Growing teratoma syndrome is an increase of tumor size containing only a mature teratoma component, during or after chemotherapy for germ cell tumors. Mature teratomatous elements are chemoresistant and have to be resected surgically. We describe three patients with malignant immature teratoma treated with chemotherapy and surgical resection. All three had an increase in the size of the mass after chemotherapy, surgery was possible, and histology revealed mature teratoma. One of the patients showed fluorodeoxy glucose positron emission tomography (FDG-PET) positivity for growing teratoma syndrome, but the histology revealed only mature teratoma. All three patients are alive, at 55, 72, and 103 months follow up after the initial diagnosis. Data collected from the literature are reviewed. Early recognition of this syndrome is essential as it offers hope for curative resection and avoids the use of ineffective chemotherapy.

Key words Immature teratoma · Tumor markers · PET scan · Chemotherapy

Introduction

Growing teratoma syndrome (GTS) is defined as an increase in tumor size in a patient with germ cell tumor (GCT) during or after chemotherapy while tumor markers are normal and histology shows only mature teratoma. Logothetis et al. first used this term in 1982. DiSaia et al., in 1977, described this phenomenon as “chemotherapeutic retroconversion.” Later it was understood that the two terminologies were synonymous. While this syndrome is well known in males (incidence varying from 1.9% to 7.6%), few cases of GCT have been reported in young girls and women. In our 10 years’ experience of 120 cases of GCT, we have encountered three such patients.
Case 2
A 26-year-old woman presented in January 2001 with abdominal pain of 4 months’ duration. Magnetic resonance imaging (MRI) showed a large pelvic mass, measuring 15.3 cm × 14.3 cm, compressing the urinary bladder and displacing the uterus. She was referred to our institute. She underwent exploratory laparotomy, which revealed a right-sided ovarian cyst. Total abdominal hysterectomy with cyst removal and omental biopsy was performed. Residual disease was gross in the form of a left adnexal mass, peritoneal deposits, and enlarged external iliac lymph nodes. Histology revealed immature teratoma, grade 3. Results for serum tumor markers were: ß HCG, negative; and AFP, 1462 ng/ml. Postoperatively, she received four cycles of BEP chemotherapy, following which serum AFP was normalized, with a persistent mass seen on CT scan. She underwent exploratory laparotomy, with complete excision of the pelvic mass. Histological examination of the pelvic mass and omental tissue revealed only mature teratomatous elements. She is on regular follow up and continues to be disease-free, 5 years after her last surgery.

Case 3
A 27-year-old parous woman presented to a local hospital in June 1998 with pain and distension of the abdomen of 1-month duration. CT scan of abdomen and pelvis revealed a pelvic mass, measuring 8 × 8.8 cm, occupying the left adnexa and pouch of Douglas. Laparotomy was performed, followed by biopsy of the mass. Histopathology revealed immature teratoma. She was referred to our institute for further management. Examination revealed a firm mass in the suprapubic region, the size of a 16-week uterus and the same mass was felt in the per-vaginal examination in the left adnexal region, pushing the uterus to the right. Serum AFP was 6000 ng/ml, lactate dehydrogenase (LDH) was 566 IU/ml, and ß HCG was undetectable. Four cycles of BEP chemotherapy were planned. After two cycles, she developed a fecal fistula, for which she underwent transverse loop colostomy. She completed four cycles of BEP in September 1998. After the four cycles, the left adnexal mass was persistent, with a slight increase in size, while her markers were negative. She underwent laparotomy with partial removal of the pelvic mass. Histopathology revealed mature teratoma. In view of this, close follow up was advised, with monitoring of tumor markers and CT scans, and closure of the colostomy later. She remained asymptomatic with negative markers. Recently, while she was being evaluated for closure of the colostomy, a CT scan showed an increase in the size of the pelvic mass and liver lesions. Positron emission tomography (PET) scan showed positive fluorodeoxy glucose (FDG) uptake in the pelvic mass (Fig. 3). She underwent laparotomy and excision of the pelvic mass. There were liver lesions, but they were not excised. Histopathology revealed mature teratoma comprising cartilage, adipose, hair follicle, brain, and thyroid tissue. She is disease free 9 months after her last surgery.

Discussion
Malignant cell differentiation into mature teratoma and selective chemotherapy-induced destruction of immature elements are the two possible mechanisms considered for the pathogenesis of GTS. It has been suggested that chemotherapy might alter the cellular kinetics of totipotential malignant cells in some way to favor the development of mature elements rather than immature elements. Benign evolution may be an indirect property of the malignant cell. In murine teratocarcinoma systems, isolated embryonal carcinoma cells are capable of spontaneous differentiation into a broad range of somatic tissues without the persistence of some of the embryonal malignant elements.

GTS is a rare entity in females. We encountered three female patients with germ cell tumor (GCT) of the ovary among 120 GTS patients in over 10 years; this confirms the rarity of this entity. A thorough Medline search revealed only 37 cases of GTS of the ovary (Table 1). The median age at onset was 20 years, ranging from 5 to 38 years. The most common histology at diagnosis was immature teratoma, seen in 28 patients (76%). All the patients underwent surgery followed by chemotherapy for the primary treat-