

## Case Report

# How Should Immature Ovarian Teratoma with Gliomatosis Peritonei Be Treated? A Series of Three Rare Cases and Review of the Literature

 Yusuf İlhan,<sup>1</sup>  Hasan Şenol Coşkun,<sup>1</sup>  Hadice Elif Peştereli,<sup>2</sup>  Sema Sezgin Göksu,<sup>1</sup>  Elif Ocak Gedik,<sup>2</sup>  
 Havva Serap Toru,<sup>2</sup>  Ali Murat Tatlı<sup>1</sup>

<sup>1</sup>Department of Medical Oncology, Akdeniz University Faculty of Medicine, Antalya, Turkey

<sup>2</sup>Department of Pathology, Akdeniz University Faculty of Medicine, Antalya, Turkey

### Abstract

Immature ovarian teratoma (IT), also called malignant ovarian teratoma, is one of the ovarian germ cell tumors. Histologically, these neoplasms are typically differentiate towards the three germ cell layers. The metastatic implantation of mature glial tissue on the surface of the peritoneum, omentum, and abdominal lymph nodes is defined as gliomatosis peritonei (GP). It is an extremely rare disease and usually associated with ovarian teratomas, especially in IT. Because of its rarity, the prognostic effect of GP is unclear. Here, we presented three different patients who were diagnosed as IT with GP, and we also reviewed the literature to understand this disease better.

**Keywords:** Ovarian germ cell tumors, immature teratoma, gliomatosis peritonei, prognosis

**Cite This Article:** İlhan Y, Coşkun HŞ, Peştereli HE, Sezgin Göksu S, Ocak Gedik E, Toru HS, et al. How Should Immature Ovarian Teratoma with Gliomatosis Peritonei Be Treated? A Series of Three Rare Cases and Review of the Literature. EJMA 2022;2(2):90-94.

Ovarian germ cell tumors arise from primordial germ cells of the ovary. They can be benign or malignant. Unlike epithelial ovarian cancers, they are very rare. Immature ovarian teratoma (IT) is one of the ovarian germ cell tumors and it is also called malignant ovarian teratoma which is frequently observed in the first two decades of life. Histologically, these neoplasms are typically differentiate towards the three germ cell layers. The main components are usually neurogenic, also mesodermal elements are common.<sup>[1,2]</sup> ITs are the only ovarian germ cell tumors that are histologically graded. Grade is an important predictive factor for the extra-ovarian dissemination; especially to pelvic, abdominal, peritoneum, and omentum.<sup>[3]</sup> Malign germ cell tumors have a good prognosis. While surgical treatment is

mostly sufficient, in some cases platin-based chemotherapy is recommended.<sup>[4]</sup>

The metastatic implantation of mature glial tissue on the surface of the peritoneum, omentum, and abdominal lymph nodes is defined as gliomatosis peritonei (GP). It is an extremely rare disease and usually associated with ovarian teratomas, especially in IT. GP is considered as grade 0 according to the WHO grading system for ITs.<sup>[5]</sup> Only about 100 cases have been reported in the literature. Although GP is associated with a good prognosis, some cases with malignant transformation have been reported.<sup>[5-7]</sup>

Here, we presented three different patients who were diagnosed as IT with GP, and we also reviewed the literature to understand this disease better.

**Address for correspondence:** Yusuf İlhan, MD. Akdeniz Üniversitesi Tıp Fakültesi, Tıbbi Onkoloji Anabilim Dalı, Antalya, Turkey

**Phone:** +90 505 608 62 51 **E-mail:** dryusufilhan@gmail.com

**Submitted Date:** February 01, 2022 **Accepted Date:** April 26, 2022 **Available Online Date:** April 28, 2022

©Copyright 2022 by Eurasian Journal of Medical Advances - Available online at www.ejmad.org

**OPEN ACCESS** This work is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License.



## Case Report

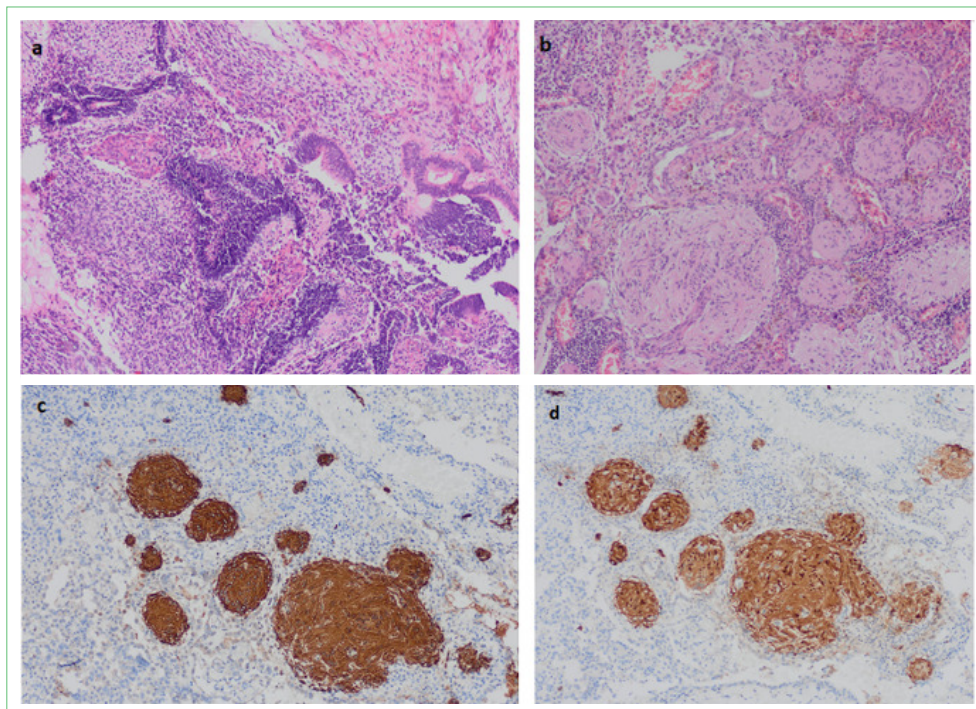
**Case 1** – A 23-year-old nulliparous-woman was referred to the clinic with abdominal pain. A huge abdominopelvic mass was found on physical examination. A computer tomography (CT) scan revealed an abdominopelvic mass originating from the right ovary. She had no family history of malignancy. Pre-operative alpha-fetoprotein (AFP) level (19 ng/ml) and ca 125 level (156 U/ml) were high, but the total hCG level was in the normal range.

Laparotomy was planned to the patient and during the operation, 300 cc ascites fluid was aspirated, no malignant cells were found. Unilateral salpingo-oophorectomy was performed with peritoneal and omental biopsies. A large solid tumor arising from the right ovary and multiple peritoneal and omental nodules were observed. Macroscopically right ovarian mass diameter was 19\*15\*10 cm. Cut sections showed cystic and solid areas containing hair and fat. On histologic examination, the tumor demonstrated predominantly mature ectodermal, mesodermal, and endodermal elements. However small foci of immature neuroectodermal tissue less than one low power field (40x) in one slide were present and it was defined as Grade 1 IT. Mature glial tissue was defined in the peritoneal and omental biopsies and immunohistochemical stains S-100 and glial

fibrillary acidic protein (GFAP) were positive. The pathology report was given as GP. Pathologic diagnosis was IT (Grade 1) with GP (Grade 0) (Fig.1). After the operation, AFP and ca 125 markers turned to normal range. Three cycles of BEP (bleomycin, etoposide, cisplatin) chemotherapy regimen and observation options were presented to the patient. She didn't want to take chemotherapy. She is still following in remission.

**Case 2** – Our second patient was a 34-year-old woman. She presented with abdominal distension and pain. A cystic-solid pelvic mass was shown on CT. As the first patient, pre-operative AFP level (1219 ng/ml) and ca 125 level (72 U/ml) were high but total hCG level was in normal range.

She underwent unilateral salpingo-oophorectomy with peritoneal and omental biopsies. All the tumor implants in the peritoneum were removed. In pathologic evaluation macroscopically 26\*18\*10-cm left ovarian mass was defined. Cut sections showed solid areas containing cartilage tissue, cystic areas, keratinous material. On histologic examination, the tumor showed a large amount of immature neuroepithelial tissue occupying more than three low power fields (40x) in any slide and it was defined as grade 3 IT. In addition, mature glial tissue was defined in the peritoneal samples and immunohistochemical stain GFAP were positive for mature glial tissue. The final pathological report was



**Figure 1.** Immature Ovarian Teratoma with Gliomatosis Peritonei. **(a)** Immature neuroectodermal epithelium with rosettes and tubules. (H&E stain, x100 magnification) **(b)** Nodules of mature glial tissue in the peritoneal implant. (H&E stain, x100 magnification). **(c)** The glial nodule was immunoreactive for GFAP. (x100 magnification). **(d)** The glial nodule was immunoreactive for S-100 protein. (x100 magnification).

given as grade 3 IT with grade 0 GP (Fig. 2) Tumor markers returned to normal range after the operation. Subsequently, she received three cycles of BEP chemotherapy regimen. She completed her treatment, and she is in the follow-up visits every 3 months.

**Case 3** – The third patient was an 18-year-old woman. She was admitted to the hospital with a 2-month history of progressively worsening abdominal pain. A cystic-solid pelvic mass was shown on CT. As the other two patients, pre-operative AFP level (126 ng/ml) and ca 125 level (165 U/ml) were high but total hCG level was in normal range. She was operated and a cystic-solid mass was removed from the right pelvic area. Tumor implants in the peritoneum of douglas were also removed. On macroscopic evaluation, a large ovarian mass (30\*21\*13 cm) and peritoneal implants largest 0,7-cm were seen. Cut sections showed cystic areas with haemorrhagic fluid and solid areas. On histological examination, the tumor showed a large amount of immature neuroepithelial tissue occupying more than three low power fields (40x) in any slide, and the primary lesion was defined as grade 3 IT. Furthermore, mature glial tissue was seen in the peritoneal sample. The pathology report was given as grade 3 IT with GP (Fig. 3) Tumor markers were also in the normal range after the operation. After the oocyte cryopreservation, three cycles of adjuvant BEP chemotherapy regimen was suggested to the patient. She was in the

third cycle of treatment while this paper was written.

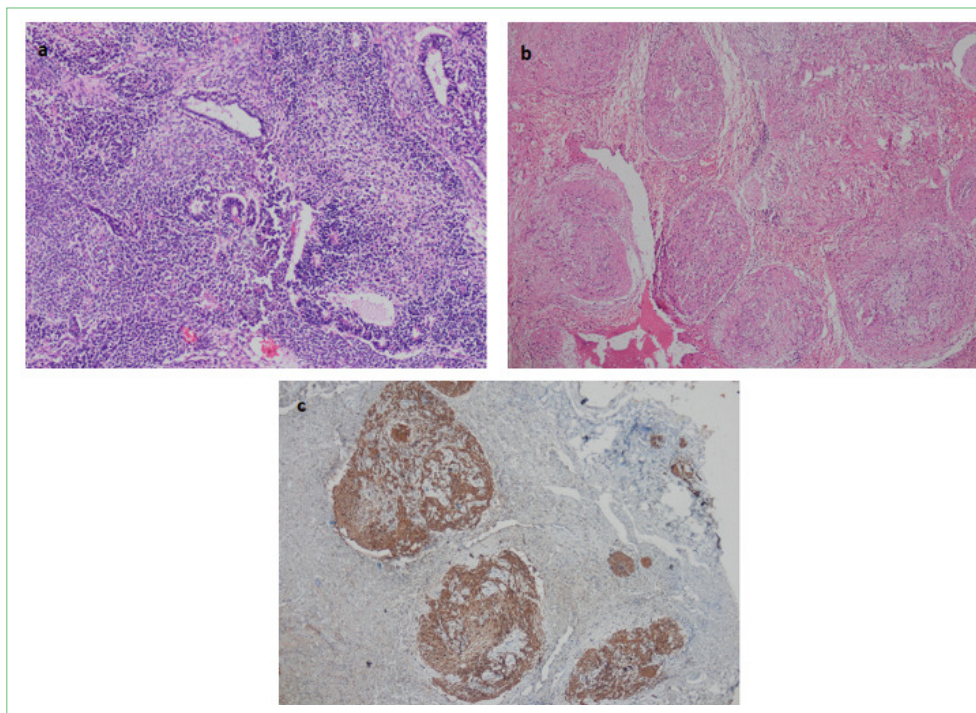
The clinical and pathological features of 3 cases with GP were given in Table 1.

## Discussion

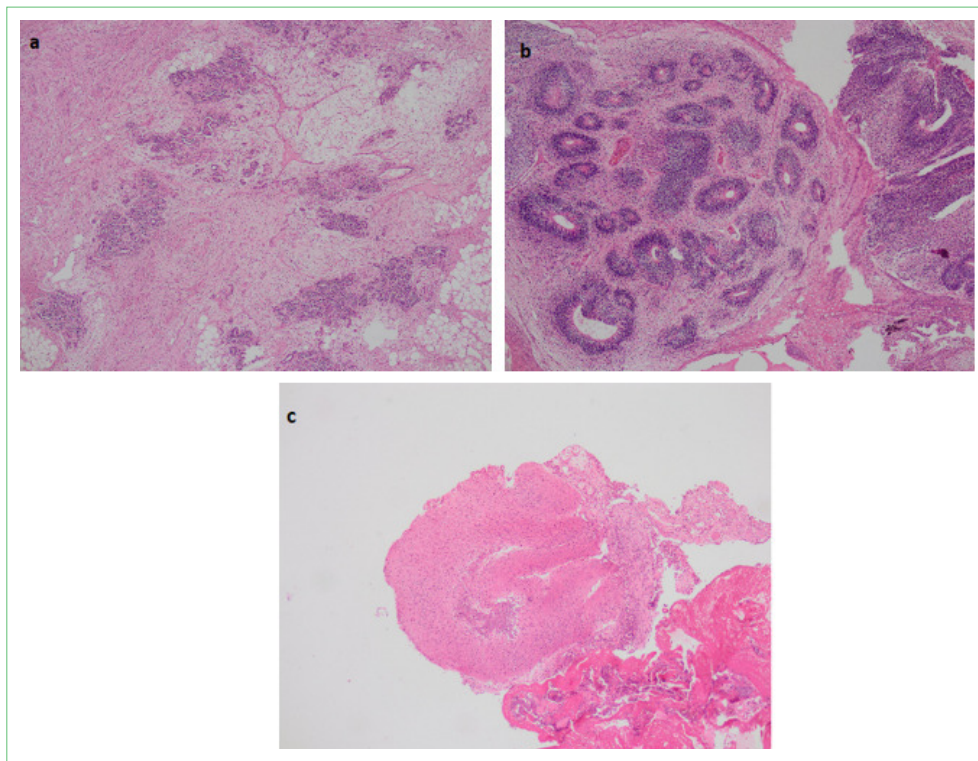
The metastatic implantation of mature glial tissue on the surface of the peritoneum, omentum, and abdominal lymph nodes is defined as GP. It is an extremely rare disease and usually associated with ovarian teratomas, especially in IT.

Most of the articles about this topic are case reports and small case series. Wang et al. reported 8 cases and they thought that the presence of mature glial implants does not affect the prognosis of ovarian teratoma. Moreover, Liang et al reported 14 cases who had IT with GP, and they demonstrated that GP is associated with favorable prognosis.<sup>[5,8]</sup> Contrary to these findings; Yoon et al. investigated the clinicopathologic features of IT associated with GP (n=15) or without GP (n=27). Although there was no difference in overall survival, recurrence rates were higher in IT with GP.<sup>[6]</sup> Here, we have reported 3 new cases from Turkey.

Prognosis for IT of the ovary is associated with the stage and grade of the tumor. Recurrence can be minimized by



**Figure 2.** Immature Ovarian Teratoma with Gliomatosis Peritonei. **(a)** Extensive immature neuroectodermal epithelium with rosettes and tubules. (H&E stain, x100 magnification). **(b)** Nodules of mature glial tissue in the peritoneal implant. (H&E stain, x40 magnification). **(c)** The glial nodule was immunoreactive for GFAP. (x40 magnification).



**Figure 3.** Immature Ovarian Teratoma with Gliomatosis Peritonei. **(a)** Extensive immature neuroectodermal epithelium with rosettes and tubules. (H&E stain, x40 magnification). **(b)** Extensive immature neuroectodermal epithelium with rosettes and tubules. (H&E stain, x40 magnification). **(c)** Nodul of mature glial tissue in the peritoneal implant. (H&E stain, x40 magnification).

postoperative adjuvant therapy with BEP if the tumor is of grade 2 or 3.<sup>[4,9]</sup> Observation can be suggested after surgery in stage 1 and grade 1 IT.<sup>[4]</sup> GP is a rare occurrence and has been found especially in women with IT. Some authors estimate that the presence of GP does not affect adversely the prognosis of ovarian teratomas.<sup>[6,9,10]</sup> On the other hand, as mentioned before, Yoon et al. investigated the clinicopathologic features of ovarian teratoma associated with GP or without GP. The overall survival did not differ between the two groups, but the recurrence rate was higher in the GP group.<sup>[6]</sup> Because of all gliomatosis foci were evaluated as

grade 0, we didn't think chemotherapy would be helpful. In our knowledge, there is no evidence-based role of chemotherapy for these grade 0 lesions. To sum up, because of its rarity, the effect of prognosis is still unclear. In our first patient who has grade 1 immature teratoma with GP; we suggested her to treat with 3 cycles of BEP regimen because of her young age, huge mass, peritoneal dissemination, and its unclear effect of GP on prognosis. Adjuvant 3 cycles of BEP regimen were also recommended to our second and third patients who had grade 3 IT with GP.

**Table 1.** The clinical and pathological features of 3 cases with gliomatosis peritonei

Case	Age	Tumor Size (cm)*	Pre-op† Ca-125 U/ml‡	Pre-op† AFP § ng/ml?	Surgical Procedure	Grade	Adjuvan Therapy	GFAP**	Outcome
1	23	18	156	19	USO ††, Peritonectomies, Omenctomy	1	3 cycles BEP ††	+	Alive 6 months
2	34	26	72	1219	USO, Peritonectomies, Omenctomy	3	3 cycles BEP	+	Alive 3 months
3	18	30	165	126	USO, Peritonectomies, Omenctomy	3	3 cycles BEP	NA ***	Alive

\* cm: centimeter; † pre-op: pre-operative; ‡ U/ml: Units per millilitre; § AFP: alpha-fetoprotein; ? ng/ml: nonogram per millilitre; \*\*GFAP: glial fibrillary acidic protein; ††USO: unilateral salpingo-oophorectomy; †† BEP: bleomycin, etoposid, cisplatin; \*\*\* NA: not available.

## Conclusion

In conclusion, there are no standard treatment approaches or guidelines for IT with GP. Adjuvant chemotherapy should be directed by the grade and stage of primary tumors regardless of the presence of GP. Treatment should be considered on a case-by-case.

## Disclosures

**Informed Consent:** Written informed consent was obtained from the parents of the patient for the publication of the case report and the accompanying images.

**Peer-review:** Externally peer-reviewed.

**Conflict of Interest:** The authors declare that they have no conflict of interest.

**Authorship Contributions:** Concept – Y.I., H.S.C.; Design – Y.I.; Supervision – H.S.C., H.E.P.; Materials – Y.I., E.O.G., H.S.T.; Data collection &/or processing – Y.I., E.O.G., H.S.T., H.E.P.; Literature search – Y.I.; Writing – Y.I.; Critical review – S.S.G., A.M.T., H.S.C.

## References

- Gheorghisan-Galateanu A, Terzea DC, Carsote M, Poiana C. Immature ovarian teratoma with unusual gliomatosis. *J Ovarian Res* 2013;6:28. [\[CrossRef\]](#)
- Heda SA, Patrikar AD, Bothale KA, Mahore SD. A rare case of immature ovarian teratoma with gliomatosis peritonei. *J Basic Clin Reprod Sci* 2014;3:126–9. [\[CrossRef\]](#)
- Norris HJ, Zirkin HJ, Benson WL. Immature (malignant) teratoma of the ovary: a clinical and pathologic study of 58 cases. *Cancer* 1976;37:2359–72. [\[CrossRef\]](#)
- Mangili G, Scarfone G, Gadducci A, Sigismondi C, Ferrandina G, Scibilia G, et al. Is adjuvant chemotherapy indicated in stage I pure immature ovarian teratoma (IT)? A multicentre Italian trial in ovarian cancer (MITO-9). *Gynecol Oncol* 2010;119:48–52.
- Wang D, Jia CW, Feng RE, Shi HH, Sun J. Gliomatosis peritonei: a series of eight cases and review of the literature. *J Ovarian Res* 2016;9:45. [\[CrossRef\]](#)
- Yoon NR, Lee JW, Kim BG, Bae DS, Sohn I, Sung CO, et al. Gliomatosis peritonei is associated with frequent recurrence, but does not affect overall survival in patients with ovarian immature teratoma. *Virchows Arch* 2012;461:299–304. [\[CrossRef\]](#)
- Shefren G, Collin J, Soriero O. Gliomatosis peritonei with malignant transformation: a case report and review of the literature. *Am J Obstet Gynecol* 1991;164:1617–21. [\[CrossRef\]](#)
- Liang L, Zhang Y, Malpica A, Ramalingam P, Euscher ED, Fuller GN, et al. Gliomatosis peritonei: a clinicopathologic and immunohistochemical study of 21 cases. *Mod Pathol* 2015;28:1613–20. [\[CrossRef\]](#)
- Mrabti H, El Ghissassi I, Sbitti Y, Amrani M, Hachi H, Errihani H. Growing teratoma syndrome and peritoneal gliomatosis. *Case Rep Med* 2011;2011:123527. [\[CrossRef\]](#)
- Gratama S, Swaak-Saeys AM, van der Weiden RM, Chadha S. Low-grade immature teratomas with peritoneal gliomatosis; a case report. *Eur J Obstet Gynecol Reprod Biol* 1991;39:235–41. [\[CrossRef\]](#)