Growing teratoma syndrome: A case report*

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ABSTRACT

Growing teratoma syndrome is a rare phenomenon. Presented is a case of a 36 year old, G2P2 (2002) who consulted for abdominal enlargement and subsequently underwent exploratory laparotomy, peritoneal fluid cytology, left salpingooophorectomy, right oophorocystectomy, infracolic omentectomy and random peritoneal biopsy. Histopathology revealed immature teratoma of the ovary, FIGO grade III, stage IIIC. She received adjuvant chemotherapy using Bleomycin, Etoposide, Cisplatin. After the second cycle of chemotherapy, new lesions were appreciated in the right ovary and at the cul de sac for which she underwent exploratory laparotomy, peritoneal fluid cytology, total hysterectomy with right salpingooophorectomy, tumor debulking, infragastric omentectomy, random peritoneal biopsy. Histopathologic study showed mature teratoma. No further treatment was given. Presently, patient has no evidence of disease for 5 months.

Keywords: Chemotherapeutic retroconversion, Growing teratoma syndrome, Ovarian immature teratoma

INTRODUCTION

Germ cell tumors of the ovary signify a small ratio of all ovarian malignancies with immature teratoma being the third most common among them. It is usually diagnosed in the adolescent and reproductive age women who would benefit from fertility sparing surgery, with or without chemotherapy. Growing teratoma syndrome (GTS) is a rare occurrence in patients with ovarian immature teratoma. In this report, a case of growing teratoma syndrome is discussed.

CASE REPORT

R.D. is a 36-year-old, Gravida 2 Para 2 (2002), who consulted for enlarging abdominopelvic mass of two months duration. There was no history of heredofamilial diseases and previous surgery.

The patient denied use of cigarettes, alcohol and illicit drugs. Her first coitus was at 25 years of age with one monogamous partner. She had Pap test last February 2016 with normal results. Her menarche was at 15 years old with regular monthly intervals. Her last menstrual period was February 2017. All her to pregnancies were delivered vaginally with no complications.

Her condition started two months when she experienced gradual enlargement of the abdomen associated with early satiety, pelvic heaviness and weight loss. She consulted with a gynaecologist with findings of ovarian new growths on transvaginal ultrasound. She underwent exploratory laparotomy, peritoneal fluid cytology, left salpingooophorectomy, right oophorocystectomy, infracolic omentectomy and random peritoneal biopsy (July 2016) from a different institution. Lymphadenectomy was not performed due to the unavailability of a gynecologic oncologist. Intraoperatively, there was approximately one liter of mucoid ascitic fluid. The left ovary was converted to a cream to grayish multicystic mass measuring 18.0 x 15.0 x 11.0 cms with some calcifications and hair within. It was partly covered by the omentum. The right ovarian cyst measured 4.0 x 4.0 x 3.5 cm with intact smooth capsule. There were multiple implants on the pelvic peritoneum and cul de sac with an aggregate diameter of 2.0 cm. Histopathology revealed immature teratoma, grade II of the right ovary (Figures 1 & 2), mature cystic teratoma of the left ovary (Figure 3) and with metastatic immature teratoma, grade III on the peritoneum (Figure 4), gliomatosis peritonei in omentum biopsy, giving the diagnosis of immature teratoma, FIGO grade III, right ovary, stage IIIC. She was advised chemotherapy but prior to that, baseline physical examination and imaging studies were all normal. The alpha fetoprotein (AFP), however, was elevated at 23.2 IU/ml (0-5.8 IU/ml). Chemotherapy was given in the form of Bleomycin 30 u/m2 at Day 1, 8, 15, Etoposide 100 mg/m2 at Day 1 to 5 and Cisplatin 20mg/m2 at Day 1 to 5 (BEP regimen) every 28 days. After the second cycle of BEP, a 10 x 10 cm pelvic mass and a 6.0 x 8.0 cm cul de sac mass were appreciated on pelvic examination. Transvaginal ultrasound confirmed these masses. (Figure 5) AFP was

*Third Place, SGOP 2017 Interesting Case Contest

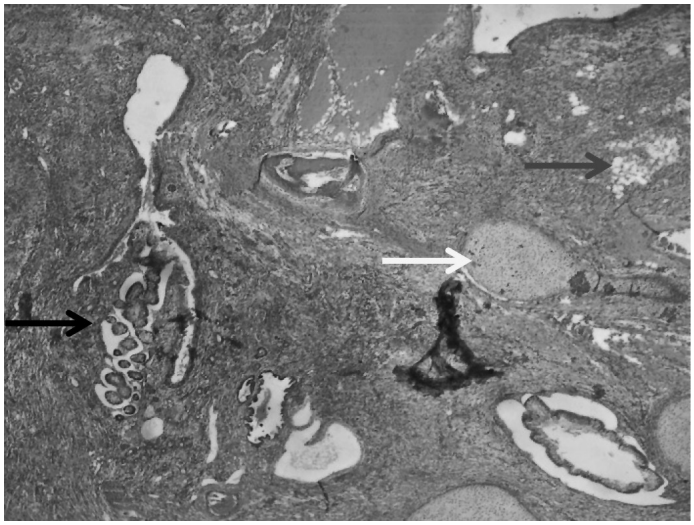

Figure 1. Immmature Teratoma, Right Ovary (40x) showing mature intestinal elements (black arrow), mature cartilaginous elements (yellow arrow), and mature fat elements (blue arrow)

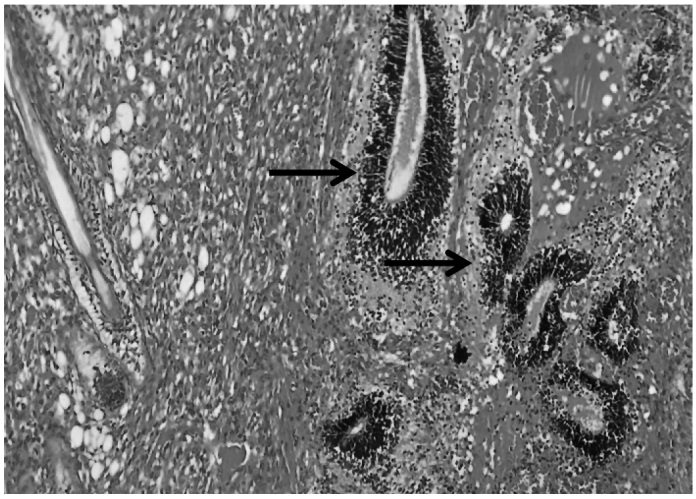

Figure 2. Immature Teratoma, Right Ovary (100x), showing numerous immature neuroepithelium (black arrows)

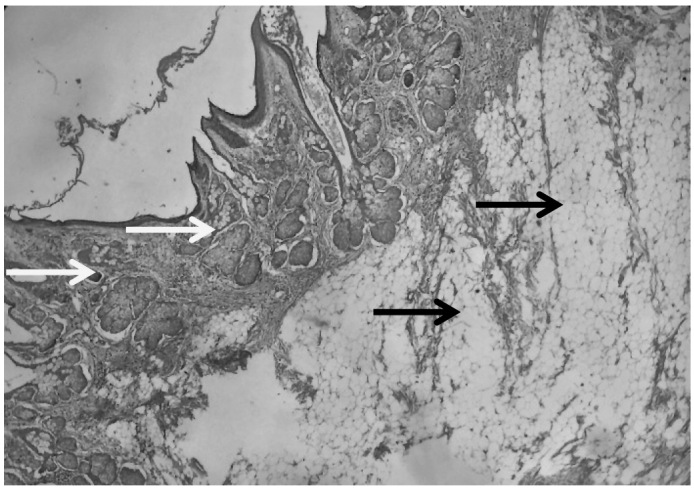

Figure 3. Left Ovary, Mature Teratoma (40x), showing mature fat elements (black arrows) and mature skin adnexal structures (yellow arrows)

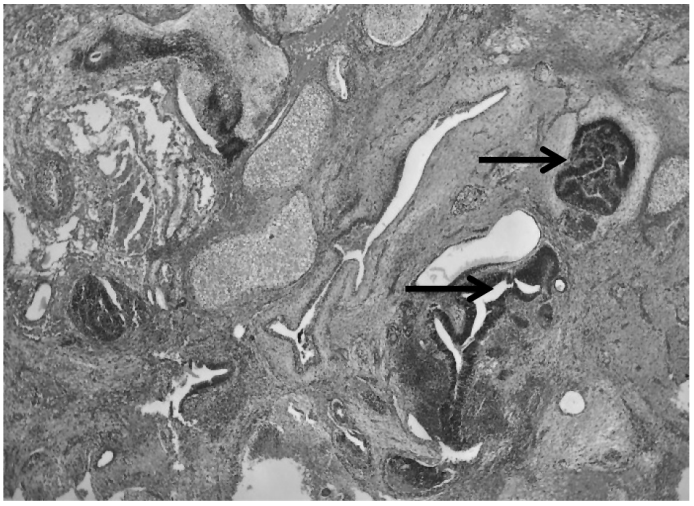

Figure 4. Peritoneum, Immature Teratoma (40x), showing numerous immature neuroepithelium (black arrows)

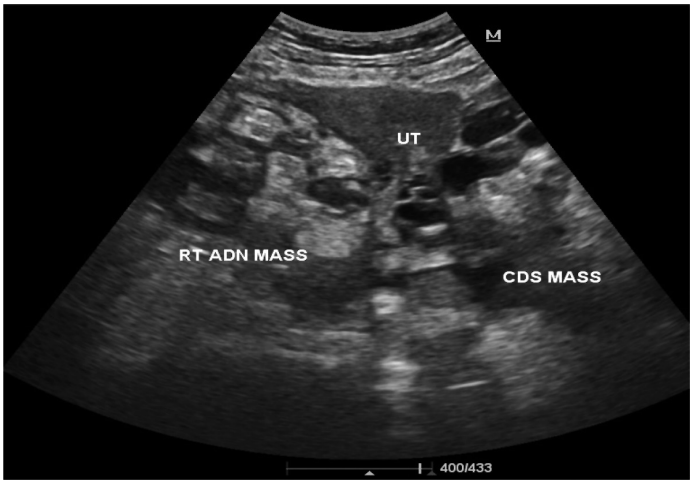

Figure 5. Transvaginal ultrasound, transverse view of the uterus, right adnexal mass and cul de sac mass. At the right adnexal area (RT ADN MASS) is a heterogenous predominantly solid mass measured 9.3 x 10.6 x 8.1 cm. A cul de sac mass (CDS MASS) with heterogeneous predominantly solid measured 6.9 x 8.5 x 4.5 cm

normal at 3.3 IU/ml (0-5.8 IU/ml). She then underwent exploratory laparotomy, peritoneal fluid cytology, total hysterectomy with right salpingooophorectomy, tumor debulking, infragastric omentectomy, random peritoneal biopsy (March 2017). Intraoperatively, the right ovary was converted to a uniloculated predominantly solid mass with cystic and necrotic areas on cut section measured 14.0 x 11.0 x 6.0 cm. (Figure 6). There were two cul de sac masses which measured 8.0 x 8.0 x 3.0 cm and 9.0 x 6.0 x 5.0 cm with the same characteristics as the ovarian mass. (Figure 7). All tumors were completely resected. Final histopathologic result showed mature cystic teratomas with no malignant cells or tissues seen (Figures 8 & 9). Gliomatosis peritonei on omentum, right pelvic sidewall and paracolpic biopsies (Figure 10). Levels of AFP were

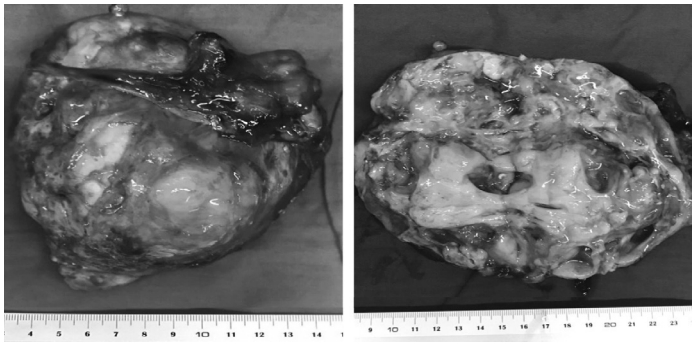

Figure 6. Right ovary converted to a uniloculated predominantly solid mass with cystic and necrotic areas on cut section measured 14.0 x 11.0 x 6.0 cm

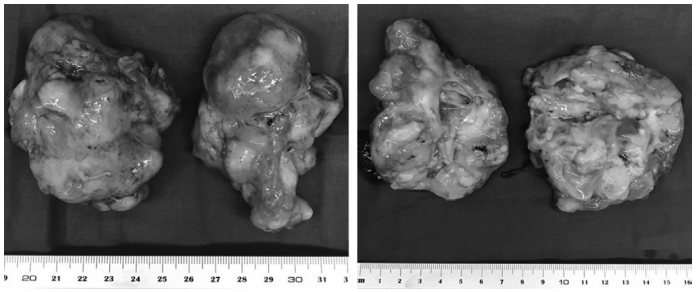

Figure 7. Two cul de sac masses predominantly solid with cystic and necrotic areas measured 8.0 x 8.0 x 3.0 cm and 9.0 x 6.0 x 5.0 cm

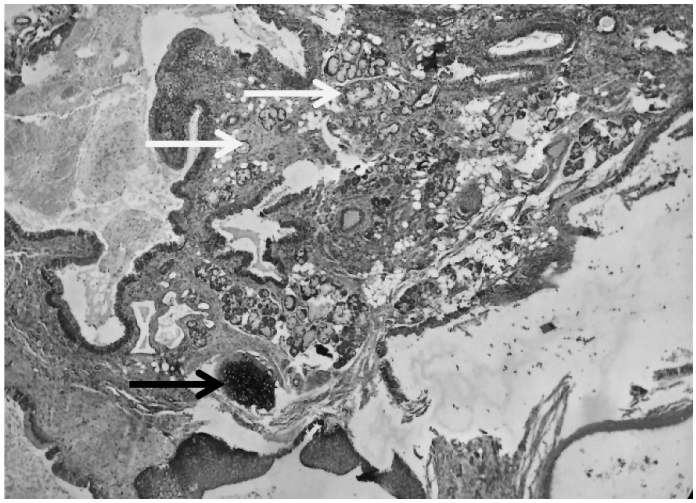

Figure 8. Mature Teratoma, Right Ovary (40x) showing mature cartilaginous elements (black arrow) and mature intestinal elements (yellow arrows)

monitored and remained within normal ranges. No subsequent treatment was given. At present, patient showed no evidence of disease for 5 months.

CASE DISCUSSION

Immature teratoma of the ovary most frequently occurs in children and in adults up to age 30 years for whom fertility-sparing surgery becomes a necessity.

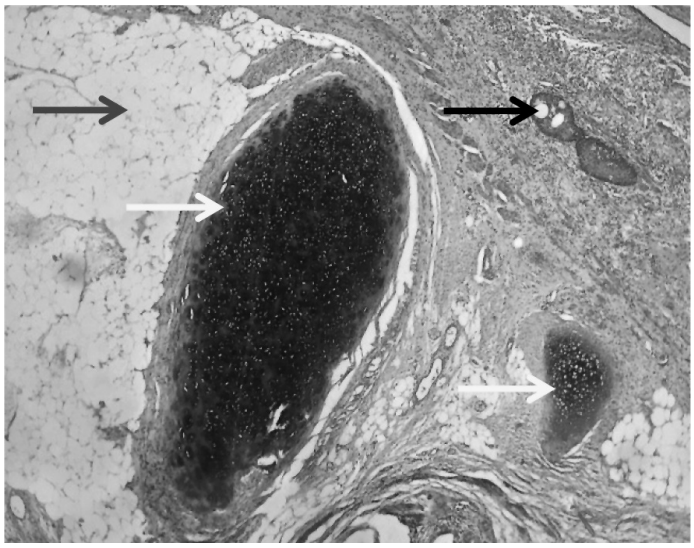

Figure 9. Mature Teratoma, Right Ovary, 40x, showing mature skin adnexal elements (black arrow), mature cartilaginous elements (yellow arrows) and mature fat elements (blue arrow)

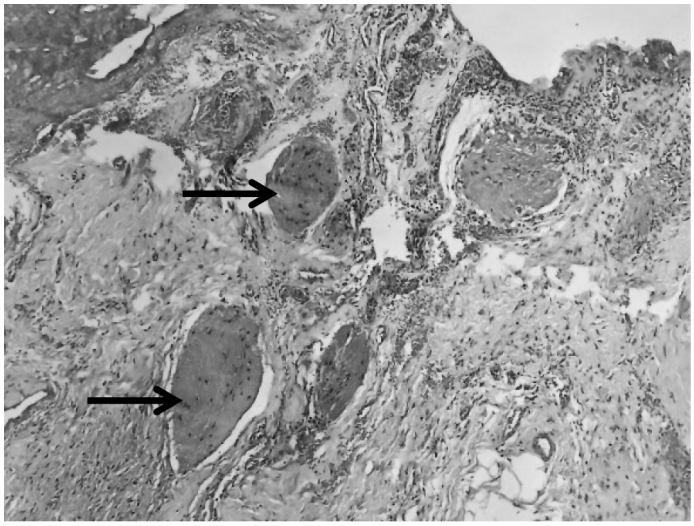

Figure 10. Gliomatosis peritonei, 40x, right pelvic sidewall showing mature neural tissues (black arrows)

Growing teratoma syndrome is a rare phenomenon in patients with primary ovarian germ cell tumors. This occurrence is defined as a subsequent growth of mature teratoma during chemotherapy or subsequently after chemotherapy for a malignant germ cell tumor.[1] These results are, as a consequence, often misinterpreted as tumor progression. The incidence of growing teratoma syndrome in nonseminomatous germ cell tumor of the testes was 1.9 to 7.9 percent.[1] It is less common after ovarian immature teratoma and has been reported to occur in 12% of ovarian germ cell tumors.[2] There has been 101 cases being reported in the literature.[3]

Di Saia et al in 1977 first described "Chemotherapeutic Retroconversion" in ovarian immature teratoma. Chemotherapeutic retroconversion is a chemotherapy induced conversion of a metastatic immature teratoma into mature teratoma.[4] They reported 3 women who received Vincristine, Actinomycin D and Cytoxan (VAC) for ovarian immature teratoma. Development of multiple tumors was noted during chemotherapy which only showed mature components on re-exploration. Two women did not receive further treatment while the other woman was treated with pelvic radiation, all of them had no evidence of disease within 6 years of follow-up.[4]

There are two proposed mechanism of this phenomenon. First, chemotherapy promotes the conversion of immature teratoma to mature teratoma. Second, chemotherapy only destroys the immature component leaving the mature elements behind intact. Logethesis et al, described "growing teratoma syndrome" in six men with nonseminomatous germ cell tumors of the testis with distant metastasis.[1] Three recommended criteria are mandatory to define growing teratoma syndrome: (1) There is an enlarging tumor or findings of new tumor during or after chemotherapy for nonseminomatous germ cell tumors; (2) There is normalization of previously increased serum tumor markers alpha fetoprotein (AFP) and/or human-beta chorionic gonadotropin (Beta-HcG) and (3) the presence of only mature teratoma in the final histopathology of the resected specimen.[1] Our index patient fulfilled the three criteria.

Growing teratoma syndrome includes enlargement of the benign teratoma implants in addition to the appearance of new tumors. Djordjevic et al pointed out that growing teratoma syndrome and chemotherapeutic retroconversion are not one and the same.[5] Chemotherapeutic retroconversion only met two out of three criteria for growing teratoma syndrome. In chemotherapeutic retroconversion, mature teratomas nodules do not increase in size while in growing teratoma syndrome, not only the mature teratoma nodules undergo chemotherapeutic retroconversion, they must have the capacity to grow. However, some authors believed that the chemotherapeutic retroconversion and growing teratoma syndrome are possibly dissimilar terms for the same phenomenon.[6]

In a review of available literature, the median age at diagnosis was 22 years (ranges 4 to 48 years).[3,11] Tumor growth rate was reported to be 0.5 to 0.7 cm per month while the volume increase of 9.2 to 12.9 cm^3 per month.[6]

The most frequent site of growing teratoma syndrome is at the retroperitoneum.[2] Shibata et al reported a stage IC ovarian mixed germ cell tumor included immature teratoma grade III (75%), mature teratoma (10%), embryonal carcinoma (10%) and yolk sac tumor (5%) with metastasis to paraaortic lymph nodes, pelvic region and lung which occurred 5.5 years after adjuvant chemotherapy.[7] In the cases presented by Andre et al which included 30 men with non-seminomatous germ cell tumors and 3 women treated with ovarian germ cell tumor, they determined the factors that would predict the development of growing teratoma syndrome were the following: presence of mature teratoma component in the primary tumor, no change in tumor size after chemotherapy and incomplete tumor resection.[8]

Growing teratoma syndrome may appear anytime during chemotherapy or after chemotherapy. Average appearance of this occurrence is from the start of chemotherapy up to 2 years, with an average of 8 months.[5] Succeeding recurrences of growing teratoma syndrome was documented with the longest interval of 19 years.[5] Due to its indolent course, long term follow-up is essential. Imaging such as computed tomography and magnetic resonance are recommended with the findings of increased in fatty component within the mass or a peritoneal mass which is solid and cystic in character.[9]

As of today, there is no standard treatment protocol proven to best manage cases of growing teratoma syndrome. Since growing mature teratomas applies pressure to the surrounding organs in addition to the fact that it does not respond to chemotherapy, complete cytoreduction with no macroscopic residual has been emphasized with subsequent favourable prognosis. Tumor rupture and incomplete resection leads to greater chance of recurrences of up to 50-83%.[10] Gliomatosis peritonei is a grade 0 teratoma according to World Health Organization grading system for immature teratoma. The presence of a mature glial tissue in the peritoneum and omentum is a rare entity which is associated with immature teratoma. This was reported to transform into malignant glial tumors.[12]

A similar reported case by Dy Echo was compared to the present case. The former case described the appearance of new masses found on CT scan after the 4^{th} cycle of Bleomycin, Etoposide, Cisplatin and she underwent 3 cycles of Carboplatin-Paclitaxel. After these chemotherapy sessions, the masses grew bigger and she underwent debulking surgery which showed 90% mature teratoma and 10% immature teratoma.[13] In our present case presented, she developed new masses after the second cycle of chemotherapy. It was initially thought of as a persistent progressive disease or a chemoresistant one. A complete cytoreductive surgery was performed with a final histologic report of mature teratoma with no immature elements seen and gliomatosis peritonei. In our opinion, chemotherapy eradicated the immature elements leaving the mature teratoma nodules propagate

and grow. No subsequent treatment was given to this patient. Patient has been noted to have no evidence of disease for 5 months.

CONCLUSION

A case of ovarian immature teratoma in a 36 year old woman with development of new lesions while undergoing chemotherapy was presented. Complete tumor debulking was done which revealed only mature teratomatous elements. This case should highlight the fact that not all masses that occur during or after chemotherapy for immature teratoma signify tumor progression or chemoresistant disease. There are rare occasions when a benign tumor may occur such as in a growing teratoma syndrome. ■

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