Virchows Arch (1998) 433:381–384

CASE REPORT

Roberto Vigliani · Maria Iandolo · Antonio Lacivita

Mature ovarian cystic teratoma with combined squamous cell carcinoma and malignant melanoma

Received: 23 October 1997 / Accepted: 30 December 1997

Abstract In a mature ovarian cystic teratoma (MOCT) in a 67-year-old woman we found associated invasive squamous cell carcinoma and nodular amelanotic malignant melanoma. The finding of foci of typical and atypical melanocytic proliferation at the junctional level of the dermal component together with the absence of other possible sources supports an ovarian origin of the melanoma. A comparative analysis of the reported MOCT-associated malignant melanomas emphasizes the singularity of our case in the amelanotic character of the melanoma, its lymphotropism and the coexistence of invasive squamous cell carcinoma.

Key words Ovary · Cystic teratoma · Squamous cell carcinoma · Malignant melanoma

Introduction

Mature ovarian cystic teratoma (MOCT) is common, representing 5–10% of all cystic ovarian tumours [1, 2, 17, 19]. Malignant transformation within a MOCT is relatively uncommon (0.2–4%) [1, 3, 6, 17, 25, 27, 29]. Squamous cell carcinoma is most frequent, followed by adenocarcinoma in a ratio of 8:1 [15]. Malignant melanoma in MOCT is extremely rare, with a hypothetical incidence of less than 5% of all malignant MOCT [4, 5, 15, 27]. We report a highly unusual case of (in situ and invasive) squamous cell carcinoma combined with (junctional and tumorigenic) amelanotic malignant melanoma in the same MOCT.

R. Vigliani (✉)[1] · M. Iandolo · A. Lacivita
Department of Pathology, E. Agnelli Hospital, Pinerolo, Italy

Mailing address:
[1] Unità Operativa di Anatomia e Istocitologia Patologica, Ospedale "E. Agnelli", AUSL 10, via Brigata Cagliari, 39, I-10064 Pinerolo, Italy
Fax: +39-121-795049

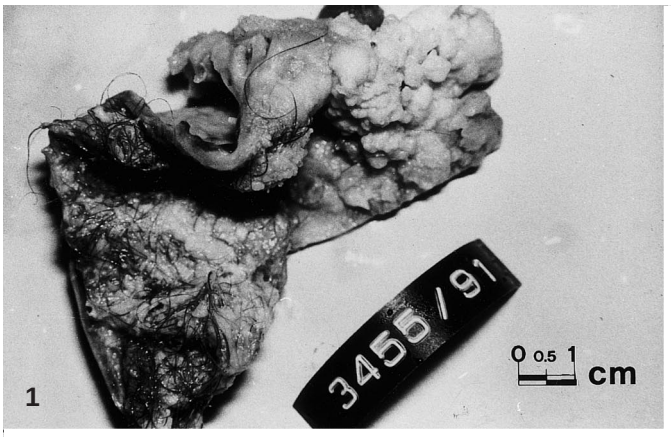
Case history

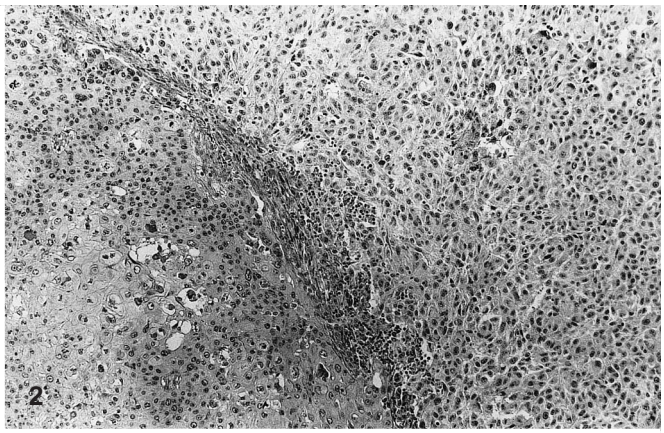
A 67-year-old woman, para 1001, was admitted to our Hospital with abdominal pain. Her medical history and laboratory data were noncontributory. Physical examination revealed an abdominopelvic mass. At surgery a tumour (suggestive of "cystoma") involving the left ovary without ascites and a small (2 cm) subserosal uterine myoma were found, and the patient underwent myomectomy and bilateral salpingo-oophorectomy without frozen section examination. The pathological finding recorded was: MOCT with malignant transformation (invasive squamous cell carcinoma). An abdominal ecographic control 2 years and 10 months later was negative.

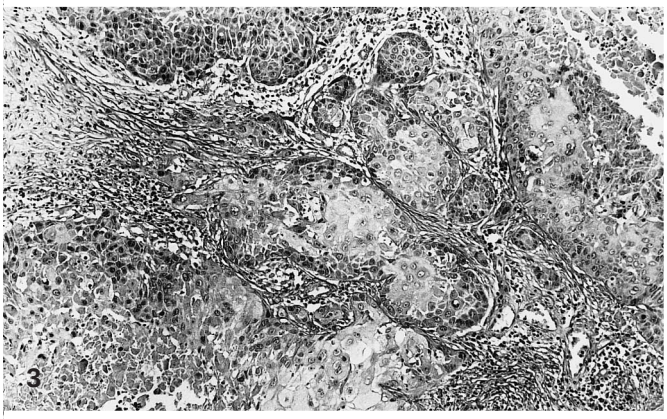
Six months later a CT scan revealed para-aortic lymphadenopathy, and 9 months later supraclavicular and laterocervical lymphadenopathy was biopsed. The histological diagnosis was metastatic neoplasm with features of malignant melanoma. A careful search for the primary possible site of origin revealed no suggestive cutaneous lesion(s). The ovarian neoplasm removed earlier was reexamined, and a few areas of more anaplastic (no stratification, no keratinization) tissue consistent with malignant melanoma according to histochemistry and immunohistochemistry were detected. A final diagnosis of invasive squamous cell carcinoma associated with tumorigenic malignant melanoma in MOCT was made. Two months later further examination showed liver (CT) and lung (X-ray) metastases. No chemotherapy was given, and the patient died 3 months later. Autopsy was not requested.

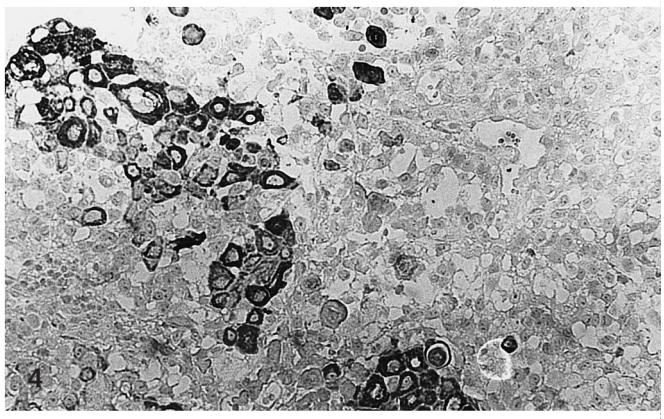
Pathology and laboratory findings

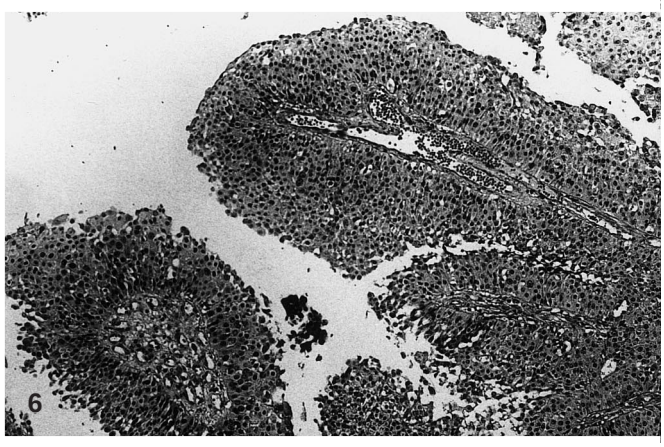
Grossly (Fig. 1) the tumour measured 13 cm in its maximum diameter, was cystic and contained greasy sebaceous material and hair. The outer surface was smooth. Most of the inner surface was whitish with diffuse papillarity and some solid areas. No brownish component was observed. Microscopically (15 blocks), in addition to mature teratomatous tissues with a dermal prevalence, invasive atypical tissue was detected. This corresponded morphologically and immunohistochemically [cytokeratin (CK) wide range, vimentin, S-100 protein and HMB-45] to dual histotypic differentiation of a squamous cell carcinoma (CK positive; vimentin, S-100 protein and HMB-45 negative), with keratinization and stromal invasion (Figs. 2–4), and a vertically growing amelanotic malignant melanoma (CK negative; vimentin, S-100 pro-











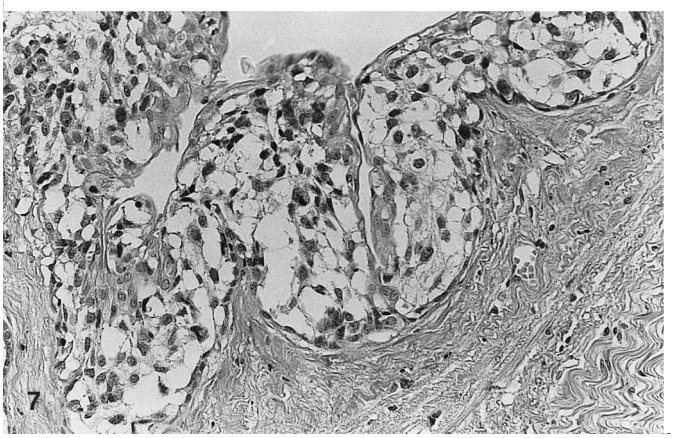


Fig. 1 Gross internal appearance of mature ovarian cystic teratoma (after preliminary sampling). Evidence of dermoid component and neoplastic projections

Fig. 2 Neoplastic tissue: collision between invasive components of malignant melanoma (*right*) and squamous cell carcinoma. Note stratification, maturation and unicellular keratinization in squamous cell carcinoma; different cytomorphology, amelanotic character and lesser degree of cellular cohesiveness in malignant melanoma. Lymphocytic infiltration at the interface. H&E, ×100

Fig. 3 Evidence of invasive squamous cell carcinoma. Mallory trichrome stain, ×100

Fig. 4 Immunostaining for cytokeratin (wide range) shows different degrees of positivity of squamous cell carcinoma within a negative melanomatous background. The *top* of the picture represents a desquamating area towards the cavity of the tumour. ×250

tein and HMB-45 positive) (Figs. 2, 4, 5). The amount of squamous cell carcinoma greatly exceeded the amount of melanoma. The Masson-Fontana method for melanin was positive in sporadic melanoma cells. The mitotic index was higher for the carcinoma (5–10 times that of melanoma), but the mean mitotic rate in the melanoma was more than 6/mm^2, with a maximum thickness of 12 mm. The melanoma was measured by micrometer from the internal surface (epithelial lining cells were inconspicuous or absent) to the deepest (external) cells. PCNA correlated with both the mitotic activities. Other histological findings included focal flat squamous cell carcinoma in situ, extensive in situ papillary carcinoma with transitional cell features (Fig. 6), a melanocytic junctional component (ranging from typical to increasingly atypical) (Fig. 7) and abundant granulation tissue with macrophages. The outer surface of the cyst wall was not infiltrated by neoplastic cells. The myoma was confirmed and the right ovary was normal. Of the blood laboratory tests only the LDH level (1290 l U/l, normal range 30–460) was abnormal terminally; CEA, AFP, CA 19-9 were normal.

Discussion

Malignancy in MOCT has been reported in several reviews [4, 5, 15, 16, 21, 24, 25, 27]. In 1993 Carlson and Wheeler [3] recorded 14 cases of malignant melanoma in MOCT. Two additional cases have since been published [14, 26], but to our knowledge the simultaneous occurrence of carcinoma and malignant melanoma in the same MOCT has not been previously reported. In our case the diagnosis of primary ovarian melanoma was supported by the clinical data (no evidence of an extraovarian origin) and the presence of junctional melanocytic activity with and without nuclear atypia. Histochemical and immunohistochemical [12, 13] results also support the diagnosis of melanoma.

Primary ovarian melanomas without evidence of teratoma have been described, but the review by Cronje and Woodruff [6] expresses reservations about their origin. However, there are occasional reports of cutaneous melanoma metastasizing to MOCT [8]. Junctional activity was detected in 8 out of 16 cases (typical in 3 [6, 20, 23], atypical in 4 [1, 17, 22, 29], unspecified in 1 [26]), but none had combined typical and atypical junctional activity. Ueda et al. [33] found a transition between dermal melanocytic naevus and melanoma in MOCT.

◀ **Fig. 5** Immunostaining for HMB-45 shows granular cytoplasmic positivity in the melanoma cells (a deep field of stromal invasion, scanty lymphocytic infiltration). ×250

Fig. 6 In situ papillary carcinoma with transitional cell features (internal side of the cystic teratoma). H&E, ×100

Fig. 7 Junctional melanocytic activity within epidermoid epithelium (internal surface). Note the mixture of typical and atypical melanocytes. H&E, ×250

Other singular features in our case were the substantial amelanotic character of the melanoma cells, the aggressiveness of the melanomatous component despite the lower mitotic and proliferative indices (than in the coexistent carcinoma) and the lymphotropism of the melanomatous spread. Areas of papillary carcinoma reminiscent of transitional cell carcinoma and foci of intraepithelial flat squamous cell carcinoma are clearly unusual. This case also showed the longest survival (52 months) of the patients who died from melanoma [2, 6, 10, 22, 30]. In the literature on malignant melanoma in MOCT only 1 case was frankly amelanotic [20], and none with lymph node metastases was described.

The aggressiveness of our case can be explained in terms of advanced pT (TNM staging system). In all the 15 well-documented cases of melanoma [1–3, 6, 10, 14, 17, 19, 20, 22, 23, 29, 30 32, 33] there was macroscopic evidence of a large mass and/or pigmentation, and a vertical invasive pattern was present in 14 of them.

Among these melanomas measured at least one dimension was 2 cm or more (the maximum was 6 cm) [32], with a smallest thickness of 5.6 mm [29]. Multifocality was observed in 5 cases [2, 3, 10, 22, 33].

An intraepithelial carcinoma component in invasive squamous cell carcinoma in MOCT is rarely mentioned [24], and the occurrence of squamous cell carcinoma exclusively in situ in MOCT is exceptional [5]. Interestingly, this was reported by Sworn et al. [28] in an ovarian epidermoid cyst associated with cervical intraepithelial neoplasia grade III. Transitional cell features in our case could be interpreted as immature and/or teratomatous squamous neoplastic epithelium. The high level of LDH found presumably reflects liver metastases [7], but this finding could be directly ascribed to melanoma [9]. Nanbu et al. [20] also reported this in their case.

Several melanocytic lesions (alone or associated) in MOCT have been described that may be correlated with vertically growing malignant melanoma, including intraepithelial melanocytosis [29], melanocytic naevi without or with junctional (typical/atypical) activity [1, 6, 11, 17, 18, 20, 22, 23, 26, 29, 31, 33] and radial spread, in situ and invasive [1, 19, 29]. Occasionally other melanocyte-related lesions including blue naevus, pigmented (benign) schwannoma and leptomeningeal melano(cyto)sis have been described in association with MOCT melanoma [29, 33].

It is interesting to speculate on how many precursor lesions related to malignancy are missed in daily practical examination of MOCT and how worthwhile an appropriate search for them would be. The problem concerns not only the detection of malignancy for clinical purposes, but also the incidence of multipotential dysplasia in mature germ cell tumours. In the case of MOCT, we suggest a careful macroscopic evaluation (no more than 3-mm-thick consecutive sections), followed by generous sampling for histology, with special attention to sampling from different areas. Systematic cytological monitoring of ascites tumours may be a useful additional examination in MOCT.

Acknowledgements We are very grateful to Ms. Mariangela Cavandoli for technical assistance.

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