EJGO European Journal of Gynaecological Oncology

Malignant transformation of mature cystic teratoma of the ovary: 30-year experience of a single tertiary care center

A. Al Wazzan[1,2], S. Popowich[1], E. Dean[1], C. Robinson[1], R. Lotocki[1], A.D. Altman[1]

[1] Winnipeg Health Sciences Centre & CancerCare Manitoba, Department of Obstetrics & Gynecology and Reproductive Sciences, Division of Gynecologic Oncology, University of Manitoba, Winnipeg, Manitoba (Canada)
[2] King Abdulaziz University Hospital, Department of Obstetrics & Gynecology, Division of Gynecology Oncology, King Abdulaziz University, Jeddah (Saudi Arabia)

Summary

Objective: To review the authors' experience with this rare disease and describe their management modality and the outcome. *Material and Methods:* From January 1983 to December 2013, 13 patients with malignant transformation arising in ovarian MCT were treated at the Division of Gynecologic Oncology in the University of Manitoba. Demographic characteristics, symptoms, signs, stage, mode of therapy, and results of follow-up were reviewed retrospectively. *Results:* Median age at diagnosis was 53 years (range 25-65). The most common presenting symptom was a palpable mass in nine cases. Squamous cell carcinoma (SCC) was found in 38% (five cases), adenocarcinoma in 15% (two cases), anaplastic carcinoma in 8% (one case), and papillary thyroid carcinoma in 38% (five cases). Eight cases were Stage I, two cases were Stage II, and three cases were Stage III. All patients underwent surgery. Five patients received adjuvant treatment with platinum-based chemotherapy + pelvic radiation. Four patients had recurrent disease (two SCC and two adenocarcinoma). Three patients died of disease after recurrence. The median follow up period of the entire patient population was 60 months, with a three-year overall survival of 76%. *Conclusion:* Malignant transformation of MCT is large ovarian tumors that mainly occur in patients in their fifth and sixth decades of life. They often present as incidental pathologic findings after surgery for MCT. SCC has traditionally been the most common pathology, however in the present series, the authors found that papillary thyroid carcinoma was equally common. Platinum-based chemotherapy with pelvic radiation in early stage (including Stage IA) and locally recurrent disease should be offered. Advanced stages and mucinous adenocarcinoma represent a poorer prognosis despite adjuvant treatment. In patients with papillary thyroid carcinoma, conservative surveillance in early stage and adjuvant total thyroidectomy with radioactive iodine treatment in advanced stage disease appears to be an effective treatment.

Key words: Malignant transformation; Mature cystic teratoma; Ovary; Platinum-based chemotherapy.

Introduction

Malignant transformation occurs in 0.5-2% of mature cystic teratomas (MCTs) [1, 2] and accounts for 3% of all primary ovarian malignant tumors [3]. Although any of the components of a mature cystic teratoma may undergo malignant degeneration, squamous cell carcinoma (SCC) arising from the ectoderm is considered the most common [4, 5]. Other malignant neoplasms include (but are not limited to) basal cell carcinoma, melanoma, adenocarcinoma, sarcoma, and thyroid carcinoma [4, 5].

Compared to benign cystic teratomas, malignant transformation tends to occur in older patient populations, with a mean age of 45-60 years [4, 5]. Other possible risk factors for malignant transformation include tumor diameter greater than ten cm, rapid growth, and suspicious findings on imaging (e.g. low resistance intra-tumor flow on Doppler) [4, 5].

Preoperative diagnosis of malignant transformation is very difficult due to its similarity to benign teratoma with regards to clinical signs and symptoms. The most common symptoms include: abdominal mass, distension, and pain [6-9]. The diagnosis is often made unexpectedly in the operating room or, more commonly, on final pathology; this presents a dilemma regarding the need for surgical staging and/or adjuvant therapy [6-9].

The prognosis of these malignancies has been reported to be poor, especially with distant metastases [4, 9-12]. However, because of the rarity of these tumors, the clinicopathologic characteristics, treatment and prognostic factors are not yet well established. The literature is limited to descriptive case series, and there is no consensus within gynecologic oncology regarding optimal management.

The aim of this study was to review the experience of a single tertiary care center in Winnipeg, Manitoba with this rare disease, and describe the management and outcomes data.

Materials and Methods

This study is a retrospective analysis of patients with malignant transformation of mature cystic teratomas that were referred to

Revised manuscript accepted for publication August 3, 2015

the Division of Gynecologic Oncology at CancerCare Manitoba, Winnipeg, Manitoba; it is the only tertiary care center in Manitoba, Canada. All female patients older than 18 years with an unequivocal diagnosis of malignant transformation of mature cystic teratoma, and treated by the Gynecologic oncology group at CancerCare Manitoba over a 30-year period (1983 to 2013) were included.

After institutional ethics board approval (REB # H2013:426; December 15, 2013), women were identified within the cancer registry by the Division of Gynecologic Oncology and the Department of Epidemiology, at the University of Manitoba. Clinical data were abstracted and follow-up information was obtained on all women until August 2014.

Data recorded for each patient included age, gravity, parity, symptoms at presentation, type and details of surgery, pathology of tumor, residual disease, stage, serum tumor markers levels (alfa-fetoprotein (αFP), β-subunit of human chorionic gonadotropin (β-hCG), lactate dehydrogenase (LDH), alkaline phosphatase (ALP), carcinoemberionic antigen, and CA125), type of chemotherapy regimen, and follow-up data (date of last follow up in gynecology oncology clinic, status at the time of the study, date of recurrence, date of death). Surgical stage was assigned retroactively as outlined by the International Federation of Gynecology and Obstetrics (FIGO 2014) [13].

Time to progression was calculated from the date of initial surgery to the time of progression or recurrence. Overall survival was defined as time from the date of initial surgery to the time of death or last follow-up in gynecology oncology clinic.

Table 1. — *Patient's characteristics.*

Age - median (range)	53 years (25-65)
Presenting symptom	
Abdominal distention with palpable mass	9 (70%)
Abdominal pain (ovarian torsion)	3 (23%)
Incidental finding	1 (7%)
Stage	
I	8 (61%)
A	6 (46%)
B	0 (0%)
C	2 (15%)
II	2 (15%)
III	3 (23%)
B	1 (7%)
C	2 (15%)
Histology	
Squamous cell	
Mucinous adenocarcinoma	5 (38%)
Anaplastic	2 (15%)
Papillary thyroid carcinoma within a surrounding	1 (7%)
Mature teratoma	5 (38%)
Tumor markers	
Elevated Ca125	4 (30%)
CEA	2 (15%)
Type of surgery	
TAH, BSO, and complete staging	11 (85%)
TAH, BSO, and debulking	2 (15%)
Follow-up — median (range)	60 months (36-60)
Overall three-year survival	10 (76%)

TAH: total abdominal hysterectomy, BSO: bilateral salpingo-oophorectomy, CEA: carcinoembryonic antigen. Complete staging: washing, bilateral pelvic lymph node dissection, para-aortic lymph node dissection, peritoneal biopsies, omentectomy, and diaphragmatic scraping.

Results

According to the present authors' health record and cancer registry, 606 patients with ovarian MCT underwent surgery at the health sciences center in the University of Manitoba during the study period. After review of pathologic reports of these patients, the authors identified 13 women with malignant transformation of MCT treated in the present center (2.1%). Median age at diagnosis was 53 years (range 25-65). Median tumour diameter was 16 cm (range 8-20). The most common presenting symptom was a palpable mass (nine cases; 70%); three patients (23%) presented with severe abdominal pain and had confirmed intraoperative ovarian torsion. The remaining one patient had an incidental finding of an ovarian mass during cesarean section. SCC was found in 38% (five cases), mucinous adenocarcinoma in 15% (two cases), anaplastic carcinoma in 8% (one case), and papillary thyroid carcinoma within a surrounding MCT in 38% (five cases). Stage distribution was Stage I in 61% (eight cases), Stage II in 15% (two cases), and Stage III in 23% (three cases). The median follow up period of the entire patient population was 60 months, with a three-year overall survival of 76% (Table 1).

Tumor markers were available in all identified patients. CA125 was elevated in 30% of the patients (two squamous carcinoma and two mucinous). CEA was elevated in two patients (15%) all had mucinous adenocarcinoma. No other elevated tumor markers were identified (αFP, β-hCG, LDH, ALP) (Table 1). Preoperative evaluation and impression was consistent with a benign teratoma in nine patients (five papillary thyroid carcinoma, one anaplastic carcinoma, and three squamous carcinoma) due to normal tumor markers and non-suspicious imaging. Malignant ovarian cancer was suspected in four patients (two squamous carcinoma and two mucinous) who had elevated tumor markers and suspicious finding on imaging.

All patients underwent primary surgical treatment. Seven Stage I patients had their initial surgery done by a general gynecologist in the form of total abdominal hysterectomy and bilateral salpingo-oophorectomy. They were referred to gynecologic oncology postoperatively with an incidental finding of malignant transformation within a surrounding mature teratoma in final pathology. Those patients were taken back to the operation room for complete staging procedure (washing, bilateral pelvic lymph node dissection, para-aortic lymph node dissection, peritoneal biopsies, omentectomy, and diaphragmatic scraping). Six patients had their initial surgery done by the present gynecology oncology team (two patients underwent complete staging procedures and two patients had debulking procedures). Optimal cytoreduction was achieved in 92% (12 cases).

Table 2. — *Recurrence.*

Patient	Age	Stage	Surgery	Residual	Histology	Adjuvant Treatment	Time to Relapse (mo)	Site of Relapse	Second-Line Treatment	Follow up After Second-line treatment	Current status
1	31	IA	TAH BSO and Complete Staging	NONE	Mucinous	NONE	6 months	Pelvis and upper abdomen	EB X 2 Cycles	N/A	Died
2	39	IIIC (omental, small and large bowel involvement)	TAH BSO Omentectomy	>1cm	Mucinous	Chemotherapy FOLFOX X12 cycles	6 months	Pelvis and upper abdomen	Not a candidate	N/A	Died
3	60	IA	TAH BSO and Complete Staging	NONE	Squamous	NONE	12 months	Pelvis	EP X 4 cycles + WPRT 50 Rad in 31 fraction	60 months	Still Alive
1	61	IIIC (omental, small and large bowel involvement)	TAH, BSO, Sigmoid resection with colostomy	<1cm	Squamous	Chemotherapy EP X 4 cycles + WPRT 50 Rad in 31 fraction	8 months	Pelvis, upper abdomen, lung	Not a candidate	N/A	Died

TAH: Total Abdominal Hysterectomy, BSO: Bilateral Salpingo-oophorectomy, EB: Cisplatinum/Etoposide.

One patient had suboptimal debulking with more than one cm residual disease (Table 1).

Four patients (three Stage IA papillary thyroid and one Stage IA anaplastic carcinoma) received no adjuvant treatment; they were followed in the gynecology oncology clinic on a regular basis for five years, and they are still alive with no evidence of recurrence at the completion of this study according to the present authors' database and medical records. Five patients received adjuvant treatment with no documented recurrence. Two Stage IC SCC and one Stage II received four cycles of cisplatin/etoposide followed by whole pelvis radiation (50 rad in 31 fractions). They finished five years of clinic follow up after that and are still alive with no evidence of recurrence. One Stage II papillary thyroid carcinoma and one Stage IIIB had adjuvant total thyroidectomy followed by radioactive iodine treatment; both patients also finished five years of follow up and still alive with no evidence of recurrence.

Four patients had recurrent disease. One patient with Stage IA SCC presented during regular clinic visit one year after primary treatment (surgery with no adjuvant treatment) complaining of abdominal bloating and progressive nausea. A CT scan was done in an urgent basis that demonstrated a pelvic recurrence. Second line treatment with chemotherapy (four cycles of cisplatin/etoposide), followed by whole pelvic radiation was successful in treating the patient, who is alive at five years with no evidence of disease of recurrence at the time of this study. One patient with Stage IA mucinous adenocarcinoma presented to the emergency department six months after primary treatment (surgery with no adjuvant treatment) complaining of severe nausea and vomiting. CT scan confirmed disease recurrence in the pelvis and upper abdomen. The patient was started on cisplatin/etoposide with a plan to give four cycles. After two cycles the patient functional status deteriorated and a repeat CT scan confirmed progression of disease. The patient died of her disease one month later. One patient with Stage IIIC SCC, who had optimal debulking, and had finished four cycles of cisplatin/etoposide, presented eight months later with severe nausea, poor oral intake, and severe weight loss. CT scan confirmed disease recurrence in the pelvis, upper abdomen, and lung. The patient was not a candidate for second line treatment, and died of her disease. One last patient with Stage IIIC mucinous adenocarcinoma, who had a suboptimal debulking and received 12 cycles of FOLFOX chemotherapy as an adjuvant treatment, returned six months after treatment with extensive metastatic disease on CT scan and poor functional status. She also was not a candidate for second line treatment, and died of her disease (Table 2).

Discussion

MCT is the most common ovarian neoplasm, especially during adolescence and the reproductive age period [14]. Malignant transformation of mature cystic teratoma has been previously reported with an average frequency of 1-3%. The incidence rate of this rare malignancy in the present study is 2.1% of all MCTs, and is consistent with previously published reports [15, 16]. According to previous literature, SCC is the most common form of malignant transformation, followed by adenocarcinomas, malignant melanomas, sarcomas, sebaceous carcinomas, and thyroid papillary carcinomas [15, 16]. The present study confirms the high rate of SCC transformation at 35%, but surprisingly, papillary thyroid carcinoma within a surrounding mature cystic teratoma was equally common (35%) [10, 15, 17].

The median age at diagnosis was 53 years and most of the patients were in the postmenopausal period. The most common presenting symptoms were palpable mass and abdominal pain. Three patients presented with ovarian torsion and

underwent emergency surgery; these findings are consistent with previous reports [15, 18-21].

Preoperative diagnosis of malignant tumors arising in teratoma tissue remains very difficult. In most cases, the diagnosis is not suspected until final pathological examination has been performed [22, 23]. The presence of a solid component with contrast enhancement, transmural extension, and irregular invasion through the septa to the peritoneum on MRI has been reported to be beneficial in preoperative diagnosis of malignant transformation [8, 24]. Tumor size also has been reported to predict malignant transformation from mature cystic teratoma of the ovary, with a diameter greater than ten cm representing an increased risk of malignancy [8, 24, 25]. Intraoperative findings that suggest malignant transformation include: adherence to surrounding pelvic structures, thickening in the cyst wall, areas of necrosis, or hemorrhage [21, 22]. In the present study, the mean tumor size was 14 cm and preoperative imaging showed that 80% of patients had some solid portions within the typical MCT. Although preoperative diagnosis remains enigmatic, in the preset series malignancy was suspected in 66% of cases preoperatively.

The utility of tumor markers in this patient population is unclear and has been investigated in multiple series, with variable results [20, 24]. SCC antigen seems to be the most useful tumor marker. SCC antigen can be elevated in some benign MCTs and may not be sensitive in early-stage malignancy; it is therefore still insufficient to diagnose malignant transformation preoperatively. In cases of recurrence, SCC antigen has been shown to be useful and its elevation preceded the clinical presentation by several months [7, 21, 26]. In a study performed by Chen *et al.* (2008) [27], CA125 was found to be elevated in 60% of the reported cases and was associated with poorer prognosis and survival rates. In the present study, CA125 was elevated in four patients (30%), two of them had advanced stage disease (two Stage IIIC), and both died with recurrence. Since the present authors do not routinely perform SCC antigen test, they cannot comment about its role in this case series.

Patients with malignant transformation of MCT are known to have a poor prognosis. Stage of disease, histological type, and optimal debulking are the most important reported prognostic factors [23, 28]. Other prognostic factors include tumor grade, growth pattern, capsular rupture, and lymph-vascular invasion [29, 30]. Patients with advanced stage disease, suboptimal cytoreduction, and mucinous adenocarcinoma histolologies were noted to have the worse outcome in the present study, which is consistent with other reports.

Due to the rarity of this tumor, adjuvant treatments have not been evaluated in prospective randomized trials, and only case reports and small series have been reported with different regimes and modalities of treatments. Multimodality therapy including aggressive cytoreduction followed by chemotherapy and/or radiation therapy has been advocated by several authors in diseases that are more than Stage IA [21, 23].

For Stage IA disease, conservative treatment with unilateral salpingo-oophorectomy for fertility preservation, or full surgical staging, and close follow-up with no adjuvant treatment has been proposed [21]. In the present study two out of six Stage IA patients (one squamous cell and one mucinous adenocarcinoma) were treated in such way, but unfortunately developed a recurrence within one year of treatment. One patient (SCC) was cured using a combination of chemotherapy and pelvic radiation. The other patient (mucinous adenocarcinoma) did not respond to treatment and died of her disease (Table 2). Only the patients with Stage IA papillary thyroid carcinoma were noted to be cured with conservative treatment and no adjuvant treatment.

For Stage IC disease and greater, diverse adjuvant regimens have been described in individual cases, with variable results. Platinum-based multi-agent chemotherapy, with or without pelvic radiation, after aggressive cytoreduction, showed better overall disease-free survival in multiple small series [21, 31, 32]. In the present study cisplatinum + etoposide for four cycles with adjuvant pelvic radiation was used postoperatively in four patients (Stage IC, II, and IIIC); only one patient (Stage IIIC) recurred and died of disease. Cisplatin/etoposide x four cycles followed by pelvic radiation also resulted in a complete clinical response in one patient with local recurrence (Stage IA SCC) who also remains alive with no evidence of disease.

A focus of papillary thyroid carcinoma, within a surrounding mature cystic teratoma, is an extremely rare condition, and has only been reported in case reports and small series [33-36]. There is no consensus with regards to treatment. Conservative treatment for Stage IA, with no adjuvant therapy, and adjuvant total thyroidectomy with radioactive iodine ablation for more advanced stages has been reported to be successful [33-36]. In the present study the authors encounter five such cases (three Stage IA, one Stage IIIB, and one Stage II). Three patients were treated conservatively and received no adjuvant treatments and two patients had total thyroidectomy with radioactive iodine treatment. They are all still alive with no evidence of recurrence after they completed five years of regular clinic follow up.

In conclusion, malignant transformation of MCT is commonly large ovarian tumors that mainly occur in patients in their fifth and sixth decades of life. These tumors often present as incidental pathologic findings after surgery for MCT. SCC has traditionally been the most common pathology, however in the present series, the authors found that papillary thyroid carcinoma was equally common.

In patients with SCC, early stage appears to be an important prognostic factor for long-term survival and although there is lack of consensus in the literature regarding adjuvant treatment, the present authors strongly believe that platinum-based chemotherapy, with pelvic radiation, in early stage (including Stage IA) and locally recurrent disease should be offered. Platinum-based chemotherapy followed by pelvic radiation showed great promise in the present series, with

evidence of complete clinical response. Advanced stages and mucinous adenocarcinoma represents a poorer prognosis despite adjuvant treatment. In patients with papillary thyroid carcinoma, conservative surveillance in early stage disease, and total thyroidectomy with radioactive iodine treatment in advanced stage disease appears to be an effective treatment. Larger trials are needed to confirm these finding and to explore more adjuvant treatment option for advanced stage disease.

References

[1] Westhoff C., Pike M., Vessey M.: "Benign ovarian teratomas: a population-based case-control study". *Br. J. Cancer*, 1988, *58*, 93.

[2] Singh P., Yordan E.L., Wilbanks G.D., Miller A.W., Wee A.: "Malignancy associated with benign cystic teratomas (dermoid cysts) of the ovary". *Singapore Med. J.*, 1988, *29*, 30.

[3] Smith H.O., Berwick M., Verschraegen C.F., Wiggins C., Lansing L., Muller C.Y., *et al.*: "Incidence and survival rates for female malignant germ cell tumors". *Obstet. Gynecol.*, 2006, *107*, 1075.

[4] Hackethal A., Brueggmann D., Bohlmann M.K., Franke F.E., Tinneberg H.R., Munstedt K.: "Squamous-cell carcinoma in mature cystic teratoma of the ovary: systematic review and analysis of published data". *Lancet Oncol.*, 2008, *9*, 1173.

[5] Dos Santos L., Mok E., Iasonos A., Park K., Soslow R.A., Aghajanian C., *et al.*: "Squamous cell carcinoma arising in mature cystic teratoma of the ovary: a case series and review of the literature". *Gynecol. Oncol.*, 2007, *105*, 321.

[6] Mori Y., Nishii H., Takabe K., Shinozaki H., Matsumoto N., Suzuki K., *et al.*: "Preoperative diagnosis of malignant transformation arising from mature cystic teratoma of the ovary". *Gynecol Oncol.*, 2003, *90*, 338.

[7] Suzuki M., Tamura N., Kobayashi H., Ohwada M., Terao T., Sato I.: "Clinical significance of combined use of macrophage colony-stimulating factor and squamous cell carcinoma antigen as a selective diagnostic marker for squamous cell carcinoma arising in mature cystic teratoma of the ovary". *Gynecol. Oncol.*, 2000, *77*, 405.

[8] Kikkawa F., Nawa A., Tamakoshi K., Ishikawa H., Kuzuya K., Suganuma N., *et al.*: "Diagnosis of squamous cell carcinoma arising from mature cystic teratoma of the ovary". *Cancer*, 1998, *82*, 2249.

[9] Miyazaki K., Tokunaga T., Katabuchi H., Ohba T., Tashiro H., Okamura H.: "Clinical usefulness of serum squamous cell carcinoma antigen for early detection of squamous cell carcinoma arising in mature cystic teratoma of the ovary". *Obstet. Gynecol.*, 1991, *78*, 562.

[10] Sakuma M., Otsuki T., Yoshinaga K., Utsunomiya H., Nagase S., Takano T., *et al.*: "Malignant transformation arising from mature cystic teratoma of the ovary: a retrospective study of 20 cases". *Int. J. Gynecol. Cancer*, 2010, *20*, 766.

[11] Chen P., Yeh C.C., Lee F.K., Teng S.W., Chang W.H., Wang K.C., *et al.*: "Squamous cell carcinoma occurring in the pelvis after total hysterectomy and bilateral salpingo-oophorectomy for an ovarian mature teratoma with malignant transformation". *Taiwan J. Obstet. Gynecol.*, 2012, *51*, 446.

[12] Kadoya A., Okada J., Iikuni Y., Kondo H.: "Risk factors for Pneumocystis carinii pneumonia in patients with polymyositis/dermatomyositis or systemic lupus erythematosus". *J. Rheumatol.*, 1996, *23*, 1186.

[13] Prat J., FIGO Committee on Gynecologic Oncology: "Staging classification for cancer of the ovary, fallopian tube, and peritoneum". *Int. J. Gynaecol. Obstet.*, 2014, *124*, 1.

[14] Curling O.M., Potsides P.N., Hudson C.N.: "Malignant change in benign cystic teratoma of the ovary". *Br. J. Obstet. Gynaecol.*, 1979, *86*, 399.

[15] Tham K.T., Ma P.H., Kung T.M.: "Malignant melanoma in an ovarian cystic teratoma". *Hum. Pathol.*, 1981, *12*, 577.

[16] Pantoja E., Rodriguez-Ibanez I., Axtmayer R.W., Noy M.A., Pelegrina I.: "Complications of dermoid tumors of the ovary". *Obstet. Gynecol.*, 1975, *45*, 89.

[17] Climie A.R., Heath L.P.: "Malignant degeneration of benign cystic teratomas of the ovary. Review of the literature and report of a chondrosarcoma and carcinoid tumor". *Cancer*, 1968, *22*, 824.

[18] Kashimura M., Shinohara M., Hirakawa T., Kamura T., Matsukuma K.: "Clinicopathologic study of squamous cell carcinoma of the ovary". *Gynecol. Oncol.*, 1989, *34*, 75.

[19] Rim S.Y., Kim S.M., Choi H.S.: "Malignant transformation of ovarian mature cystic teratoma". *Int. J. Gynecol. Cancer*, 2006, *16*, 140.

[20] Stamp G.W., McConnell E.M.: "Malignancy arising in cystic ovarian teratomas. A report of 24 cases". *Br. J. Obstet. Gynaecol.*, 1983, *90*, 671.

[21] Tseng C.J., Chou H.H., Huang K.G., Chang T.C., Liang C.C., Lai C.H., *et al.*: "Squamous cell carcinoma arising in mature cystic teratoma of the ovary". *Gynecol. Oncol.*, 1996, *63*, 364.

[22] Kelley R,R,, Scully R.E.: "Cancer developing in dermoid cysts of the ovary. A report of 8 cases, including a carcinoid and a leiomyosarcoma". *Cancer*, 1961, *14*, 989.

[23] Peterson W.F.: "Malignant degeneration of benign cystic teratomas of the overy; a collective review of the literature". *Obstet. Gynecol. Surv.*, 1957, *12*, 793.

[24] Yamanaka Y., Tateiwa Y., Miyamoto H., Umemoto Y., Takeuchi Y., Katayama K., *et al.*: "Preoperative diagnosis of malignant transformation in mature cystic teratoma of the ovary". *Eur. J. Gynaecol. Oncol.*, 2005, *26*, 391.

[25] Kido A., Togashi K., Konishi I., Kataoka M.L., Koyama T., Ueda H., *et al.*: "Dermoid cysts of the ovary with malignant transformation: MR appearance". *AJR Am. J. Roentgenol.*, 1999, *172*, 445.

[26] Kimura T., Inoue M., Miyake A., Tanizawa O., Oka Y., Amemiya K., *et al.*: "The use of serum TA-4 in monitoring patients with malignant transformation of ovarian mature cystic teratoma". *Cancer*, 1989, *64*, 480.

[27] Chen R.J., Chen K.Y., Chang T.C., Sheu B.C., Chow S.N., Huang S.C.: "Prognosis and treatment of squamous cell carcinoma from a mature cystic teratoma of the ovary". *J. Formos. Med. Assoc.*, 2008, *107*, 857.

[28] Amerigo J., Nogales F.F. Jr., Fernandez-Sanz J., Oliva H., Velasco A.: "Squamous cell neoplasms arising from ovarian benign cystic teratoma". *Gynecol. Oncol.*, 1979, *8*, 277.

[29] Hirakawa T., Tsuneyoshi M., Enjoji M.: "Squamous cell carcinoma arising in mature cystic teratoma of the ovary. Clinicopathologic and topographic analysis". *Am. J. Surg. Pathol.*, 1989, *13*, 397.

[30] Pins M.R., Young R.H., Daly W.J., Scully R.E.: "Primary squamous cell carcinoma of the ovary. Report of 37 cases". *Am. J. Surg. Pathol.*, 1996, *20*, 823.

[31] McGuire W.P., Hoskins W.J., Brady M.F., Kucera P.R., Partridge E.E., Look K.Y., *et al.*: "Cyclophosphamide and cisplatin compared with paclitaxel and cisplatin in patients with stage III and stage IV ovarian cancer". *N. Engl. J. Med.*, 1996, *334*, 1.

[32] McGuire W.P., Blessing J.A., Moore D., Lentz S.S., Photopulos G.: "Paclitaxel has moderate activity in squamous cervix cancer. A Gynecologic Oncology Group study". *J. Clin. Oncol.*, 1996, *14*, 792.

[33] Tanaka H., Sakakura Y., Kobayashi T., Yoshida K., Asakura T., Taniguchi H.: "A case of thyroid-type papillary carcinoma derived from ovarian mature cystic teratoma, resected by laparoscopic surgery". *Asian J. Endosc. Surg.*, 2011, *4*, 86.

[34] Ferrer J., Herrero-Zapatero A., Orille V., Llaneza P., Perez-Rodrigo C.: "Thyroid carcinoma originating in a teratoma of the ovary". *Eur. J. Gynaecol. Oncol.*, 1995, *16*, 396.

[35] Bougerra B., Fitouhi L., Daaloul W., Ben Zina H., Klibi-farah F., Zidi-Mouafek Y.H., *et al.*: "Papillary thyroid carcinoma in a mature ovarian teratoma associated with a mucinous cystadenoma: case report and review of the literature". *Tunis Med.*, 2010, *88*, 210.

[36] Lataifeh I., Abdel-Hadi M., Morcos B., Sughayer M., Barahmeh S.: "Papillary thyroid carcinoma arising from mature cystic teratoma of the ovary". *J. Obstet. Gynaecol.*, 2010, *30*, 884.

Address reprint requests to:
A.D. ALTMAN, M.D.
RS 406, 810 Sherbrook St.
Winnipeg, Manitoba
R3A-1R9 (Canada)
e-mail: alondaltman@gmail.com