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Case Report

# Recurrent immature teratoma in a 47 year old with maturation in subsequent laparotomies and a grave course

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**Summary**

Ovarian immature teratoma (IT) is uncommon after the first two decades of life. Management is largely surgical, and recurrences are rare. Ovarian IT has the potential to convert into mature disease at the time of recurrence. The current case report describes a 47-year-old female patient who developed two recurrences within three years. The primary disease and first recurrence were managed surgically, whereas the second recurrence was managed surgically plus adjuvant chemotherapy with bleomycin, etoposide and cisplatin (BEP) regimen. Histopathology was immature teratoma grade 3 initially which progressed to immature teratoma grade 1 in last recurrence. Alpha-feto protein levels were never raised except two months after the last laparotomy when the patient was diagnosed to have hepatic metastases and succumbed to disease. Prognosis was grave in our patient. Advanced age may be a one contributing factor. Relapse of ovarian IT is uncommon and its optimal management remains debatable.

*Key words*: Recurrent immature teratoma; Ovarian; Surgery.

## Introduction

Immature teratomas (ITs) comprise less than 1% of all ovarian malignancies. They most commonly occur in the first two decades of life; they extremely seldom occur after menopause [1]. They most often present to clinical attention in the form of abdomino-pelvic mass, abdominal pain or belly distension [2, 3]. They characteristically tend to rapidly grow, aggressively infiltrate ovarian capsule and unfavorably form adhesions to surrounding structures. Alpha-fetoprotein (AFP) level is often raised at the time of diagnosis, and its measurement may serve as a useful tool to monitor for tumor recurrence. Treatment is largely surgical; staging/debulking is indicated for most patients, whereas fertility-sparing surgery is indicated in young adults who anticipate childbearing. Adjuvant chemotherapy with bleomycin, etoposide and cisplatin (BEP) is usually administered for tumors with high grade (grade 2/3) or extraovarian spread. The five-year overall survival rate ranges from almost 100% in early stages to around 75% in advanced stages [4, 5].

Relapse of ovarian IT is uncommon and must be differentiated from the rare condition growing teratoma syndrome (GTS) [6]. GTS rarely follows the treatment of IT of the ovary [7-9]. Moreover, GTS typically occurs during or after administration of chemotherapy, and It is characterized by the presence of enlarging intraabdominal masses as well as normal tumor markers. Histologic examination of the resected surgical specimens of GTS shows mature elements. GTS was first described in 1982 by Logothetis *et al*. [10]. Notably, even if patients are not exposed to chemotherapy, ovarian ITs have the potential to convert into mature diseases if post-surgical recurrences occur [11]. Optimal management at the time of ovarian IT relapse remains controversial, and is largely attributable to the paucity of published literature. This lack of data is multifactorial, including the extreme rare prevalence of the ovarian IT disease. There is an ongoing debate surrounding the role of adjuvant chemotherapy in ovarian IT following surgery. Adjuvant chemotherapy has been almost universally administered to adult patients [12, 13], except patients with International Federation of Gynecology and Obstetrics (FIGO) stage IA, grade 1 disease. Recent data suggests a primary surgical management of ovarian IT recurrences. Some authors believe that ovarian IT is a chemotherapy-resistant disease, and thus principally suggest an exclusive surgical management [14].

The current case report describes a 47-year-old female patient with a known history of immature teratoma who developed two recurrences within three years despite intensive surgical debulking. Histopathology was immature teratoma grade 3 initially which progressed to immature teratoma grade one in her last recurrence. Adjuvant chemotherapy was administered after the second recurrence but she succumbed to the disease eventually.

## Case report

A 47-year-old female patient presented to our center with intermittent abdominal pain and distention for the past six months. She also reported difficult and painful defecation. Past medical history was remarkable for two prior laparo-

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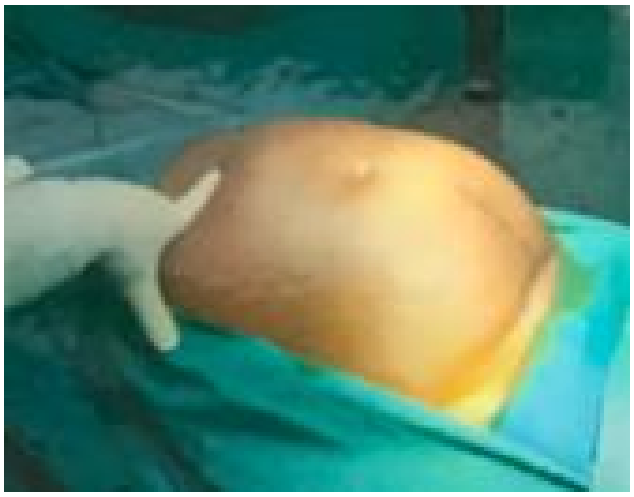

Figure 1. — Abdominopelvic mass- hard and fixed with irregular margins and surface.

tomies for ovarian masses. In September 2015, she underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy and omental biopsy for a 20 × 20 cm multilobulated and friable mass arising from the right ovary. Postoperative histopathology of the resected mass was suggestive of mature teratoma of right ovary. Subsequently in April 2017, she developed recurrence of a large abdomino-pelvic mass, which was managed surgically by excision, omentectomy and adhesiolysis. The mass measured 3.7 kg and was adherent to the small bowel and omentum. Post-operative histopathology of the resected abdomino-pelvic mass showed mature teratoma; the omentum was tumor-free. We reviewed the histopathology of prior two surgeries and it was immature teratoma grade 3.

Clinical examination revealed a 15 × 15 cm abdomino-pelvic mass, which demonstrated hard consistency, non-mobility and irregular margins (Figure 1). Contrast-enhanced computed tomography (CECT) scan of the abdomen and pelvis displayed a 13 × 11 × 9 cm heterogeneous mass with multiple foci of calcifications causing bilateral moderate hydroureteronephrosis (Figure 2). Laboratory testing for tumor markers showed: cancer antigen 125 (CA-125) 31.3 U/mL, carcinoembryonic antigen (CEA) 7.1 ng/mL, cancer antigen 19-9 (CA 19-9) 36.5 U/mL, lactate dehydrogenase (LDH) 214 U/L, beta human chorionic gonadotropin (beta-HCG) 3.1 mIU/mL and AFP 4.0 ng/mL.

In July 2018, the patient underwent bilateral ureteric stenting, abdomino-pelvic mass excision, sigmoid colon resection and end colostomy. The resected mass measured 30 × 30 cm mass with cheesy consistency, and it was adherent to the rectus sheath and sigmoid colon. The mass was solid and had formed teeth and hair in some areas (Figure 3). The postoperative course was uneventful. Postoperative histopathology of the resected mass revealed immature teratoma grade 1; the resected sigmoid colon was tumor-free.

After a multidisciplinary review, the patient was started on adjuvant chemotherapy of six cycles of BEP regimen. In October 2018, that is, two months after the surgery and during adjuvant chemotherapy, the patient had a complaint of abdominal pain. The clinical examination was unremarkable. Laboratory testing was significant for a raised AFP level of 140.3 ng/mL. Ultrasonography of abdomen and pelvis revealed a progressive disease with two rounded and heterogeneous hepatic masses of 8 × 8 cm and 5 × 4 cm. Poor prognosis was explained to the patient. Two months later, the patient died in December 2018.

## Discussion

Ovarian teratomas are divided into mature and immature types. Both types comprise of tissues of ectodermal, mesodermal and endodermal origins. However, mature tissues are found in mature teratomas (MTs) whereas immature elements are found in ITs. MT is the most common type of ovarian teratoma, and it occurs between 20-40 years of age. Ovarian MTs are commonly benign tumors although malignancies may arise from constituent elements in a few cases [11]. In contrast, ovarian ITs present in patients under 20 years of age. In a study of 244 patients with ovarian ITs, only 4 patients (1.6%) were over 40 years of age [15]. Imaging of ovarian teratomas show large, heterogeneous, complex and cystic ovarian masses with small areas of fat and scattered calcification. MTs contain much larger areas of fat and calcification. Large amounts of solid areas and heterogeneity are features that can help in differentiating ovarian MTs from other malignant germ cell tumor types. Our patient was in her late fourth decade of life and CT findings were suggestive of MT.

In one third of ovarian ITs, AFP levels are elevated [16]. In our case, AFP level was initially normal which further directed us toward mature elements. Originally, Norris grading system was used to classify ovarian IT into three grades (grades 1-3) depending on the quantity of immature neuroepithelium. In 2014, the World Health Organization (WHO) suggested two grades, low grade (former grade 1) and high grade (former grades 2 and 3).

Generally, management of ovarian teratoma includes surgery followed by adjuvant chemotherapy in select cases. During surgery, the entire peritoneal cavity is inspected, washings are obtained for cytology and biopsies are taken from suspicious areas. Primary lesions are removed en bloc without rupture. Ovarian teratomas with advanced stages require debulking, and the extent of debulking depends on the age and fertility status of the patient. Our patient underwent complete resection of tumor mass in all her laparotomies. Histopathology was grade 3 in the first two laparotomies and grade 1 in the last resection.

Since the histopathological report for the two laparotomies in 2015 and 2017 was reported as MT initially, the patient did not receive any adjuvant treatment. In fact, there is a controversy regarding the role of adjuvant chemotherapy in ovarian IT. Currently the standard of care in gynecologic oncology practice is chemotherapy for all women with ovarian IT, except in patients with FIGO stage IA, grade 1

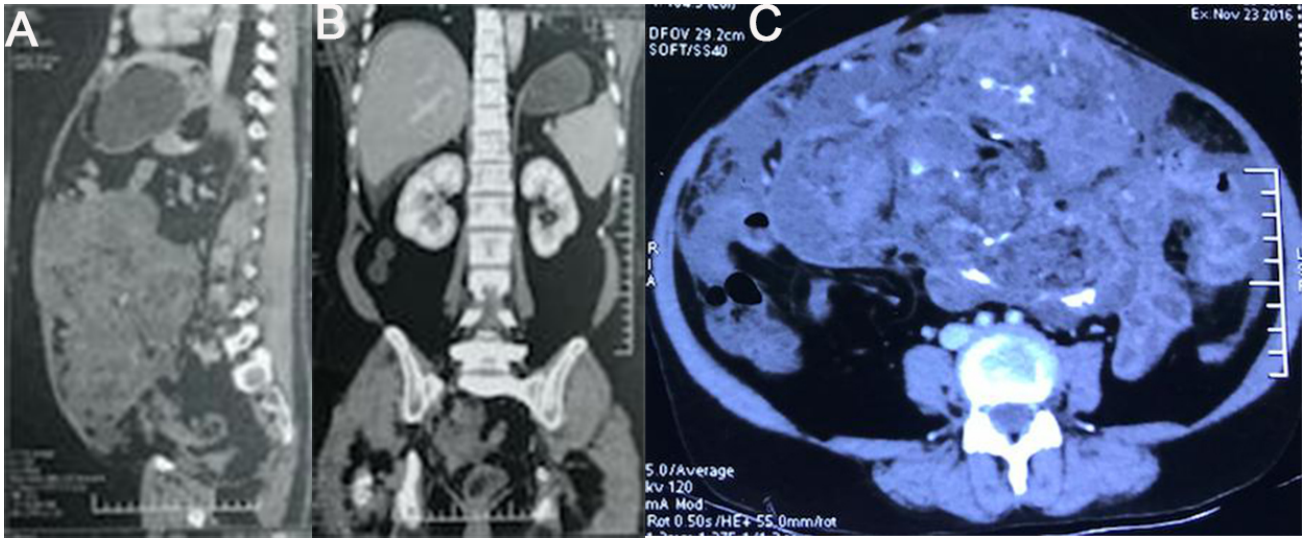


Figure 2. — 13 × 11 × 9 cm heterogenous mass with multiple foci of calcification causing bilateral moderate hydroureteronephrosis.

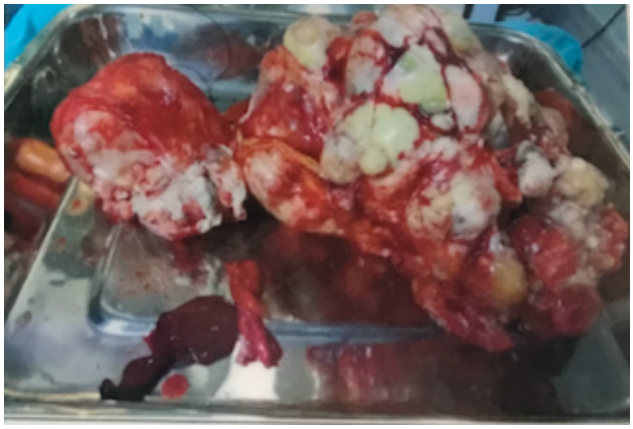

Figure 3. — Solid mass with formed tooth and hair in some areas.

disease [12]. Due to lack of evidence of benefit in children, pediatric patients are treated with fertility-preserving surgery alone with similar excellent outcomes [17]. In 2016, the Malignant Germ Cell International Consortium reviewed a large series of both pediatric and adult ovarian IT cases to determine the role of chemotherapy in the management of ovarian ITs [12]. The Consortium merged data from seven pediatric and two adult trials to generate a dataset of 179 patients (98 pediatric and 81 adult patients). The study showed that there was no evidence that administration of adjuvant chemotherapy at first presentation would decrease the rate of recurrence in the small number of pediatric cases treated with adjuvant chemotherapy (eight out of 98 cases). The five-year event-free survival (EFS) and overall survival (OS) rates were 91% and 99% for the pediatric cohort, respectively, and 87% and 93% for the adult cohort, respectively. Among grade 3 pediatric patients, the five-year EFS was 92% for stage I/II cohort, however, it was statistically significantly lower for stage III cohort at 52% ($p = 0.005$). Similar outcomes were observed in adult patients with grade 3 disease, with five-year EFS of 91% for stage I/II patients and 65% for stage III/IV patients ($p = 0.01$).

Newton et al. explored the role of adjuvant chemotherapy after surgery for adult patients with ovarian IT [14]. The authors studied a sum of 138 patients across four large United Kingdom cancer centers over a period of 12 years. The five-year EFS and OS rates were 72% and 93%, respectively. They showed that adjuvant chemotherapy did not reduce future relapse or progression in ovarian IT patients. Moreover, they observed no radiologic responses to chemotherapy. The authors concluded that ovarian IT is a chemotherapy-resistant disease, and suggested exclusive surgical management of ovarian IT in all patients irrespective of age. To assess this conclusion prospectively, the AGCT1531 trial (ClinicalTrials.gov identifier: NCT03067181) is currently enrolling pediatric and adult patients (aged 0–50 y) with stage I ovarian IT (both FIGO IA and IB), regardless of grade. Optimal management at the time of ovarian IT relapse remains open to debate due to the difficulty in distinguishing between recurrence of ovarian IT and gliomatosis peritonei/GTS, especially in the presence of normal AFP levels. GTS has been reported to occur in 12% of all ovarian ITs. Moreover, GTS takes place in the retroperitoneum [18-20]. GTS is an uncommon aftermath of teratoma that may happen when ovarian IT is treated by adjuvant chemotherapy. The most plausible explanation is that chemotherapy transforms and differentiates malignant cells into benign cells. The second explanation is that the chemotherapy destroys malignant cells, leaving behind chemoresistantteratoma cells although it does not explain why such lesions become larger. Notably, ovarian IT has the potential to convert into mature disease in postsurgical recurrence even in the absence of adjuvant chemotherapy [11]. Our patient did not receive prior adjuvant chemotherapy and there was subsequent maturation of elements as ev-

idenced by normal tumor markers, imaging and histopathology. The decision to administer BEP was made due to prior high grade histology and two recurrences within three years.

## Conclusions

Relapse of ovarian IT is uncommon and must be differentiated from the rare GTS disease. The optimal management of recurrent ovarian IT remains debatable. Our patient had poor prognosis despite intensive debulking and adjuvant chemotherapy. Advanced age may be a one contributing factor.

## Author contributions

JBS contributed to investigations and management of the case and drafting the manuscript. SK contributed to literature search and drafting of the manuscript. Both authors have reviewed the manuscript for intellectual and editorial comments. Both authors have read and approved the final draft of the manuscript, and agreed to be held accountable for the presented content.

## Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki, and written informed consent was obtained from the patients' kin (daughter) due to patients' demise. As per Institute Ethics Committee guidelines, protocol approval is not required for case reports and hence was not sought, however written permission was taken from the faculty in-charge of the case who is also one of the co-authors.

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## Conflict of Interest

Authors report no conflict of interest.

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