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Original Research Article

Immature Teratoma of the Ovary: A Series of Rare Cases and Review of Literature

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Abstract:

Introduction: Immature teratomas account for less than 1% of all ovarian cancers but is the second most common germ cell malignancy and accounts for 10%-20% of all ovarian malignancies in women younger than 20years. Preoperative diagnosis of immature cystic teratoma can be challenging for clinicians because of varied radiological findings and tumor markers level.

Aims and Objectives: To elaborate on the varied presentation, prognostic markers and challenges for diagnosis and management of immature teratoma. To emphasize on the need of timely referrals, multidisciplinary team management and need for continuous follow up.

Materials and Methods: The hospital records of patients with confirmed histopathological diagnosis of immature teratoma in last one year was reviewed and these patients were closely followed up for further management at AIIMS, New Delhi. All the cases have been discussed via graphic presentation for detailed and in-depth understanding.

Results: Histopathological examination is the only confirmatory diagnosis. Age of presentation was between 16-32 years. The clinic-radiological diagnosis was challenging because of varied presentations. Tumor markers were not specific for all of them. Grade of the tumor is the most important prognostic factor followed by stage. Even with adjuvant chemotherapy, there are chances of recurrences.

Conclusion: Immature teratoma of ovary primarily involves younger patients; hence clinicians should strongly have a high sense of suspicion whenever the diagnosis of a germ cell tumour is entertained and timely intervene.

Keywords: Immature teratoma, germ cell malignancy, ovarian malignancies, clinic-radiological, Tumor markers.

Introduction

Immature teratoma is defined as a teratoma containing variable amount of immature neuroectodermal tissue. It is the second most common germ cell malignancy. Pure immature teratoma constitutes less than 1% of all ovarian cancers but it accounts for 10%-20% of all ovarian malignancies in women younger than 20years [1,4,5]. These atypical neoplasms contains tissue representative of all or two out of the three germ cell layers.

The tumor histology incorporates varying amounts of immature tissue, most frequently with neural differentiation. [2,3] Immature teratoma is the only ovarian germ cell neoplasm that is histologically graded. Grade of the tumor is decided by the proportion of immature neural elements in the histopathology review.[2] The histological grade of these tumors constitute an important prognostic factor and it is one of the deciding factor for extra ovarian spread and ultimately the overall survival.[3] Preoperative diagnosis of immature teratomas are challenging for clinicians because of varied clinical presentation, radiological findings and tumor markers level. These patients have a very good prognosis and better overall survival with adjuvant chemotherapy after surgery as compared to historical controls.

At least 90% of women with early-stage ovarian germ cell tumors (stage I and II) and upto 75% of those with advanced disease (stage III and IV) are long-term survivors.[7] Currently, the most widely used combination is bleomycin, etoposide, and cisplatin (BEP). Alternatively, etoposide/cisplatin (EP) can be used to decrease toxicity and increase compliance. There are no prospective trials to inform clinicians of the optimal number of treatment cycles. 3 cycles of BEP are usually administered for patients at a low risk of recurrence, and 4 or

more cycles are administered to high-risk cohorts. [8,9]

Objective

1. To elaborate on the varied presentation and challenges for diagnosis and management of immature teratoma of the ovary.
2. To stress on the need of timely referrals, multidisciplinary team management and need for continuous follow up.

Material and Methods

The hospital record of patients with confirmed histopathological diagnosis of immature teratoma over a span of one and a half year from January, 2021 till April, 2022 was reviewed and these patients were closely followed up for further management. We describe the clinico-radiological profile of 5 cases of immature teratoma along with their management and follow up plan.

Case 1: Miss A visited a private hospital in Jan'2021 with pain abdomen and distension for 10-20 days. There she was evaluated initially with ultrasound followed by MRI which was suggestive of a solid-cystic mass from right ovary. CA 125 was within normal range. No other tumor markers were done. FNAC was suggestive of right ovary mature teratoma. She underwent emergency laparotomy followed by right salpingo-oophorectomy in view of acute abdomen. She self referred herself to us when her histopathology report was suggestive of high grade immature teratoma. We reviewed her slide and all the tumor markers. Only AFP was raised which was repeated after 2 months and it had risen by 4.5 times. The patient was started on BEP chemotherapy. Though her AFP levels decreased significantly, her CECT was suggestive of a progressive disease and thereby fertility preserving cyto-reductive surgery was done for her. She was followed every 2 monthly for recurrence.

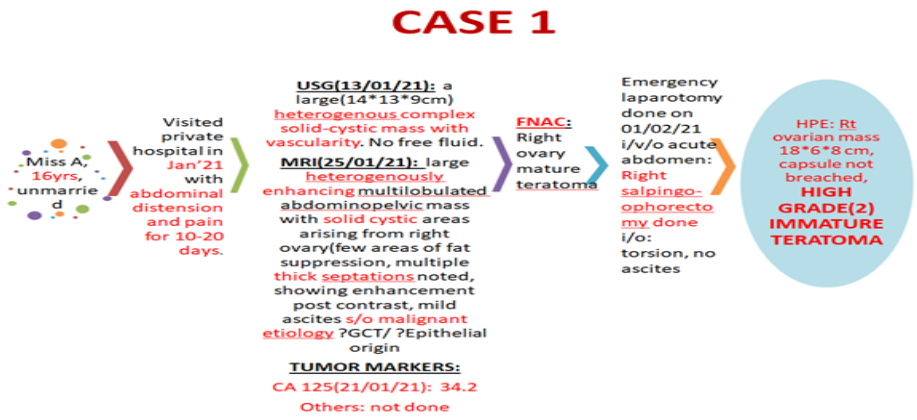

Figure 1: Flowchart of Case 1

Case 2: 18yrs old Miss B presented with painful lump in abdomen for 7 months. Her USG suggested of a 16 cm solid cystic mass. She had a 30weeks size solid cystic abdomino-pelvic mass with restricted mobility. Her CA125, AFP, LDH were raised and CECT suggested of multiple peritoneal and omental deposits. She underwent omental and adnexal mass biopsy but the findings were inconclusive. She thereby underwent right salpingo-oophorectomy with omentectomy. Intra-op frozen section only suggested teratoma but her final HPE report turned out to be Grade 1 Immature teratoma. She was upstaged to Stage IIIC and taken up for BEP chemotherapy.

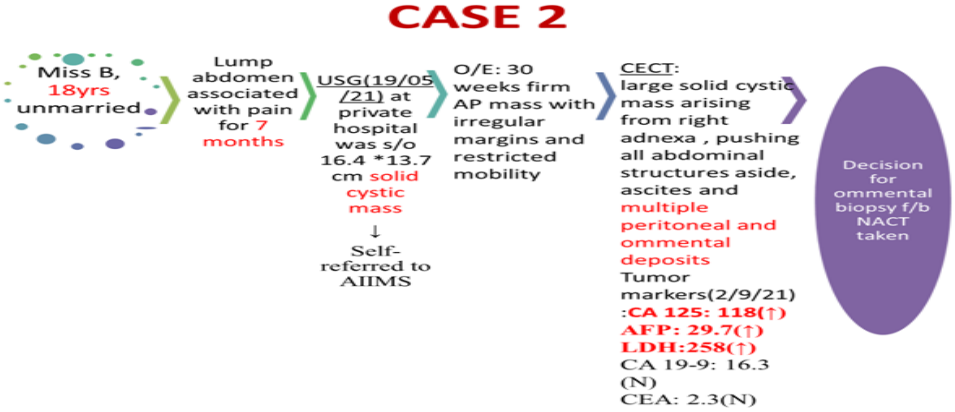

Figure 2: Flowchart of Case 2

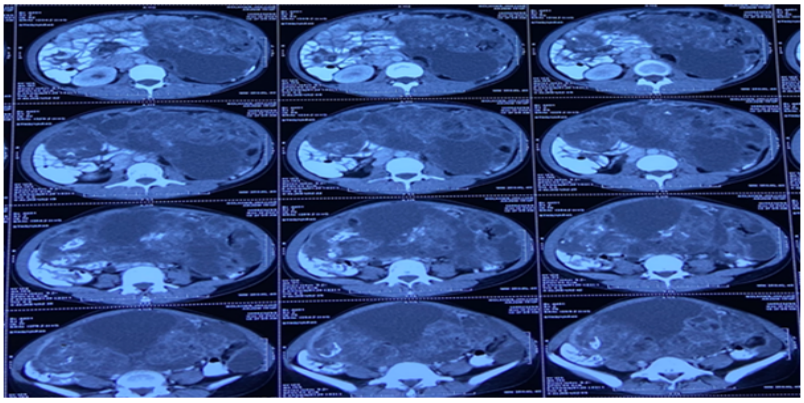

Figure 3: CECT image of Case 2

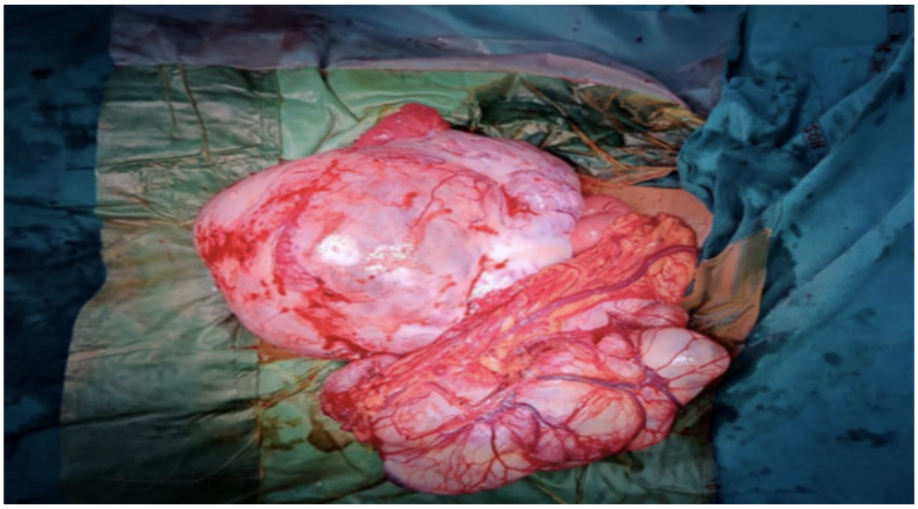

Figure 4: Intra-op finding of case 2. A 30x 35 cm right ovarian solid cystic mass seen adherent to bladder. Right tube was dilated, tortuous & adherent over mass. Mass was adherent to anterior abdominal wall. No spill occurred. FROZEN section - Teratoma

Case 3: 23yrs old unmarried Miss C presented with heaviness in lower abdomen for one week associated with increased frequency of micturition for 4-5 days. She underwent ultrasound to elicit right adnexal solid-cystic mass. Her PET CT suggested of a large inactive cystic mass with an area of soft tissue within it. Her tumor markers were within normal limits. She underwent staging laparotomy and right salpingo-oophorectomy. Intra-op frozen section was suggestive of immature teratoma. R0 resection was done. She received 3 cycles of BEP in post-op period and then following up with two monthly ultrasound and AFP levels.

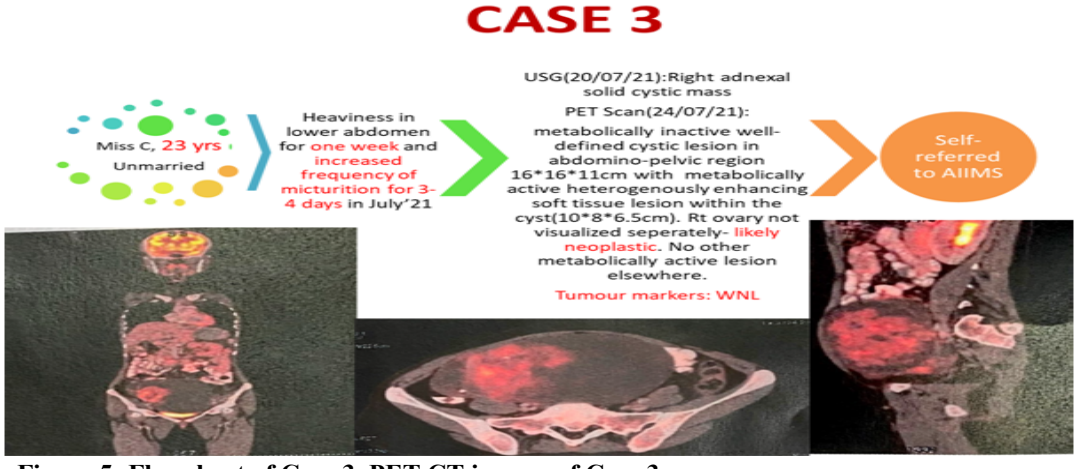

Figure 5: Flowchart of Case 3. PET CT images of Case 3

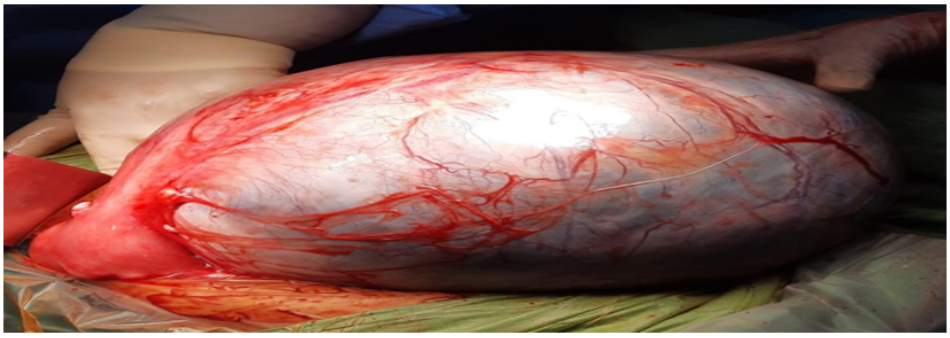

Figure 6: Intra-op image of Case 3. Staging laparotomy + PWC + rt salpingoophorectomy done for this case. Frozen section: Immature Teratoma Stage 1C1. After frozen section report, left ovarian cystectomy + ovarian reconstruction + Infracolic ommentectomy + pelvic lymph node dissection+ peritoneal biopsy was done.

Case 4: 29yrs old Mrs D presented with abdominal distension with pain abdomen for 1.5 months. She had on and off fever for 1 month. Her USG and CECT suggested of a large complex solid cystic pelvic mass with gross ascites and raised CA-125, AFP, CA19-9, LDH levels. Her adnexal mass biopsy was inconclusive. After stabilizing her haematological parameters, she was taken up for staging laparotomy and left salpingo-oophorectomy. Intra-op frozen section was suggestive of immature teratoma with neuroepithelial components.

Final histopathology report suggested of high grade immature teratoma with gliomatosis peritonei. Patient received 3 cycles of BEP chemotherapy, but she developed Growing teratoma syndrome for which she underwent relook laparotomy with peritonectomy. She is now following up USG and AFP 2 monthly.

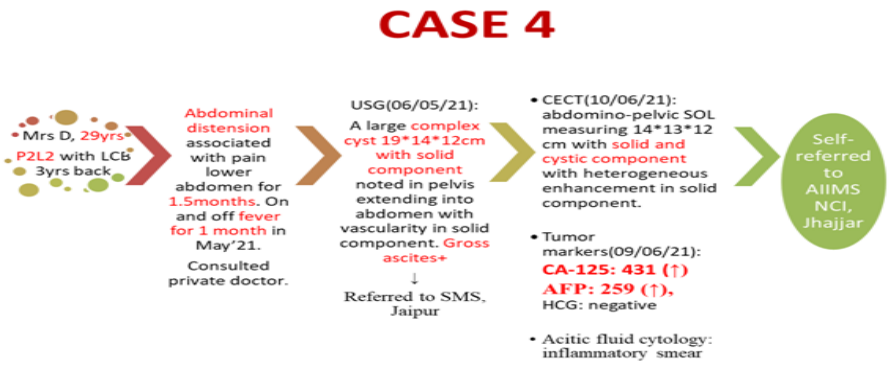

Figure 7: Flowchart of Case 4

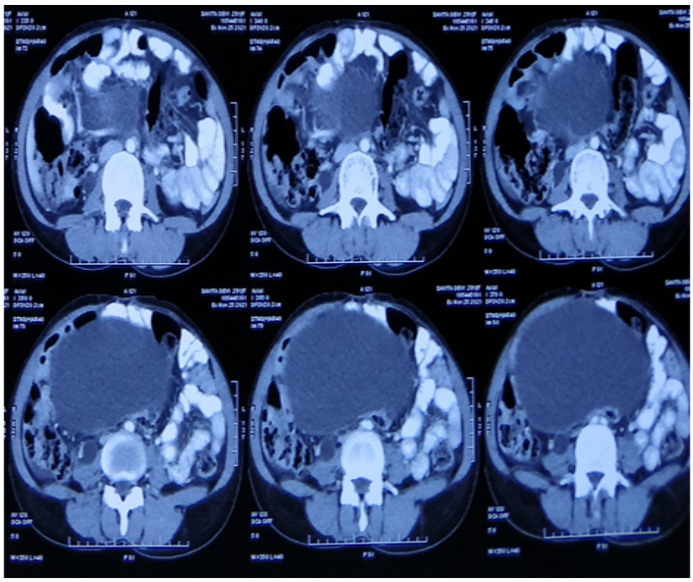

Figure 8: CECT image of Case 4

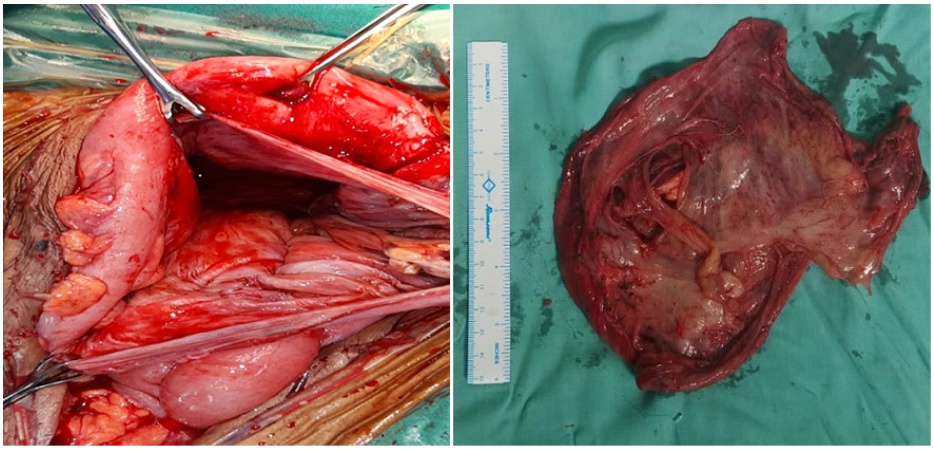

Figure 9: Intra-Op Image of Growing Teratoma Syndrome

Laparotomy+ peritoneal cyst excision+ bladder peritonectomy+ rt paracolic ommentectomy was done for Case 4.

Case 5: 31yrs old unmarried Miss E presented with heaviness in lower abdomen and decreased appetite for one month. Her USG and CECT suggested of large heterogeneous abdomino-pelvic mass with numerous tiny calcification and lipid infilteration and CA125, AFP levels were significantly raised. She underwent staging laparotomy and right salpingo-oophorectomy (R1 resection).

Her HPE report came as low grade immature teratoma with gliomatosis peritonei. She received 4 cycles of BEP but developed Growing Teratoma Syndrome and underwent relook laparotomy.

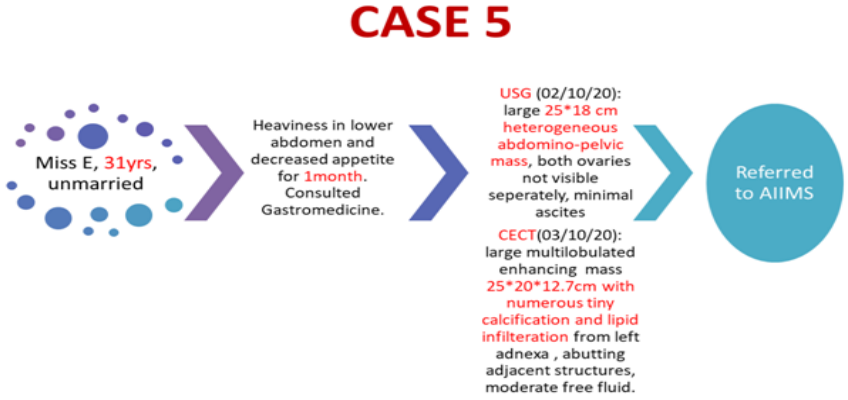

Figure 10: Flowchart of Case 5

Results

Age of presentation was between 16-32 years. The clinic-radiological diagnosis was challenging because of varied presentations. Tumor markers were not specific for all of them (4 cases had raised AFP of which one case had raised CA125, CA 19-9, LDH). In remaining 1case, all tumor markers were normal.

Final histopathological examination is the only confirmatory diagnosis. Though intra-operative frozen section helps in decision making especially in young patients where fertility preservation is of paramount importance, it is not always confirmatory in immature teratoma patients. Grade of the tumor is the most important prognostic factor followed by stage. Even with adjuvant chemotherapy, there are chances of recurrences and Growing Teratoma Syndrome which warrants re-look laparotomy.

Discussion

The median age at diagnosis in case series was 23yrs (16-31yrs) which is comparable to that observed by Alwazzhan et al in 2015 (18-36yrs) and other observational studies [5,2,10,11]. All the patients presented with abdominal distension of varied duration similar to Deodhar et al observation in 2016, though one of our patients presented with increased frequency of micturition and other one with fever.

These symptoms subsided after surgery suggesting its correlation with the disease entity. Tumor markers are non-specific in patients with immature teratoma. Only AFP holds its significance in follow up of patients [12] but it cannot be relied upon for preop diagnosis of immature teratoma. Its levels are

not correlated to stage or grade of tumor.[13-16] Though in our study, 80 percent patients had raised AFP pre-operatively, only 2 out of 27 cases had raised AFP in a study by Alwazzhan et al [5]. They had raised CA125 levels in only 2 cases while we had it raised in 60 percent of our cases. One of our patient had raised levels of multiple tumor markers including LDH and CA19-9 apart from AFP and CA125. Fertility-sparing surgery in the form of unilateral salpingo-oophorectomy should be the primary treatment modality in young patients.[17-19] Although optimal debulking is the standard recommendation in advanced disease, conservative surgery may not compromise the chances of cure given the high rate of chemotherapy sensitivity seen in these tumors.[20] According to Alwazzhan et al. fertility preserving surgery could be done in majority (88%) but not all cases.[5] The other patients either received NACT followed by debulking or directly complete debulking as per clinicians discretion. All of the patients were young in our study hence fertility preserving surgery was done for all of them. Only one patient had R1 resection, but she responded satisfactory to post op BEP chemotherapy. Early stage and low grade immature teratoma is treated adequately with surgery alone. The rate of recurrence in this group of patients is low (15%-25%); if it occurs, the patient can be effectively salvaged with chemotherapy.[21-24] Adjuvant chemotherapy using BEP is the current standard of care for the remaining stages and grades. Treatment results in an overall disease-free survival of more than 95% and 75% in early- and advanced-stage disease, respectively. All our patients were administered post op BEP chemotherapy and all of them tolerated it very well. Two of our patients had presence of mature glial tissue in the peritoneum as was evident from final histopathology report. This condition which is referred to as Gliomatosis Peritonei was not related to the grade of tumor but was seen in patients who were around 30 yrs of age. Both these patients had significantly raised AFP levels in pre-op period. Though AFP levels decreased significantly after surgery and BEP chemotherapy, these patients developed growing teratoma syndrome (GTS) and needed additional surgery. Both the patients had breach of capsule, significant ascites, omental and POD deposits in the pre-op stage. The GTS can be correlated to advanced stage immature teratoma with gliomatosis peritonei. The patients with later histopathology report needs to be counselled about the risk of GTS which mostly needs a second surgery at later stage. Hence, both the doctor and the patient needs to be watchful for GTS. These patients have normal AFP levels and silently develop GTS, which can be picked up by advanced imaging modality like CECT or MRI. This is contradictory to Alwazzhan et al [5] where even though few patients had advanced disease at the time of presentation, none of them had recurrences or GTS in post op follow up period. There are several limitations to this study. First, this is a retrospective study, very small number of patients are included and the results may be subject to bias, incomplete information, or misdiagnosis. Because of the rarity of this tumor, it is challenging to perform big case series, prospective trials, or randomized control trials.

Table 1: Comparison of our study findings with other studies

Parameters	Literature	Our Study
Median age at diagnosis	27 (18-36yr)[5]	23 (16-31yrs)
Clinical presentation	Abdominal pain and distension (Ind J Pathol & Microbiol Oct-Dec 2011;54(4):730-5: Deodhar et al)	Abdominal distension of varied duration One pt had increased frequency of micturition One had fever which subsided after surgery
Pre-op tumour markers	2 cases had raised CA125, 2cases had raised AFP, Other markers not raised (Total: 27 cases) AFP level in IT is not correlated to either stage or grade[5]	AFP raised in 4 cases CA125 raised in 3 cases One case had raised CA 19-9 No raised markers in one case
Surgery	Fertility-sparing surgery was undertaken in 24 of 27 patients, including 2 stage III patients, with complete recovery and no evidence of recurrence[5]	Fertility sparing surgery was done for all our cases though one was referred with incomplete surgery
Post-surgery Chemotherapy	In selected cases	All our patients received post-op chemo with BEP
Follow up	No recurrences[5]	2 cases with gliomatosis peritonei had radiological progressive disease. (Growing teratoma Syndrome). They underwent 2nd surgery.

Conclusion

Immature ovarian teratoma affects primarily younger patients. It is important for clinicians to have a high sense of suspicion whenever the diagnosis of a germ cell tumour is entertained and timely intervene. This case series provide a brief idea of the clinico-radiological and clinic-pathological features, the challenges faced by clinicians in diagnosing and managing immature teratoma. Both stage and grade are important to decide post-op chemotherapy.

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