Immature teratoma in pregnancy: a case report and literature review

A. Daponte[1], *M.D., F.C.O.G.*, E. Kostopoulou[2], *M.D.*; A. Zavos[1], *M.D.*; H. Skentou[1], *M.D.*
A. Kallitsaris[1], *M.D.*; G. Koukoulis[2], *M.D.*; I.E. Messinis[1], *M.D.*

[1]Department of Obstetrics and Gynecology, [2]Department of Pathology, University Hospital of Larissa (Greece)

Summary

Background: The management of a Stage I immature teratoma during pregnancy with a review of the literature is reported. *Case Report:* A growing adnexal mass was removed at 12 weeks of gestation. Although the frozen section was negative, because of intraoperative clinical suspicion, a right salpingo-oophorectomy and surgical staging were performed. Histological examination revealed a Stage Ia, grade 1 immature ovarian teratoma. Appropriate surgical staging enabled avoidance of chemotherapy despite the unexpected histological diagnosis. The pregnancy was terminated because of fetal distress, with cesarean section at 34 weeks of gestation. At that time the peritoneal cavity was inspected and biopsies were taken as in second-look laparotomy. Two years after the first operation the patient remains disease free. *Conclusion:* For adnexal masses removed during pregnancy frozen section is useful but when there is clinical suspicion surgical staging must be performed.

Key words: Immature teratoma; Pregnancy; Adnexal mass in pregnancy; Explorative laparotomy; Surgical staging.

Introduction

Germ-cell malignancies are just as common as epithelial ovarian malignancies in pregnancy [1].

Immature ovarian teratomas are germ cell tumors, characterized by a variety of tissues derived from all three germ cell layers. Most commonly, the immature elements are of neural origin [2, 3]. The occurrence of immature teratoma with a coexisting pregnancy is exceedingly rare. Only 15 papers could be detected in the world literature [3-17] (Table 1). The management of a Stage I, grade 1, (only three reported as yet) immature ovarian teratoma in a 33-year-old pregnant woman is reported and the literature reviewed.

Case Report

A 5-week pregnant 33-year-old primigravida was referred to our hospital because of a 7 x 7 cm mass in the right adnexa. The tumor was increasing in size at the examinations and at the 12th week it measured 20 x 20 cm. The tumor was by then multilocular with both solid and cystic components. Two tumor markers were slightly elevated; serum alpha-fetoprotein was 15.94 IU/ml (normal range 0-7 IU/ml outside pregnancy), and serum CA-125 was 89.6 U/ml (normal range 0-35 IU/m). Laparotomy with frozen section was performed. Ascites was absent, the contralateral ovary and tube had normal morphology and there were no macroscopic implants or palpable lymph nodes in the peritoneal cavity. Although the frozen section was negative for malignancy a right salpingo-oophorectomy and surgical staging (peritoneal washings, peritoneal and omentum biopsies) were performed because of clinical suspicion of a non benign tumor. Histological examination revealed a grade 1 immature ovarian teratoma with rare nests of neuroepithelial tissue (limited to low magnification field in every slide (x 40) according to the criteria of Norris *et al*. [19] (Figure 1). Peritoneal washings and all biopsies were negative for malignancy. Thus surgical stage was designated as FIGO Stage Ia (AJCC TNM and FIGO staging classification 2002) [20] and after discussion in the Multidisciplinary Oncology Meeting no adjuvant treatment was given. The pregnancy continued without complications until 34 weeks of gestation, when the patient gave birth to a healthy infant by cesarean section which was indicated for fetal distress. Cesarean section was performed through a midline incision, the peritoneal cavity was inspected, and biopsies were taken as in second-look laparotomy. Laboratory tumor markers were at normal levels during the pregnancy and at the time of the cesarean section. Two years after the first operation the computed tomography and tumor markers were negative for any recurrence of the teratoma.

Discussion

Already in 1963 Munnell [20] suggested that removal of an adnexal mass during pregnancy was indicated for: 1) elimination of a possible cause of dystocia, 2) danger of torsion, rupture, or hemorrhage, and 3) danger of malignancy.

Our patient had a growing complex adnexal mass (> 30% increase) [2, 21] with suspicious ultrasound characteristics which persisted after the 12th week [2, 22-24]. Fetal survival is markedly improved if surgery is delayed until after the 12th week of gestation as in our case, since up to one-third of all surgeries performed in the first trimester may result in spontaneous abortion [25, 26].

AFP and CA-125 were found slightly elevated but it would be difficult to indicate laparotomy on this finding alone. CA-125 can be elevated in the first trimester of pregnancy [22]. In cases of germ cell tumors of either gonadal or extragonadal origin only AFP levels > 7.0

Revised manuscript accepted for publication September 24, 2007

Table 1. — *Literature review of immature teratoma in pregnancy.*

	Name	No. of cases	Age	Patient findings, outcome, survival	Surgery time/type	Stage	Grade	Chemotherapy/ Radiation	Fetal outcome
1	Klein 1953	1	26	Growing tumor of the ovary	31st excision of the tumor of the (L) ovary		Frozen and permanent sections. Benign adult teratoma.*		
				33rd week preeclampsia metastasis found; 8 months after initial surgery carcinoma lung, abdominal cavity, ascites; Death 10 months after initial surgery	SC and excision of remaining ovary			Radiation, no chemotherapy	At SC fetal good
2	Robboy Scully 1970	1	18	Recently postpartum left ovarian teratoma; Recurrence 4 months postoperatively; Death 9 months postoperatively; Autopsy revealed metastatic carcinoma in the lungs and lymph nodes. Glial tissue lungs, peritoneum, pericardium, pleura.	Hysterectomy BSO	≥ IIIc	G3	Postoperatively RT therapy; After the recurrence thio-TERA and later methotrexate	
3	Montz *et al*. 1989	1	27	19th week AFP > 2.5 MoM. Amniotic AFP level normal.		I	G2		
				21st week complex mass in the cul-de-sac	22nd week exploratory laparotomy. (R) SO peritoneal washings, intraperitoneal evaluation and retroperitoneal nodes palpation. No further staging			23-37 weeks, 3 courses vincristine, dactinomycin, cyclophosphamide	
				37th week spontaneous vaginal delivery					3,285 g, female apgar 8,9 (1st, 5th min) alopecia, haemoglobin level normal
				No gross or micro malignant disease at second-look laparotomy	3 months postpartum second-look laparotomy			after derlivery +39 courses vincristine, dactinomycin, cyclophosphamide	
				Disease-free 1.5 years after initial surgery.					
4	Charles *et al*. 1989	2	24	13th week gross cystic mass of the ovary; Recurrent at 30th week;	13th week (R) SO	Ia	G3		
					34th week CS + TAH (L) SO			After CS actinomycine, oncovin, cisplatin	Male 2,430 g cried immediately.
				No recurrence 3.5 years after CS.	patient refused second-look laparotomy			adriamycine, bleomysine	Good 3.5 years after CS
			32	10th week US revealed tumor 10.5 cm diagnosed as fibroma; 20th week growing mass and ascites	20th week subtotal AH BHO, omenectomy.	IIIc	G3	After surgery adriamycine, cyclophosphamide, cisplatin	
				After the 3 cycles of chemotherapy, clinical improvement, no ascites, no residual mass.					
5	Christman *et al*. 1990	1	29	6th week mixed echogenic mass (R) adnexal	15th week (R) SO and surgical staging	Ic	G3	19th week (only 1 cycle) cisplatin bleomycin	
				At term spontaneous delivery				vinblastine PVB	At labor normal appearing male 3,232 g, apgar 8, 9 (1st, 5th min)
				After the 4th cycle of chemotherapy, second-look only mature glial elements.	Second-look laparotomy			2nd week postpartum next PVB treatments (3 more cycles)	55 months good development, no abnormalities, normal male karyotype.
				61 months post discovery of the teratoma doing well.					

continue Table 1.

	Name	No. of cases	Age	Patient findings, outcome, survival	Surgery time/type	Stage	Grade	Chemotheray/ Radiation	Foetal outcome
6	Poremba *et al*. 1993	1	27	Late in gestation hydrocephalus of fetus was diagnosed; at the 38th week CS was decided during which tumor of the ovary was revealed. Follow-up N/R	38th week CS; Type of operation N/R	≥ Ic	≥ G1	N/R	Died 9 weeks after delivery. Autopsy revealed intracranial immature teratoma of deferent origin of the mothers.
7	O'Connor** 1994	3	N/R	N/R	N/R	I	N/R	N/R	N/R
8	Whitecar*** *et al*. 1999	1	N/R	N/R	N/R	N/R	N/R	N/R	N/R
9	Quesada *et al*.	1	30	At 28th week great mixed echogenic mass (L) adnexal diagnosed with US during examination for bleeding; Conservative management; 34th week elective CS	34th week CS (L) SO staging	Ia	High grade (G2 or G3)	Postoperatively (postpartum) 6 cycles of carboplatin, bleomycin, etopocid	Normal 2,430 g male infant was delivered.
				Asymptomatic 6 months after last cycle of chemotherapy					
10	Kishimoto *et al*. 2002	1	28	At 35th week palpable mass in Douglas' pouch. At 38 weeks elective CS.	At 38th week CS, simple TAH-BSO and staging	IIIc	G2	Postoperatively 5 courses of chemotherapy	2,308 g foetus, good at CS.
				Alive 9 months after delivery.					
11	Agarwal 2003	1	N/R	Mass detected during pregnancy	During pregnancy excision of growth	N/R	N/R	During pregnancy not given (refusal of patient)	N/R
				Enormous recurrence during pregnancy	LSCS at 33 weeks hysterectomy cytoreductive surgery				
				Further follow-up N/R					
12	Barki 2004	2	33	10 weeks post abortion abdominal pain and palpable mass	(L) SO staging	Ia	N/R	N/R	N/R
			21	8th week abdominal pain, fever sweating, weight loss	TAH-BSO	Undetermined III?	G2	N/R	Foetal loss
				Died 2nd trimester					
13	Han 2004	1	27	16th week AFP > 7.25 MoM; 18th week AFP > 12.55 MoM; Amniotic AFP level normal; Normal karyotype; 24th week (R) mass.	26th weeks (R) SO	Ia	G3	30th weeks, 2 cycles bleomysin, etoposide, cisplatin	
				38th week prostaglandin induction delivery.				3 cycles after pregnancy	Apgar 9, 10 (1st, 5th min), no evidence of gross malformations; 7.5 months of age infant suffered from intussusception; 26 months after birth 13 k normal physiological and neurological development.
				26 months of follow-up second-look no evidence of malignant tumor.	Laparoscopic second-look dissection of bilateral pelvic and paraortic lymph nodes, omenectomy, biopsy pf (L) ovary				
14	Leiserowitz 2005****	12	N/R	N/R	N/R	N/R	N/R	N/R	N/R
15	Zhao 2006	2	24	17th week of gestation adnexal mass; 30 months after operation disease-free survival;	17+th (L) SO	I	G1	No chemotherapy	Term infant
			24	8th week of gestation adnexal mass; 18 months after operation disease-free survival.	13+th (L) SO	I	G1	No chemotherapy	Term infant

CS: cesarean section; B: Bilateral; SO salpingo-oophorectomy; N/R not recorded. *Regions suggesting neuroepithelium and resembling somewhat immature brain substances were found, as also glial structures, but were not so unorganized or irregular as to warrant the diagnosis of malignancy.
Large series for 244 Stage I immature teratomas where the reproducibility of grading was investigated; and it was reported that 3 of the patients were pregnant women. ***Large series for adnexal masses during pregnancy where in one table of 118 cases of adnexal masses in pregnancy; one with a histological diagnosis of immature teratoma was reported. *** Large series of 9,375 adnexal masses during pregnancy where 12 cases of immature teratoma in pregnancy were reported.

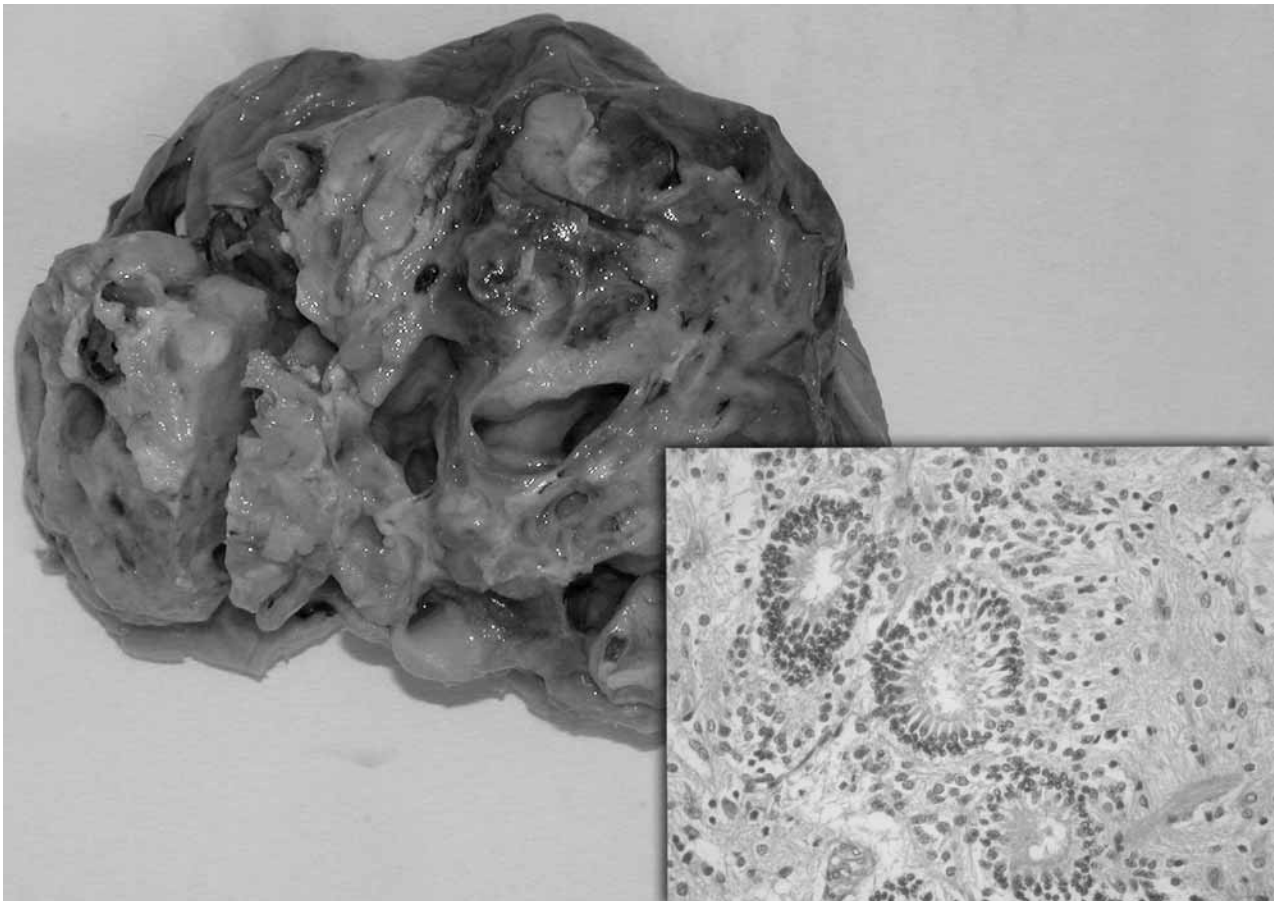

Figure — Immature teratoma of the ovary. Rare foci showing neuroepithelial tubules (no more than one focus per slide). (Original magnification 150 x).

MoM in the absence of any fetal malformation or maternal disease, should be considered diagnostic [6].

When trying to preserve the pregnancy a first estimation of the histological type of the tumor with frozen section is useful for planning the extention of the surgery although many times the results from the frozen section are incorrect [4]. Clinical assessment of possible malignancy as in our case can justify more extensive surgery to achieve optimal staging.

Bilateral malignant teratoma was not observed by Norris *et al*. [18] or in the Gynecologic Oncology Group study; therefore, conservative surgery consisting of unilateral salpingo-oophorectomy and staging is acceptable [27, 28].

All reported cases are summarized in Table 1. Most authors agree that survival is related to the stage and grade of the tumor. Our case is the fourth reported case Stage I/grade 1 in the literature. In order to decide the management we assumed that as in non pregnant women the prognosis seems dependent on the histologic grading and stage of the tumor at the time of discovery [2].

Tumors are graded according to the degree of immaturity of the tissue, and the presence and quantity of neuroepithelium. There are two grading systems: Thulderberg and Scully, and Norris (the most commonly used grading system) [18, 29]. Later on, Norris proposed only two grades to select the treatment in Stage I tumors: low grade for grade 1, and high grade for grade 2 and 3 [10].

Immature teratomas as well as others germ cell tumors can be treated and are very sensitive to chemotherapy [2, 17] with a 75% cure rate for advanced stage disease [6, 8, 15, 30, 31]. In the three reported cases (Table 1), investigators treated patients with Stage Ia/ grade 1 immature teratomas as our case with unilateral oophorectomy alone [17] and only patients with high-grade Stage Ia as well as more advanced lesions with chemotherapy post surgically [2, 3]. Chemotherapy is also proposed in incompletely staged patients and can be avoided if no relapse has occurred at second-look laparotomy [14]. Our patient was Stage Ia/grade 1 and because she was staged appropriately we managed to avoid chemotherapy during pregnancy. Also although cesarean section was indicated for obstetric reasons it was performed as a second-look laparotomy and no sign of a recurrence was observed.

In neoplasmatic masses which are removed during pregnancy frozen section is useful but when there is clinical suspicion surgical staging must be performed. It enables, in selected cases, avoidance of chemotherapy during pregnancy.

References

[1] Sivanesaratnam V.: "Gynaecological malignancies in pregnancy". In: Ratnam S.S., Sen D.K., Ng S.C., Arulkumaran S., (eds.), Contributions to Obstetrics and Gynaecology, Singapore: Churchill Livingstone, Longman Singapore Publishers (Pvt. Ltd.), 1994, 295.

[2] Di Saia P.J., Creasman W.T. (eds.). Clinical Gynecologic Oncology (6th edn.), St. Louis, MO, Mosby, 2002, 362, 446.

[3] Quesada G., Velasco M.C., Palencia R., Marina C., Garcia M., Marina J. *et al*.: "Immature teratoma of the ovary during pregnancy". *J. Gynecol. Surg*., 2000, *16,* 161.

[4] Klein J.: "Pregnancy complicated by teratoma of the ovary". *Obstet. Gynecol*., 1954, *3,* 93.

[5] Robboy S., Scully R.: "Ovarian teratoma with glial implants on the peritoneum". *Hum. Pathol.,* 1970, *1,* 643.

[6] Montz F.J., Horenstein J., Platt L.D., d'Ablaing G., Schlaerth J.B., Cunningham G.: "The diagnosis of immature teratoma by maternal serum alpha-fetoprotein screening". *Obstet. Gynecol.,* 1989, *73*, 522.

[7] Charles G., Marhic C., Ponties J.E., Meyran M.: "Advanced cancer of the ovary and pregnancy. Apropos of 2 cases". *J. Gynecol. Obstet. Biol. Reprod. (Paris),* 1989, *18*, 61.

[8] Christman J.E., Teng N.N., Lebovk G.S., Sikic B.C.: "Delivery of a normal infant following cisplatin, vinblastine, and bleomycin (PVB) chemotherapy for malignant teratoma of the ovary during pregnancy". *Gynecol. Oncol.,* 1990, *37,* 292.

[9] Poremba C., Dockhorn-Dworniczak B., Merritt V., Li C.Y., Heidl G., Tauber P.F. *et al*.: "Immature Teratomas of different origin carried by a pregnant mother and her fetus". *Diagn. Mol. Pathol.,* 1993, *2,* 131.

[10] O'Connor D.M., Norris H.J.: "The influence of grade on the outcome of Stage I ovarian immature (malignant) teratomas and the repioducibility of grading". *Int. J. Gynecol. Pathol.,* 1994, *13*, 283.

[11] Whitecar P., Turner S., Higby K.: "Adnexal masses in pregnancy: A review of 130 cases undergoing surgical management". *Am. J. Obstet. Gynecol*., 1999, *181*, 19.

[12] Kishimoto K., Ito K., Furukawa M., Ogasawara N., Matsunaga N., Nawata S. *et al*.: "Immature teratoma with gliomatosis peritonei associated with pregnancy". *Abdom. Imaging,* 2002, *27,* 96.

[13] Agarwal N., Parul, Kriplani A., Bhatla N., Gupta A.: "Management and outcome of prcegnancies complicated with adnexal masses". *Arch. Gynecol. Obstet*., 2003, *267,* 148.

[14] Bakri Y.N., Ezzat A., Akhtar, Dohami, Zahrani: "Malignant germ cell tumors of the ovary pregnancy considerations". *Eur. J. Obstet. Gynecol. Reprod. Biol*., 2000, *90*, 87.

[15] Han J.Y., Nava-Ocampo A.A., Kim T.J., Shim J.U., Parka C.T.: "Pregnancy outcome after prenatal exposure to bleomycin, etoposide and cisplatin for malignant ovarian germ cell tumors: report of 2 cases". *Reprod. Toxicol*., 2005, *19,* 557.

[16] Leiserowitz G.S., Xing G., Cress R., Brahmbhatt B., Dalrymple J.L., Smith L.H.: "Adnexal masses in pregnancy: how often are they malignant?". *Gynecol. Oncol.,* 2006, *101,* 315.

[17] Zhao X.Y., Huang H.F., Lian L.J., Lang J.H.: "Ovarian cancer in pregnancy: a clinicopathologic analysis of 22 cases and review of the literature". *Int. J. Gynecol. Cancer,* 2006, *16*, 8.

[18] Norris H.J., Zirkin H.J., Benson W.L.: "Immature (malignant) teratoma of the ovary: A clinical and pathologic study of 58 cases". *Cancer,* 1976, *37*, 2359.

[19] American Joint Committee on Cancer: "Ovary". In: AJCC Cancer Staging Manual, 6th edn., New York, Springer-Verlag, 2002, 275.

[20] Munnell E.W.: "Primary ovarian cancer associated with pregnancy". *Clin. Obstet. Gynecol.,* 1963, *30,* 983.

[21] Roberts J.A.: "Management of gynecologic tumors during pregnancy". *Clin. Perinatol.,* 1983, *10,* 369.

[22] Sivanesaratnam V.: "Gynaecological malignancies in pregnancy". *Rev. Gynaecol. Pract*., 2004, *4,* 162.

[23] Boulay R., Podczaski E.: "Ovarian cancer complicating pregnancy". *Obstet. Gynecol. Clin. N. Am*., 1998, *25*, 385.

[24] Daponte A., Stergioti E., Messinis I.E.: "Risk scoring for adnexal masses and endoscopic management". *Int. J. Gynecol. Obstet.,* 2007, *96,* 42.

[25] Sherard G.B., Hodson C.A., Williams H.J., Semer D.A., Hadi H.A., Tait D.L.: "Adnexal masses and pregnancy: a 12-year experience". *Am. J. Obstet. Gynecol*., 2003, *189,* 358.

[26] Lee G.S., Hur S.Y., Shin J.C., Kim S.P., Kim S.J.: "Elective vs conservative management of ovarian tumors in pregnancy". *Int. J. Gynaecol. Obstet*., 2004, *85,* 250.

[27] Curry S.L., Smith J.P., Gallagher H.S.: "Malignant teratoma of the ovary: Prognostic factors and treatment". *Am. J. Obstet. Gynecol*., 1978, *131,* 845.

[28] Beiner M.E., Gotlieb W.H., Korach Y., Shrim A., Stockheim D., Segal Y. *et al*.: "Cystectomy for immature teratoma of the ovary". *Gynecol. Oncol*., 2004, *93,* 381.

[29] Thurlbeck W.M., Scully R.E.: "Solid teratoma of the ovary. A clinicopathological analysis of 9 cases". *Cancer,* 1960, *13*, 804.

[30] Gershenson D.M.: "Management of early ovarian cancer: germ cell and sex cordstromal tumors". *Gynecol. Oncol.,* 1994, 55 (3 Pt 2), S62.

[31] Kojs Z., Urbanski K., Mitus J., Reinfuss M., Pudelek J., Walasek T.: "Pure immature teratoma of the ovary: analysis of 22 cases". *Eur. J. Gynecol. Oncol*., 1997, *18,* 534.

Address reprint requests to:
A. DAPONTE, M.D., FCOG
M. Skylakou, 10
41334 Larissa (Greece)
e-mail: dapontea@otenet.gr