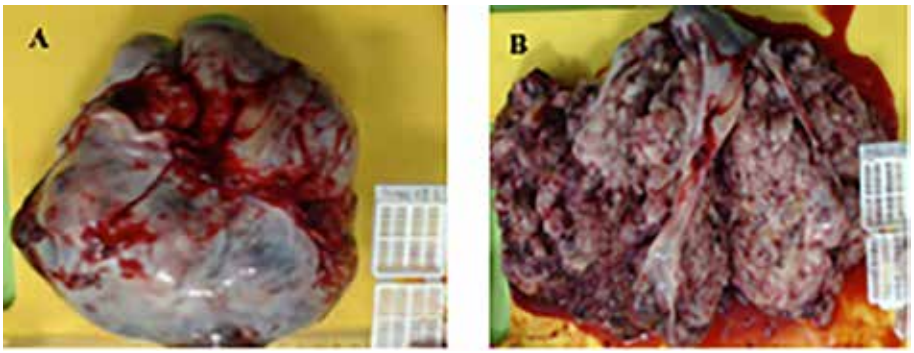

Figure 5. Case 2. Macroscopic (A) solid mass. (B) Gray white partially solid partly cystic mass and the visible area of necrosis and haemorrhage.

Histopathologic examination of the left ovary found ovarian tissue consisting of ectoderm, mesoderm, and endoderm components. The ectoderm components were squamous epithelial cells and their adnexal, hair follicles, and sebaceous glands (Figures 6A and 6B).

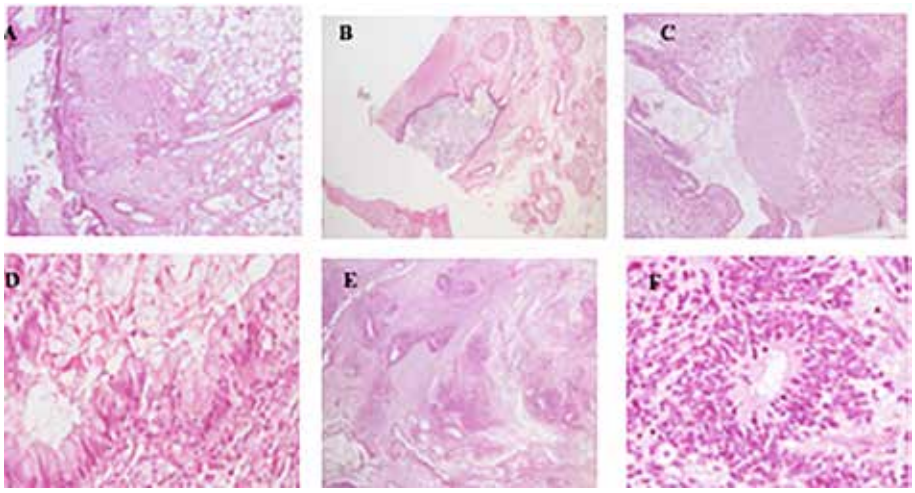

Figure 6. Macroscopic image (A) solid mass. (B) Gray white partially solid partly cystic and visible area of necrosis and haemorrhage. Ectodermal components (C) skin epithelial, hair follicles, fat tissue. (D) sebaceous gland. Mesoderm component (cartilage) (E). Endoderm component (gastrointestinal epithelial cells) (F).

The mesoderm components were cartilage, compact bone, and fat cells. The endodermal components were gastrointestinal and respiratory epithelial cells (Figures 6C and 6D).

Immature components were found in some focuses consisting of immature cartilage, immature mesenchymal, and neuroectodermal cells with a partial rosette tubular structure (Figure 6F), those primitive neuroectodermal cells with stratified oval cell morphology, narrow cytoplasm, increased N/C ratio, hyperchromatic nuclei (Figure 6E). Based on clinical, radiological, macroscopic, microscopic examination, the patient in the first case, from a routine histopathologic examination, was concluded to have grade 3 immature teratoma. Was concluded as grade 2- and second-class immature imatoma and the patient in the second case was concluded histomorphologically to have grade 3 immature Teratoma.

DISCUSSION

Immature teratomas are tumors derived from germ cell tumors of embryonic tissue consisting of three germ layers of ectoderm, mesoderm, and endoderm (14), teratomas contain various immature components (typically primitive or embryonic neuroectodermal tissue), including their most primitive forms namely embryoid bodies. Immature teratoma is the second most common germ cell tumor; this tumor can be purely a teratoma and sometimes has a mixed germ cell tumor component. Pure immature ovarian teratomas containing mature and immature tissue, only occur in about less than 1 % of all ovarian tumors, unlike cystic mature teratomas, which are commonly found during reproductive years at all ages. The incidence of immature teratomas occurs in young women in the first two decades of life and very rarely occurs in postmenopausal women (14,15). Other sources said clinical tumors are most commonly found in the first three decades of life (14). In this case, the women were 16 years old and 25 years.

Clinical features are usually asymptomatic until the tumor reaches a large size, typically larger (14-25 cm) than a cystic mature teratoma (mean 7 cm). Tumors tend to grow rapidly and may form a mass in the pelvic area and the lower abdomen can also cause symptoms of abdominal enlargement, pain, or torsion that causes acute abdominal pain. Signs and symptoms generally arise from the presence of adnexal masses in the uterus. Low serum alpha fetal protein (AFP) levels can be found in patients (14). In the

first case of a woman aged 16 years, the patient complained of abdominal enlargement over 2 months; ultrasound examination results obtained the enlarged uterus with a solid cystic mass with a size of 30x30x25 cm; lobulated, ultrasound results concluded a solid cystic mass originating from the adnexa consistent with ovarian mass suspected malignancy.

In the second case, the 25-year-old woman complained of abdominal enlargement over 4 weeks, with fever, decreased appetite, and stomach pain. Ultrasound examination (USG) revealed a normal-sized uterus, right and left adnexa showed a solid cystic mass from the adnexa to the abdominal cavity, which measured approximately 11x11x14 cm, invisible enlargement of lymph nodes in the paraorta; free fluid in the abdominal cavity and pelvic cavity was found by an echo. Impression: the cystic solid mass derived from the adnexa, consistent with ovarian mass suspected malignancy. Signs and symptoms generally arise from the presence of adnexal masses in the uterus. Low serum alpha-fetal protein (AFP) levels may be found in patients (14). In this case, low serum levels of 3.711 ng/mL (N <= 15) were examined.

Tumors macroscopically are generally unilateral, large, mostly solid, light gray, and may contain a haemorrhagic area, cysts, or necrosis (14). In the first case, there was ovarian tissue with a size of about 26x18x11 cm. The cut section revealed clear liquid, partly cystic, partially solid in consistency, a visible area of necrosis and haemorrhage. Hair, bones, teeth, and dermal plaque were also found. The second case, macroscopically, was a right ovary cyst, size 20x17x7 cm. On incision, it was found to be a solid mass, white-gray, and brittle. Also found was a clear yellow liquid, with bone and hair, and a cyst wall thickness about 0.3-1 cm in size.

Histopathological examination commonly contains immature tissue in various amounts. Most common are neuroectodermal (16) tubules and rosettes, but occasionally with active glial cell components, mitosis in significant amounts mixed with ectodermal and endodermal elements with varying levels of maturation. Neuroectodermal tubules are coated by hyperchromatic cells arranged in a stacked way with many mitose and may also contain pigments. Immature cartilage, fat tissue, bone, and striated muscle are common. Endodermal structures are liver tissue, immature gastrointestinal tissue, and a very rare form of embryonal kidney tissue. The most primitive immature teratoma component is in the embryoid bodies (embryoid bodies) composed of the yolk sac and germ disk which epithelium resembles the embryonic carcinoma composite (a predominant tumor composed of embryoid bodies called polyembriomas). The proliferation of blood vessels, with reactive features of the endothelium, can be seen in immature teratomas. Grading of immature teratoma based on the relative amount of neuroectodermal components is divided into grades 1 to 3, but the grading system into 2 (low-grade and high-grade) is now more commonly used (Table 1).

In the first case, the histopathological features of the ovarian tissue contained ectoderm, mesoderm, and endoderm components. The ectoderm component included skin epithelial cells and adnexal (hair follicles, sebaceous glands) and neural tissues comprising glial cells and choroid plexus. The mesoderm components included cartilage, compact bone, and mature fat cells. Endodermal components included gastrointestinal and respiratory epithelial cells. This tumor contained two foci of neuroectodermal components with pseudo-rosette form. The cells were arranged in a stratified, columnar, and hyperchromatic way. Sometimes immature teratoma may be associated with implantation of the peritoneal to form an infinite mature glia (gliomatosis). Histopathological examination of the omentum in the first case contained glial tissue proliferation arranged in various sizes of lobules and tissue edges surrounded by mesothelial cells which in some foci appeared to be proliferative; the surrounding stroma contained inflammatory cellular cells, blood and haemorrhage foci. Based on the histopathological examination results of the first case in correspondence with theory, it was concluded to be a grade 2 immature teratoma. In the second case, the histopathological examination of the ovarian cyst showed it contained ectoderm, mesoderm, and endoderm components. The ectoderm component included squamous epithelial cells and their adnexal (hair follicles, sebaceous glands). The mesoderm components included cartilage and compact bone and fat cells. The endodermal components

Table 1
Grading immature teratoma in the ovaries

Grade	Histological criteria
Grade 1	Tumors with immature neuroepithelial tissue at least less than 1 at 40X magnification on each slide (Low Grade)
Grade 2	Tumors with the same components, there are 1-3 at 40X magnification on each slide (High Grade)
Grade 3	Large size tumors on Immune Neuroepithel tissue more than 3 att 40X magnification on each slide (High Grade)

included gastrointestinal epithelial cells and respiratory epithelial cells. Immature components were found in some focuses consisting of immature cartilage, immature mesenchymal, and neuroectodermal cells with a partially rosette tubular structure. Primitive neuroectodermal cells were present with stratified oval cell morphology, narrow cytoplasm, increased N/C ratio, and hyperchromatic nuclei. From a routine histopathological examination, this case was concluded to be grade 3 immature teratoma.

Immature teratomas should be distinguished from the Malignant Mesodermal Mixed Tumor (MMMT), which, although it is common in the uterus, can also occur in the ovaries. MMMT often occurs in postmenopausal women aged between 50 and 70 years, in contrast to immature teratomas common in young patients (14).

Immunohistochemistry for the immature glial cell and intestinal tract components is positive for SALL4, whereas SOX2 and glypican 3 are positive in neuroepithelial. Alpha-fetoprotein (AFP) may be stained in the gastrointestinal tract (3). In this case, immunohistochemistry tests were not performed. Recommended therapy for immature teratoma grade 1 in one ovary is unilateral salpingo-oophorectomy and careful monitoring. Complete recovery is possible in all cases. For grade 2 and grade 3 tumors, adjuvant chemotherapy is recommended after unilateral salpingo-oophorectomy, resulting in complete therapy in general patients (14).

The prognosis of immature teratoma is better with chemotherapy, but the staging of the primary tumor, grade of tumor, and metastasis remain important as a predictive factors. Approximately one-third of cases are found to have uniformly distributed mature nodule glia in the peritoneum (gliomatosis peritoneii) and the abdominal lymph nodes, but the prognosis remains good (3).

CONCLUSION

Immature teratoma is a tumor derived from germ cells of embryonal tissue composed of three germ layers: ectoderm, mesoderm, and endoderm; these teratoma tumors contain an immature component in various amounts (typically a primitive or embryonic neuroectodermal tissue), including its most primitive forms which are embryoid bodies. Immature teratomas of the ovaries are generally rare with the incidence occurring in young women. Tumors tend to grow rapidly, and can form a mass in the pelvic and lower abdomen causing enlargement and pain in the abdomen. The recommended therapy for patients with grade 1 is salpingo-oophorectomy with careful monitoring. For grade 2 and grade 3 tumors, adjuvant chemotherapy is recommended after unilateral salpingo-oophorectomy, resulting in complete therapy, then chemotherapy can improve the prognosis.

REFERENCES

1. Walmiky Budi M, Matulatan F. Immature gastric teratoma in infancy: A case report. J Pediatr Surg Case Reports. 2022;78.
2. Ida Bagus Gede Ramayuda, Lies Mardiyana, Dyah Erawati IY. Diagnostic value of abdominal CT scan

in ovarian tumors in Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, from January 2017 to December 2018. Maj Obs Gin. 2021;29(2):45-52.

3. Kumar JR, Harington S, Youngkumar JR, Harington ML, Young SR. WHO classification of tumors of female reproductive organs. Edisi 4. 2014.
4. Lemaiem F, Sassy A, Bouraout SLemaiem F, Sassy A BS. Case series: Ovarian Immature Teratoma. Tunisia; 2016. Report No.: 1007.
5. Nishida M, Kawano Y, Yuge A, Nasu K, Matsumoto H, Narahara H, et al. Three cases of Immature Teratoma Diagnosed After Laparoscopic Operation. Clinical Medicine Insights: Case Reports. 2014;7(7):91-94.
6. Babacan A, Yasam KK, Cerm K, Ismet G, Ercumen M, Vedat ABabacan A, et al. Case report: A Rare Case of Postmenopausal Immature Teratoma With Recurrent Grave Course. Turkey: Departement of Obstetric and Gynecologic Ankara Mevid Military. Int J Clin Ext Med. 2014;7(4):1172-1174.
7. Kurniawati EM, Djunaidi F, Kurniasari N. Giant Fibroepithelial Polyps of the Vulva in a Woman with Uterine Myoma and Primary Infertility: A Case Report and Literature Review. Am J Case Rep. 2022;23(1).
8. Juwita PM, Yudhawati R. Secondary pleuropulmonary amoebiasis due to liver abscess rupture: A complication case report in low resource setting. Int J Surg Case Rep. 2021;85.
9. Sinaga RH, Utariani A, Wardhani P, Hardiono H. Immature granulocyte and mean platelet volume as a predictor of 30-day postoperative mortality in patients with sepsis caused by peritonitis. Bali J Anesthesiol. 2020;4(4):166-171.
10. Kos M, Nikic J LT. Ovarian Teratoma In Routine Biopsy Material During A Five-Year Period. Acta Clin Croat. 2016;55(2):265-270.
11. Bahar F, Zalika P, Lestari SW, Lunardhi H, I'tishom R, Tanojo TD. Male infertility as a bad news: A review. J Glob Pharma Technol. 2019;11(6):109-114.
12. Rahma A, Mardiyana L, Fauziah D. Malignant struma ovary: Case report of an unusual ovarian tumor with CT imaging. Radiol Case Reports. 2022;17(5):1705-1708.
13. Rizqi I, Violetta L. Abdominal and gonadal mature cystic teratomas. J Pediatr Surg Case Reports. 2022;78:102190.
14. Kurman J Robert. Blaustien's pathology of the female Genital Track. 6th edition. Philadelphia: Springer; 2013:869-872.
15. Kurata A, Hirano K, Naganee M, Fujioka YKurata A, Hirano K, et al. Immature teratoma of the ovary with distant metastases: Favorable prognosis and insights into chemotherapeutic retroconversion. Pathology of the Upper Genital Tract: Case Reports. Internat J Gynecolog Pathol. 2010;29(5):438-444.
16. Yuliana ND, Tuarita MZ, Khatib A, Laila F, Sukarno S. GC–MS metabolomics revealed protocatechuic acid as a cytotoxic and apoptosis-inducing compound from black rice brans. Food Sci Biotechnol. 2020;29(6):825-835.