Image features of growing teratoma syndrome following a malignant ovarian germ cell tumour

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Learning objectives

To access imaging findings of growing teratoma syndrome (GTS), which is rare, benign complication of malignant ovarian germ cell tumour (GCT) following chemotherapy.

Key points

• Growing teratoma syndrome (GTS) is a complication of malignant germ cell tumours with benign pathology.
• The imaging findings of GTS lesions were an increased fatty component within the mass or an entirely cystic lesion in the peritoneal cavity.
• Recognition of GTS is important for the determination of an optimal treatment strategy.
Background

In malignant germ cell tumour (GCT) patients, an enlargement or new development of tumour masses is sometimes detected, yet tumour marker levels decrease. This situation has been described as growing teratoma syndrome (GTS), since the increase of the tumour is composed of mature teratoma component. GTS is a rare metastatic complication that occurs in patients with malignant GCT following appropriate systemic chemotherapy. Three criteria are required for the diagnosis of GTS, as defined by Logothetis and colleagues: (a) Clinical or radiological enlargement of tumours during or after chemotherapy administered for non-seminomatous GCT, (b) Normalisation of previously elevated tumour markers (alpha fetoprotein [AFP] and/or human chorionic gonadotrophin [hCG]) and (c) Absence of any immature component other than a mature teratoma at tumour resection. Although GTS is a well-known complication following non-seminomatous GCTs of the testis, with an incidence of around 1.9-7.6%, GTS occurs less commonly following ovarian GCT. The distinction between GTS and the recurrence of a malignant tumour is important because of the obvious differences in management. Whereas GTS may be managed by surgical resection, a recurred tumour warrants chemotherapy. However, GTS is frequently misdiagnosed as a recurrence because of a lack of awareness of the disease entity and imaging findings. Since the initial description of this entity in the ovary, reports in the radiology literature have been limited. This study describes computed tomography (CT) and magnetic resonance imaging (MRI) findings of GTS in five female patients.
Findings and procedure details

Radiologic findings of primary ovarian GCT and GTS are summarised in Table 1 and 2. In Cases 1 and 5, there were peritoneal seeding masses at the initial presentation of the ovarian immature teratomas. The primary ovarian tumours were seen as heterogeneous masses with a scant amount of fatty tissue. After resection with the macroscopic residual disease at the resection margin and adjuvant chemotherapy for the primary tumours, the follow-up CT revealed GTS lesions which manifested as gradually enlarging, poorly-circumscribed masses with a form of diffuse peritoneal seeding. In Case 1, the GTS lesions were mixed solid and cystic peritoneal masses, which had significantly larger amounts of fatty portions than the primary tumour. After the second operation, which was performed 5 months after the initial surgery, the patient was conservatively treated and there were regrowing peritoneal masses with a similar appearance to the GTS lesions. These were continually enlarging, which was observed on a follow-up CT. In Case 5, the GTS lesions were mixed solid and cystic peritoneal masses with multifocal fatty components, as seen on the CT and MRI. These lesions also revealed significantly larger fatty components than the primary tumour. After the second operation was performed, the tumours did not recur during two years of follow-up.

In Case 2, the patient only underwent a MRI as an initial imaging study and it showed bilateral solid and cystic ovarian masses without gross fat or calcification, which were pathologically confirmed as immature teratomas. After complete resection and adjuvant chemotherapy, the patient was followed-up for 7 years with physical examination and tumour marker analysis. A CT was performed 7 years after the initial surgery and revealed four well-circumscribed GTS lesions along the peritoneum. The lesions were predominantly cystic or solid and cystic masses with multifocal fatty components and calcifications, as seen on CT. The second operation was performed and the GTS lesions were completely resected. The patient was in remission 3 years after second operation.

In Case 3 and 4, the primary ovarian GCTs were pathologically endodermal sinus tumours which were accompanied by mature teratomas. The primary tumours were seen as mixed solid and cystic ovarian masses without gross fat or calcification. After complete resection and chemotherapy for the primary tumours, a follow-up CT showed GTS lesions in the ovaries of each patient. In Case 3, the CT revealed a GTS lesion that manifested as a gradually growing, well-circumscribed fatty mass in the left ovary. The second operation achieved complete resection and the patient had no evidence of recurrence after 6 years of follow-up. In Case 4, a purely cystic mass was identified on 1-year follow-up CT after the initial resection of the primary tumour and was confirmed to be a GTS lesion. A follow-up CT scan done 1 year after the second operation showed a newly developed fatty mass in the right ovary, which has not yet been pathologically confirmed.

In summary, the GTS lesions were demonstrated to be intraperitoneal masses in all patients: poorly-circumscribed diffuse peritoneal masses in 2 patients, well-circumscribed
localised peritoneal masses in 1 and ovarian masses in 2. Two GTS lesions in the form of diffuse and poorly-circumscribed peritoneal masses were noted in patients who had peritoneal implants at the initial presentation of the malignant ovarian GCT. Upon comparison of the GTS lesions with the primary GCTs in regard to the composition of the tumours, imaging features which were more noticeable in the GTS lesions than in the primary tumour were fatty components in 3 patients, both a fatty component and calcification in 1 patient and a purely cystic lesion without a solid component in 1 patient.

18F-fluorodeoxyglucose-positron emission tomography (FDG-PET)/CT scan was performed in four patients and the GTS lesions showed hyper-metabolism in two patients.
Fig. 1: Figs. 1-8. A 13-year-old girl with growing teratoma syndrome following chemotherapy for an immature teratoma (case 1). Fig. 1. Axial CT at initial presentation demonstrates a large heterogeneously solid and cystic mass (arrows) with scattered calcifications and a scant amount of fat (arrowhead) in the pelvic cavity that was pathologically confirmed to be an immature teratoma of the right ovary.

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Fig. 3: Figs. 1-8. A 13-year-old girl with growing teratoma syndrome following chemotherapy for an immature teratoma (case 1). Axial CT in the immediate postoperative period (Fig. 2), at postoperative 2 months just before initiation of chemotherapy (Fig. 3) and at 3 months after initiation of chemotherapy (Fig. 4) showed a growing mass (arrows in Fig. 3 and Fig. 4) with an increasing volume of fat (white arrowheads in Fig. 4) and calcification (black arrowheads in Fig. 3 and Fig. 4) in the recto-uterine pouch.

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Fig. 7: Figs. 1-8. A 13-year-old girl with growing teratoma syndrome following chemotherapy for an immature teratoma (case 1). Photograph of the specimen of the mass (Fig. 7) and microscopic image (hematoxylin and eosin stain, x100) of the resected specimen (Fig. 8) showed a glistening whitish to yellowish mass which contained only mature elements without immature neuroepithelial tissue.

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Fig. 8: Figs. 1-8. A 13-year-old girl with growing teratoma syndrome following chemotherapy for an immature teratoma (case 1). Photograph of the specimen of the mass (Fig. 7) and microscopic image (hematoxylin and eosin stain, x100) of the resected specimen (Fig. 8) showed a glistening whitish to yellowish mass which contained only mature elements without immature neuroepithelial tissue.

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Fig. 9: Figs. 9-11. A 37-year-old woman with growing teratoma syndrome following chemotherapy for an immature teratoma (case 2). Fig. 9. Axial fat-suppressed T2-weighted image shows a heterogeneously solid and cystic mass (arrow) in the pelvic cavity that was pathologically confirmed as an immature teratoma of the right ovary.

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**Fig. 10:** Figs. 9-11. A 37-year-old woman with growing teratoma syndrome following chemotherapy for an immature teratoma (case 2). Axial CT performed at about 7 years after surgery shows newly developed, multiple well-circumscribed masses in the peritoneal cavity including a mixed solid and cystic mass in the perisplenic area (arrow on Fig. 10) and a predominantly cystic mass in the pelvic cavity (arrow on Fig. 11) with fat and calcification. These masses were confirmed as matured teratomas without any immature component.

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Fig. 11: Figs. 9-11. A 37-year-old woman with growing teratoma syndrome following chemotherapy for an immature teratoma (case 2). Axial CT performed at about 7 years after surgery shows newly developed, multiple well-circumscribed masses in the peritoneal cavity including a mixed solid and cystic mass in the perisplenic area (arrow on Fig. 10) and a predominantly cystic mass in the pelvic cavity (arrow on Fig. 11) with fat and calcification. These masses were confirmed as matured teratomas without any immature component.

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**Fig. 12:** Figs. 12-14. A 16-year-old girl with growing teratoma syndrome following chemotherapy for an endodermal sinus tumour (case 3). Fig. 12. Coronal CT image at initial presentation shows a solid and cystic mass (arrows) which was pathologically confirmed as an endodermal sinus tumour of the right ovary. A concomitant mature teratoma (*) is also noted.

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Fig. 13: Figs. 12-14. A 16-year-old girl with growing teratoma syndrome following chemotherapy for an endodermal sinus tumour (case 3). Fig. 13. Axial CT performed at 2 weeks after the initial surgery before initiation of chemotherapy shows a cystic lesion in the left adnexa (arrow) which was regarded as a functional cyst or postoperative change.

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Fig. 14: Figs. 12-14. A 16-year-old girl with growing teratoma syndrome following chemotherapy for an endodermal sinus tumour (case 3). Fig. 14. Axial CT performed at 15 months after termination of chemotherapy demonstrates a newly developed fatty mass in the left adnexa (arrow).

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**Fig. 15:** Figs. 15-16. A 21-year-old woman with growing teratoma syndrome following chemotherapy for an endodermal sinus tumour (case 4). Fig. 15. Axial CT performed at initial presentation shows a mixed solid and cystic mass (arrows) which was pathologically confirmed as an endodermal sinus tumour of the left ovary. Concomitant mature teratomas (*) are also noted bilaterally.

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Fig. 16: Figs. 15-16. A 21-year-old woman with growing teratoma syndrome following chemotherapy for an endodermal sinus tumour (case 4). Fig. 16. Axial CT performed 9 months after termination of chemotherapy shows a newly developed cystic mass (arrow) with a discernible wall in the pelvic cavity. This mass was confirmed to be a mature cystic teratoma of the right ovary.

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**Fig. 17:** Figs. 17-20. A 13-year-old girl with growing teratoma syndrome following chemotherapy for an immature teratoma (case 5). Opposed-phase gradient-echo pulse sequence T1-weighted MR image (Fig. 17.) and non-enhanced axial CT scan (Fig. 18) performed at initial presentation demonstrate a large heterogeneous mass with scant calcification (white arrowhead) and fat (black arrowheads) in the pelvic cavity which was pathologically confirmed as an immature teratoma of the left ovary.

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Fig. 18: Figs. 17-20. A 13-year-old girl with growing teratoma syndrome following chemotherapy for an immature teratoma (case 5). Opposed-phase gradient-echo pulse sequence T1-weighted MR image (Fig. 17.) and non-enhanced axial CT scan (Fig. 18) performed at initial presentation demonstrate a large heterogeneous mass with scant calcification (white arrowhead) and fat (black arrowheads) in the pelvic cavity which was pathologically confirmed as an immature teratoma of the left ovary.

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**Fig. 19:** Figs. 17-20. A 13-year-old girl with growing teratoma syndrome following chemotherapy for an immature teratoma (case 5). Fig. 19. Axial CT scan performed 9 months after termination of chemotherapy shows newly developed solid and cystic masses (arrows) with a fatty area (arrowhead) in the perihepatic space.

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Fig. 20: Figs. 17-20. A 13-year-old girl with growing teratoma syndrome following chemotherapy for an immature teratoma (case 5). Fig. 20. Axial opposed-phase gradient-echo pulse sequence T1-weighted images show multiple foci with signal drop within the masses (arrows). These masses were confirmed as mature teratomas without immature components.

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Fig. 2: Figs. 1-8. A 13-year-old girl with growing teratoma syndrome following chemotherapy for an immature teratoma (case 1). Axial CT in the immediate postoperative period (Fig. 2), at postoperative 2 months just before initiation of chemotherapy (Fig. 3) and at 3 months after initiation of chemotherapy (Fig. 4) showed a growing mass (arrows in Fig. 3 and Fig. 4) with an increasing volume of fat (white arrowheads in Fig. 4) and calcification (black arrowheads in Fig. 3 and Fig. 4) in the recto-uterine pouch.

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Fig. 4: Figs. 1-8. A 13-year-old girl with growing teratoma syndrome following chemotherapy for an immature teratoma (case 1). Axial CT in the immediate postoperative period (Fig. 2), at postoperative 2 months just before initiation of chemotherapy (Fig. 3) and at 3 months after initiation of chemotherapy (Fig. 4) showed a growing mass (arrows in Fig. 3 and Fig. 4) with an increasing volume of fat (white arrowheads in Fig. 4) and calcification (black arrowheads in Fig. 3 and Fig. 4) in the recto-uterine pouch.
Fig. 6: Figs. 1-8. A 13-year-old girl with growing teratoma syndrome following chemotherapy for an immature teratoma (case 1). Fig. 6. Axial fused PET-CT demonstrates multifocal fluorodeoxyglucose activity within the mass.

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**Fig. 5:** Figs. 1-8. A 13-year-old girl with growing teratoma syndrome following chemotherapy for an immature teratoma (case 1). Fig. 5. Axial CT at the level of the upper abdomen which was performed at 3 months after initiation of chemotherapy demonstrates multiple peritoneal implants (arrows) with scattered fatty areas and calcifications.

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Table 2: Radiologic findings of growing teratoma syndrome in 5 patients

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Number (Location)</th>
<th>Size (cm)</th>
<th>Imaging features</th>
<th>Distinctive CT findings between primary tumor and GTS masses</th>
<th>Metabolism on PET-CT</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Uncountable (recto-uterine pouch, peripheatic and perisplenic space)</td>
<td>unmeasurable</td>
<td>Poorly-circumscribed</td>
<td>Mixed solid and cystic</td>
<td>Fat</td>
</tr>
<tr>
<td>2</td>
<td>Right subphrenic space, splenic hilum, left paracolic gutter, and recto-uterine pouch</td>
<td>2.2-6.4 (mean, 4.1)</td>
<td>Well-circumscribed</td>
<td>Predominantly cystic or mixed solid and cystic</td>
<td>Fat, calcification</td>
</tr>
<tr>
<td>3</td>
<td>One (left ovary)</td>
<td>3.3</td>
<td>Well-circumscribed</td>
<td>-</td>
<td>fat</td>
</tr>
<tr>
<td>4</td>
<td>One (right ovary)</td>
<td>5.5</td>
<td>Well-circumscribed</td>
<td>Cystic</td>
<td>none</td>
</tr>
<tr>
<td>5</td>
<td>Uncountable (perihepatic space and recto-uterine pouch)</td>
<td>unmeasurable</td>
<td>Poorly-circumscribed</td>
<td>Mixed solid and cystic</td>
<td>Fat</td>
</tr>
</tbody>
</table>

Note - NA, not available; hyper, hypermetabolic; iso, isometabolic.

Table 2: Table 2, Radiologic findings of growing teratoma syndrome in 5 patients

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Table 1: Clinical and radiological manifestations of primary ovarian germ cell tumours in 5 patients

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Primary ovarian germ cell tumor</th>
<th>Histology</th>
<th>Concomitant mature teratoma</th>
<th>FIGO stage</th>
<th>CT and/or MR findings</th>
<th>Presence of peritoneal implants</th>
<th>Extent of initial surgery</th>
<th>Result of resection</th>
<th>Time interval (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Immature teratoma</td>
<td>N</td>
<td>III</td>
<td>Heterogeneous, mixed solid and cystic mass with scattered calcification and scanty amount of fat tissue</td>
<td>Y</td>
<td>RSO, peritoneal resection and omentectomy</td>
<td>partial</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Immature teratoma</td>
<td>N</td>
<td>I</td>
<td>Heterogeneous, solid and cystic mass</td>
<td>N</td>
<td>RSO, wedge resection of left ovary</td>
<td>complete</td>
<td>83</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Endodermal sinus tumor</td>
<td>Y, bilateral</td>
<td>I</td>
<td>Heterogeneous, mixed solid and cystic mass</td>
<td>N</td>
<td>RSO, wedge resection of left ovary</td>
<td>complete</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Endodermal sinus tumor</td>
<td>Y, bilateral</td>
<td>I</td>
<td>Heterogeneous, mixed solid and cystic mass</td>
<td>N</td>
<td>LSO, right ovarian cystectomy and omentectomy</td>
<td>complete</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Immature teratoma</td>
<td>N</td>
<td>III</td>
<td>Heterogeneous predominantly solid mass with scattered scanty amount of fat and calcification</td>
<td>Y</td>
<td>LSO, peritoneal resection and omentectomy</td>
<td>partial</td>
<td>16</td>
<td></td>
</tr>
</tbody>
</table>

Note – NA, not available; N, no; Y, yes; AFP, alpha fetoprotein, * time interval between initial surgery for germ cell tumor and subsequent surgery for growing teratoma syndrome
Table 1: Table 1, Clinical and radiological manifestations of primary ovarian germ cell tumors in 5 patients

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Conclusion

GTS is a rare benign complication following chemotherapy of malignant ovarian GCT. Although it is not always possible to differentiate GTS from tumour recurrence, GTS should be considered in the differential diagnosis when there are newly developed or enlarged masses in the peritoneal cavity showing an increased fatty component compared to the primary tumour or an entirely cystic lesion without a solid portion on follow-up imaging studies. Knowledge of this rare entity and its imaging findings is important because a correct diagnosis is critical to determine the appropriate treatment strategy and to avoid unnecessary additional chemotherapy.
References


