Growing Teratoma Syndrome: An Asian Woman With Immature Teratoma of Left Ovary After Chemotherapy

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Growing teratoma syndrome (GTS) was first described by Logothetis et al [1] and is characterized by an enlarged neoplastic mass of nonseminomatous germ cell tumors (NSGCTs) following chemotherapy, with normalization of previously elevated serum tumor markers and absence of any NSGCT components. The incidence of GTS in metastatic NSGCTs of the testis is estimated to be around 1.9–7.6% [1,2], while GTS is less common in ovarian NSGCT. Tonkin et al [3] reported the first ovarian case of GTS in 1991. To date, only a few case reports of ovarian GTS have been documented in the medical literature [4], and no case reports of Asian women have been published. Furthermore, the use of three-dimensional (3D) ultrasound for the diagnosis and management of ovarian GTS has not been reported. We present the case of a 29-year-old Asian woman with a primary diagnosis of immature teratoma and GTS. We used 3D ultrasound and computed tomography (CT) for diagnosis and follow-up in this patient.

A previously healthy, 29-year-old Taiwanese woman was referred to a local clinic with abdominal discomfort and a palpable abdominal mass in January 2006. An exploratory laparotomy and left salpingo-oophorectomy were performed. Histopathologic examination of the pelvic mass (about 21 × 21 × 13 cm) revealed an immature teratoma grade I. Microscopically, the tissue sections had the appearance of an immature teratoma, composed of abundant mature tissues including skin and respiratory type epithelium, intermixed with some slightly immature cartilage and loose stroma. Focal areas of neural tissue with no obvious mitotic activity were also seen.

After surgery, she was transferred to our medical center for adjuvant therapy because of the detection of a progressively elevated serum α-fetoprotein (AFP) level (1,839 ng/mL). Pelvic two-dimensional sonography disclosed a right adnexal mass (3.5 × 5 cm) with suspicious recurrent disease. CT scan revealed a lower-density pelvic mass with an ill-defined irregular shape near to the uterus (Figure 1).

Chemotherapy with cisplatin, etoposide and bleomycin (PEB) were promptly administered because of the suspicion of malignancy. After three cycles of PEB chemotherapy, the AFP level normalized (6.16 ng/mL). However, after completion of the chemotherapy, pelvic two-dimensional sonography revealed a progressively enlarged heteroechogenic tumor mass (6.3 × 5.3 cm) in the cul-de-sac, even though her serum tumor markers, including AFP, CA-125, CA-199, carcinoembryonic antigen, squamous cell carcinoma antigen and human chorionic gonadotropin, remained normal. Notably, 3D sonography depicted the pelvic mass, which was characterized by an echogenic mass, scattered anechoic areas, punctate calcification, and smooth margins over the three axes (Figure 2). In addition, 3D power Doppler and 3D color Doppler sonography showed no flow over or within the mass. After chemotherapy, a CT scan of the abdomen revealed an enhanced nodule (about 1.5 cm) over the segment VI surface of the liver, and a well-circumscribed, irregularly shaped soft-tissue mass (about 8 cm in size) with streak-like calcifications and heterogeneous enhancement occupying the cul-de-sac (Figure 3). Scanty ascites and para-aortic lymph node enlargement were also seen.

The patient underwent a second intentional laparotomy to investigate these findings. In order to preserve fertility, partial omentectomy, retroperitoneal lymph node dissection and complete resection of the multiple solid masses over the cul-de-sac, omentum and peritoneal cavity were undertaken. Histopathologic examination of sections of the masses showed only mature teratoma consisting of normal skin elements, respiratory tract

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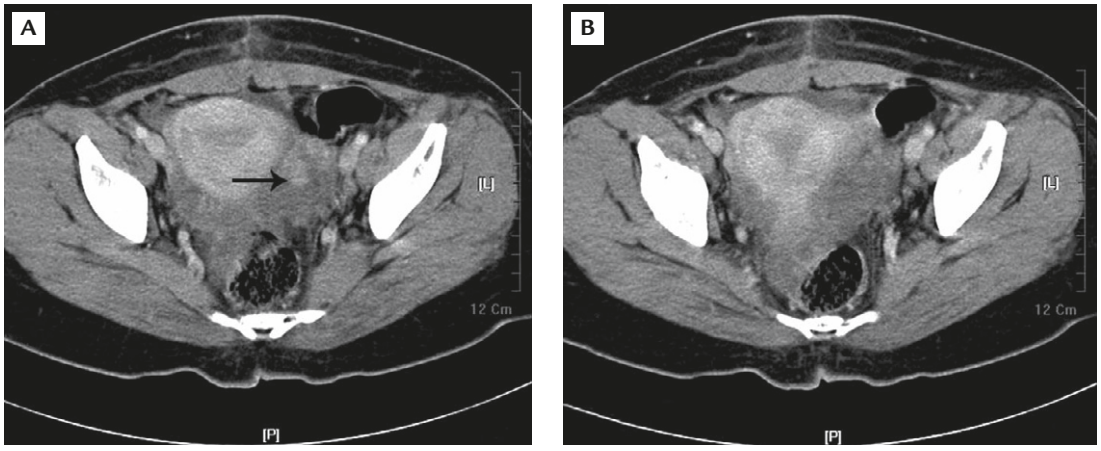

Figure 1. Contrast-enhanced axial pelvic computed tomography scans of the lower pelvis, (A) 295 mm below benchmark, and (B) 300 mm below benchmark. Both were obtained after initial surgery with elevated α-fetoprotein, demonstrating a heterogeneous mass with ill-defined margins (A, arrow).

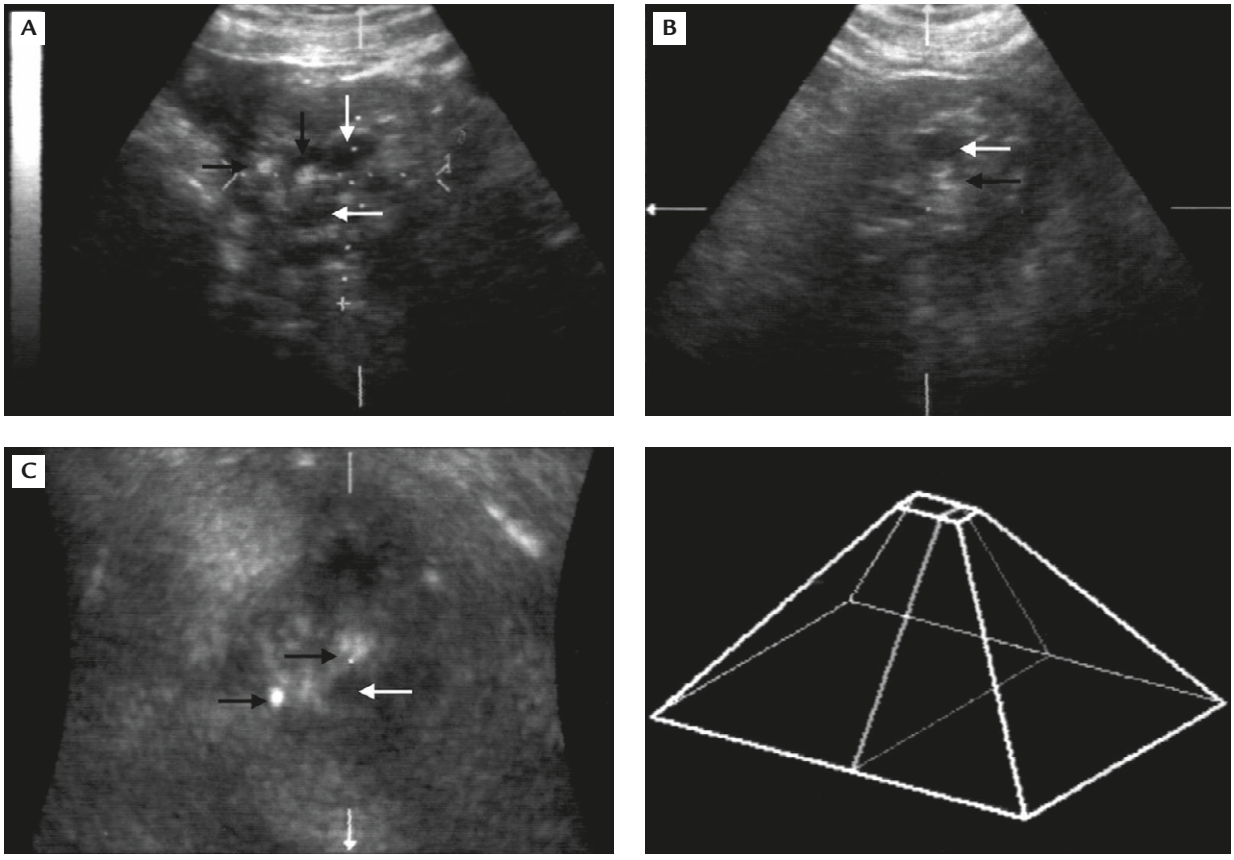

Figure 2. Three-dimensional orthogonal sonography of the growing teratoma syndrome tumors, obtained after completion of six cycles of the cisplatin, etoposide and bleomycin chemotherapy with normal α-fetoprotein. Three (A) X, (B) Y, and (C) Z axial images disclosed punctate calcifications (black arrows), scattered anechoic holes (white arrows), and smooth margins in all three axis.

mucosa, more mature cartilage, bone, glial tissue with degenerative astrocytes, ganglion cells, fat tissue, and occasional retinal-like structures. No evidence of immature tissue or malignant components could be found in any of the sections. The lymph nodes were normal.

The patient received no further treatment at follow-up, and all the tumor markers remained within normal limits. No signs of recurrence had appeared at the time of this report, 6 months after the second debulking operation for GTS.

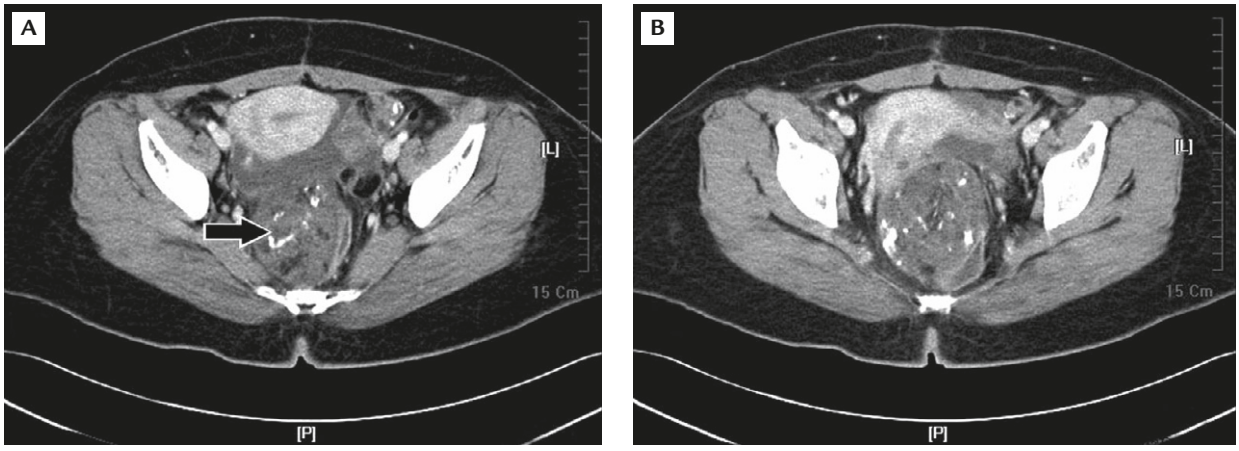

Figure 3. Contrast-enhanced axial pelvic computed tomography scans of the lower pelvis, (A) 336 mm below benchmark and (B) 351 mm below benchmark, obtained after completion of six cycles of the cisplatin, etoposide and bleomycin chemotherapy, disclosed an enlarged, smoothly marginated mass with streaked multiple calcifications (A, arrow).

Although GTS was first described by Logothetis et al [1] in 1982, DiSaia et al [5] had described a similar phenomenon 5 years earlier, which they called "chemotherapeutic retroconversion". It is now thought that GTS and chemotherapeutic retroconversion are different names representing the same disease entity [6]. The underlying mechanism of GTS, however, is not clearly understood. Elimination of the malignant components of NSGCT after chemotherapy is a possible mechanism responsible for this pathology. This chemotherapeutic retroconversion phenomenon of GTS means that clinicians often misinterpret it as a chemoresistant tumor or recurrent malignancy because of its radiologic or clinical presentation as a growing or persistent mass. Complete resection is the standard treatment for mature teratomas because of the risk of malignant transformation and of organ damage, owing to their uncertain growth rate.

Female ovarian GTS is extremely rare, and no reports of ovarian GTS in Asian women have been described. No racial differences in female GTS have been mentioned in the literature, and the reason for this lack of reports is unknown. Further international collaborative studies are warranted.

To our knowledge, no 3D sonographic features of GTS have previously been reported. In this study, we describe the 3D sonography findings, including a scattered anechoic area and miliary punctate calcifications which may represent mature components of fatty tissue and bony tissue, respectively. Furthermore, clear and smooth margins were noted on all three axes. To our knowledge, this is the first case illustrating the GTS characteristics of multiple anechoic areas and calcifications using 3D ultrasound.

No peripheral or penetrating flow over the mass was detected by 3D color Doppler or 3D power Doppler scanning. Combining these findings of 3D sonography, color Doppler and power Doppler indicated the development of a mature teratoma without neovascularization, a sign of malignancy. However, we could not exclude the possibility of a recurrence of NSGCT, especially when an obviously growing tumor was observed. From the follow-up of this case, 3D sonography was no less sensitive than CT for differential diagnosis, especially when combined with color flow Doppler scanning. Furthermore, 3D sonography has the advantages over CT of being convenient, safe, inexpensive, nonradioactive, and noninvasive. We, therefore, believe that 3D sonography could be a useful diagnostic tool for GTS.

Although GTS has a good prognosis, close follow-up with serial tumor marker measurements and imaging studies are highly recommended, because stabilization of GTS can take as long as 10 years after diagnosis. Variable imaging findings and tumor marker results may suggest the presence of a mature lesion, and surgical resection or biopsy is necessary to exclude malignant recurrence. At the time of this report, normalization of tumor markers and no evidence of recurrence had been observed in our patient. She was disease-free 6 months after diagnosis, with preserved fertility capacity.

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