Ovarian cystic teratoma with primary epithelial cell melanoma

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Summary

We report a rare case of malignant melanoma arising in a cystic teratoma of the ovary occurring in a 60-year-old woman who died in four months despite the combined treatment administrated (surgery and chemotherapy). Diagnosis of ovarian melanoma was confirmed by immunohistochemical positivity to S-100 protein and HMB 45.

There was no evidence of extra-ovarian primary melanoma on clinical examination; therefore the diagnosis was primary ovarian melanoma. Melanoma metastases were detected on the uterus, the right ovary, the omentum and in one of the three excised left external iliac lymph nodes.

A review of the literature is analyzed and discussed.

Key words: Ovarian cystic teratoma; Ovarian dermoid cyst; Malignant melanoma; Malignant degeneration; Chemotherapy.

Introduction

Primary ovarian malignant melanoma is a rare disease and its real epidemiology is not known. We reviewed the literature spanning the period 1901-2001 (Table 1) and found 35 reports of malignant melanomas, of which 28/35 had arisen in a benign cystic teratoma [1-34].

A case of epithelial cell melanoma arising in a benign cystic ovarian teratoma is reported. The patient underwent surgery and subsequent monochemotherapy with dacarbazine but died four months postoperatively.

We report this case because of the rarity of the disease and the adverse prognosis despite surgical treatment and chemotherapy.

Case Report

In May 2002 a 60-year-old Caucasian woman, gravida 5, para 4, with unremarkable family and personal history, was admitted to our Department of Gynecology and Obstetrics, Cannizzaro Hospital, Catania, Italy, complaining of abdominal distension and pain that had onset one month before. Peristalsis, micturition and temperature were normal. General physical examination was unremarkable except for the above-mentioned symptoms (abdominal distension and pain). Gynecological examination revealed a normal sized, anteverted uterus as well as a fixed, hard mass presenting an irregular surface and measuring about 10 cm in diameter occupying the left side of the pelvis. Pelvic ultrasonography, performed by the abdominal and endovaginal route, revealed a complex mass measuring 9.1 x 8.8 cm in diameter on the left of the uterus, and free fluid in the peritoneal cavity. Ultrasound of the upper abdomen showed an enlarged hyperechoic liver with hypoechoic cyst-like lesions less than 1 cm in diameter. Computed tomography (CT) of the abdomen and pelvis confirmed these findings and also revealed the presence of an irregular intestinal profile and adhesions between the bowel and the abdominal wall. Moreover, bilateral enlarged iliac and inguinal lymph nodes were found. The pelvic mass was described as a solid, expansive formation having prevalently hypodense inhomogeneous density (20-30 UH) containing adipose dense areas (-90 UH) with irregular and focally blurred walls. Chest X-ray was negative. CA125 serum level was increased (203 UI/ml).

Xyphoid-pubic laparotomy was performed and about 2,500 ml of blood-stained peritoneal fluid aspirated. The peritoneal wall, bowel and epiploon were diffusely stained by dark pigment deposits between 0.5 and 3 cm. The epiploon did not contain solid lumps. The left ovary was a solid mass adhering firmly to the bladder and anterior uterine wall. The left tube was edematous and bloated. The uterus was normal in size, but fixed. The right ovary and tube were apparently normal. Total hysterectomy with bilateral salpingo-oophorectomy and omentectomy was performed. Intraoperative histological examination showed a malignant teratoma with melanotic areas. Therefore, peritoneal biopsies and pelvic and lomboaortic lymph node sampling were carried out. Final pathologic diagnosis was: primary melanoma arising in an ovarian cystic teratoma of the left ovary. Grossly the ovarian mass measured 13 x 8 x 4 cm and contained sebum, hairs and a brownish area of about 6 cm. Histological specimens of this dark lesion revealed a focally pigmented epithelial cell melanoma. The tumor invaded blood vessels and infiltrated the left ovarian pedicle. Melanoma metastases were detected in the uterus, the right ovary, the omentum and in one of the three excised left external iliac lymph nodes. Diagnosis of ovarian melanoma was confirmed by immunohistochemical positivity to S-100 protein and HMB 45.

The patient's postoperative course was uneventful. Five days after surgery the CA125 serum level was 106 UI/ml. She was discharged and transferred to the Department of Clinical Oncology for chemotherapy which was initiated on postoperative day 20 and consisted of 21-day cycles using 150 mg/m^2 dacarbazine alone. Her condition deteriorated in August 2002 when she presented diarrhea, melena and abdominal skin metastases. Repeated abdominal and pelvic CT scans revealed peritoneal carcinomatosis with ascites. No changes were observed in the liver; chest X-ray was negative. The patient decided to suspend chemotherapy after the third cycle as a result of the progression of the disease and her poor quality of life. Thereafter, she was administered pain relief and support treatment. She died about four months after surgery.

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Table 1. — *Review of literature.*

No.	First author	Year	Age	Findings	FIGO stage	Metastasis	Treatment	Follow-up
1	Andrews	1901	35	Melanoma with spread	–	n.i	Surgery	NED 2 months
2	Amann	1903	59	Teratoma	IA2	Bone, liver	Surgery	Died, 18 months
3	Lorrain	1905	50	Teratoma	IA2	n.i.	Surgery	Died, 1 day
4	Winterwitz	1909	26	Bilateral melanoma	–	n.i.	Surgery	Died, 12 months
5	Soubevran	1911	48	Bilateral melanoma	–	n.i.	Surgery	None
6	Van Hoosen	1922	40	Inoperable	–	n.i.	Surgery	None
7	Schokaert	1938	33	Teratoma bilateral with melanoma	–	n.i.	Surgery	NED 4 months
8	Otken	1942	33	Teratoma	–	n.i.	Surgery	None
9	Marcial Rojas	1956	77	Teratoma - pagetoid - ja	IA1	n.i.	SO	None
10	Jernstroma	1959	55	Melanoma with spread	–	n.i.	Surgery	NED 30 months
11	Bruening	1963	50	Teratoma	IIIB	Peritoneum	O	Died, 2 months
12	Park	1970	49	Teratoma - ja	IA1	n.i.	HSO	NED 1 month
13	Hameed	1970	64	Melanoma with spread	–	n.i.	Surgery	Died, 46 days
14	Leo	1973	72	Teratoma - ja	IA2	None	SO	NED 8 months
15	Ladouch	1975	63	Teratoma	IIIC	Pancreas	Surgery	Died, 8 days
16	Cronje	1981	74	Teratoma - ja	IA1	Bone	SO	Died, 18 months
17	Tham	1981	44	Teratoma	IIB	Abd. wall, peritoneal cavity, liver, lungs	HBSO	Died, 8 months
18	Gregg	1982	56	Teratoma bilateral - ja	IA1	Spleen, liver	HBSO	Died, 4 months
19	Parekh	1985	26	Teratoma - ja	IA1	Lung-pelvic recurrence	HBSO + chemo	Died, 8 months
20	Siu	1986	45	Melanoma with spread	–		Surgery + chemo	Died, 2 months
21	Tsukamoto	1986	46	Teratoma - ja	IA1	Skin	HBSO + chemo + immuno	NED 12 months
22	Boughton	1987	28	Teratoma - ja	IA1	None	O	NED 24 months
23	Nambu	1990	47	Teratoma - ja - amelanotic	IA1	None	HBSO + chemo	NED28 months
24	Takubo	1991	65	Teratoma – ja	IA1	None	HBSO	NED24 months
25	Ueda	1991	87	Teratoma	IA1	None	None	Died, 1 day
26	Selak	1991	66	Teratoma – ja	IIB	None	HBSO	NED 24 months
27	Borup	1992	66	Teratoma - amelanotic	III	Controlateral ovary, peritoneum	HSO	Died, 12 months
28	Carlson	1993	20	Teratoma Melanoma with spread	IIIC	Peritoneum, omentum, uterus, mesentery	HBSO + chemo	NED 60 months
29	Di Vagno	1993	62	Teratoma - amelanotic	IA1	Paracholic lymph nodes	HBSO	NED 12 months
30	Davis	1996	54	Teratoma bilateral - ja	IA1	Bone, brain, liver	HBSO	Died, 18 months
31	Davis	1996	47	Teratoma - uveal ja	IA	n.i	HBSO	n.i.
32	Vigliani	1998	67	Teratoma - ja - amelanotic + squamous cell carcinoma	IV	Paraortic-supraclavicular-cervival lymph nodes, liver, lung	BSO	Died, 52 months
33	Liberati	1998	74	Teratoma - ja	IA1	None	BSO	NED 7 months
34	Vimla	2001	42	Teratoma	IA1	Lungs (after 2 years - left pneumonectomy)	SO - HMSO + chemo	NED 18 months
35	Moerle	2001	56	Teratoma - uveal (?)	IA1	Vertebral column - liver	HBSO	Died 14 months
36	Present case	2002	60	Teratoma	IIIC	Left iliac lymph node - Skin – liver (?)	HBSO - LN sampling omentectomy + chemo	Died, 4 months

ab: abdominal; JA: junctional activity; NED: no evidence of disease; n.i.: no information; O: oophorectomy; SO: salpingo-oophorectomy; BSO: bilateral salpingo-oophorectomy; HSO: hysterectomy with salpingo-oophorectomy HMSO: hysterectomy with monolateral salpingo-oophorectomy HBSO: hysterectomy with bilateral salpingo-oophorectomy; LN: lymph nodes; chemo: chemotherapy; immuno: immunotherapy.

Discussion

Although melanotic spread to the ovary has been well documented [35], primary malignant ovarian melanoma is very rare. Only 35 cases were reported in the time interval 1901 to 2001 [1-34], and most of them (28/35) arose in a benign cystic teratoma. The incidence of malignant ovarian teratoma is 0.2-0.8% [36], and the transformation of benign teratoma into a malignant tumor is even rarer.

A teratoma is made up of tissue from three germ layers and thus may give rise to any type of malignancy. At times mixed tumors can be present, as in the case reported by Vigliani *et al.* [31] where a melanoma and a squamous cell carcinoma were observed in the same teratoma. Melanocytes can be found in epidermal structures, in the meninges and in ocular structures, such as the iris. In fact, presence of nevus inside dermoid cysts has been reported in the literature [37]. Furthermore, three cases of

g. 1A

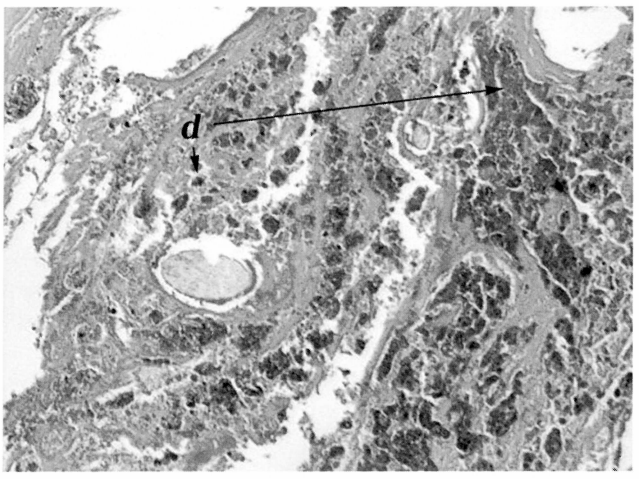

Fig. 1B

Figures 1A-B — Photomicrograph x 20 (H&E staining).
A: a) tumor infiltrate containing epithelioid elements with severe atypia; b) cystic teratoma wall; c) pilar appendages.
B: d) melanin pigment partially phagocyted by melanophages.

melanoma arising in uveal tissue within a benign cystic teratoma have been described [13, 30, 34]. Melanotic metastases from other organs can spread to the ovary; hence it is difficult to claim that the ovarian neoplasia observed is a primary melanoma. In fact, some cases reported as ovarian primary tumors could be secondary metastases from misdiagnosed peripheral melanomas that had been previously excised, had spontaneously regressed or had not been evident because they were amelanotic [23, 27, 38, 39].

In 1981 Cronje and Woodruff [16] proposed the following criteria for diagnosing primary ovarian melanoma:

– absence of other primary tumors;

– unilateral ovarian tumor with associated teratoid elements;

– good correlation of patient age and symptoms;

– demonstration of melanocytic junctional activity.

Analysis of the literature reveals the weakness of the above-mentioned diagnostic criteria:

– absence of other primary tumors: in all the cases reported, primary ovarian melanoma was diagnosed as there was no evidence of primary melanoma in other sites at the moment of histological diagnosis on the surgical specimen, or after reviewing the histological specimen following detection of a peripheral lung metastasis [33];

– site and presence of teratoid elements: 3/35 cases presented a bilateral teratoma; 28/35 cases were detected in a benign cystic teratoma. FIGO staging was available in 27/35 cases: Stage I was reported in 19 cases, Stage II in two, Stage III in five, and Stage IV in one patient. In 8/35 cases FIGO staging was unknown: in one patient the melanoma was monolateral, in three cases bilateral, and in the remaining four cases disseminated disease was observed;

– age and symptoms: there was no correlation between primary ovarian melanoma and age because the patients' age ranged between 20 and 87 (mean age 52.4 years). There was no evidence of pathognomonic related symptoms; it is reported that abdominal distension and pain are the most common [33];

– melanocytic junctional activity: this was reported only in 15/35 patients, while it was not observed in the remaining cases, including ours (Table 1).

Melanotic metastases mainly involve the surrounding structures or spread via the vascular or lymphatic systems. The most common sites of spread are the lymph nodes, liver, lungs and bones. Some authors underline the role of radioimmunoscintigraphy 99mTc-F(ab')2 bound to antimelanoma antibodies in assessing spread [29].

Surgical management is the gold standard (hysterectomy and salpingo-oophorectomy), but prognosis is generally poor, unlike that observed in common epithelial ovarian tumors [40]. Regardless of the type of treatment administered, 8/17 FIGO Stage I patients (47%) died within ten months (range 1 day-18 months), whereas the remaining 9/17 patients (53%) were disease-free after a mean time interval of 15 months (range 1-28 months).

Chemotherapy with dacarbazine and cisplatin achieved the best long-term results and Legha *et al.* reported that α-interferon and interleukin-2 treatment of metastatic melanoma gives encouraging results [41]. Nevertheless, there is no clear evidence of the efficacy of chemotherapic drugs in prolonging survival. More than 50% (4/7) of the patients who underwent surgery and postoperative chemotherapy were disease-free for a mean time interval of 29.5 months (range 12-60 months) [21, 23, 28, 34], whereas the remaining three (including our case) showed a mean survival of 4.7 months (range 2-8 months) [19, 20]. On the contrary, a disease-free interval of two to 30 months was reported in patients where the disease, even disseminated melanoma, was managed only by surgery [1, 7, 10, 14, 22, 24, 26, 29, 33].

Therefore, we believe that it is too early to draw definitive conclusions on the possible role of chemotherapy to date as there are no standard parameters, such as tumor stage, size and spread or follow-up long enough to verify previous studies to set a recommended therapeutic protocol.

Conclusions

Primary malignant ovarian melanoma is extremely rare, the natural history is unknown, the clinical and pathological diagnostic criteria are not specific and the prognosis is poor. In the cases reported in the literature, the tumor was diagnosed only after examination of the postoperative specimen (generally a benign cystic ovarian teratoma).

Surgery is the first choice treatment in primary malignant ovarian melanoma. Some authors have reported positive results after surgery associated with cisplatin and dacarbazine chemotherapy. Moreover it has been reported that treatment using combined a-interferon and interleukin-2 gives encouraging results.

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