ANTICANCER RESEARCH *25*: 1603-1606 (2005)

Malignant Melanoma and Fibrothecoma - an Ovarian Mixed Tumor

J. NICKEL[1], V. BRIESE[1], J. BRIESE[2] and E. REHDA[1]

[1]*Department of Gynaecology and Obstetrics, University Clinic of Rostock;*
[2]*Department of Pathology and German Reference Centre for Malignant Lymphomas, University Clinic of Schleswig-Holstein, Campus Luebeck, Germany*

Abstract. *There are only a few cases of primary ovarian melanoma described in the literature. Here, we report a rare case of ovarian mixed neoplasm with parts of malignant melanoma and fibrothecoma in a 76-year-old female who was hospitalized for a cataract operation. To our knowledge, cases of a combination of malignant melanoma and fibrothecoma in the ovary have not been described. In this study, new markers for malignant melanoma (S-100, tyrosinase mRNA) were also tested.*

Malignant melanoma – derived from melanin-producing cells – have a tendency towards an early and distant hematogenous spread, which accounts for their poor prognosis. In stage IV, the 5-year survival rate is less than 5%. Sun exposure seems to be a triggering factor since there is a higher incidence of skin cancer in people of light complexion. Moreover, woman have a two times higher risk than men (4).

Early lymphogen or hematogen metastases of malignant melanoma can be found in the lung, liver and gastrointestinal tract (2). There are only a few reports of ovarian metastases in the literature. Blaustein's Pathology of the female genital tract mentions 36 case reports of metastases to the ovaries (3). Some author's have reported solitary metastases into the ovary without, however, finding a primary tumor.

At present, there are only few useful diagnostic/prognostic tumor markers that are also potential targets for therapy in patients with malignant melanoma. The calcium-binding protein S-100 is an established marker in tumor diagnosis (2, 5). An immunoradiometric assay for S-100 in serum has been developed (6). Furthermore, it is known that RT-PCR of tyrosine kinase (tyrosinase) indicates the rate of melanin production in the blood. The level of tyrosinase mRNA seems to be a risk factor for an early metastasis (1).

Fibrothecoma – derived from fibroblasts – is a rare, benign tumor of the ovary. The lipid rich cells are typically stained with Sudan's stains. To our knowledge, no association between fibrothecoma and malignant melanoma of the ovary has been reported in the literature.

Case Report

A 76-year-old female patient was admitted to the University Eye Hospital in Rostock, Germany, for a cataract operation. A routine chest X-ray showed two pulmonary lesions. Ultrasound examination revealed findings of the right adnex and the patient was admitted to the University Hospital Department of Gynaecology in Rostock. The general history was inconspicious. There were no symptoms of any malignant disease during physical examination. The family history revealed a stomach carcinoma and a bronchial carcinoma of the patient's parents. The gynecological examination showed a palpable mass of 8 cm in the right adnex. Again the ultrasound corroborated the palpable result. A 6 x 8 cm large structure with cystic parts inside was detected sonographically. On the basis of these results, an abdominal extrafascial hysterectomy with adnexectomy, appendectomy and extirpation of omentum majus were performed. Intraoperatively we could see a large white-yellow tumor of the right adnex showing a 4-cm-wide area with dark colored pigmentation (Figure 1). The pathological examination of the extirpated tumor revealed a malignant melanoma and a fibroma. The patient was sent for consultation to the Department of Dermatology at the University of Rostock. No signs of any skin lesions or malignant melanoma were found. Further, an ophthalmological consultation did not reveal a primary tumor. Preoperative measurement of ovary tumor marker

Correspondence to: Prof. Dr. Volker Briese, Department of Gynaecology and Obstetrics, University Clinic of Rostock, Doberaner Strasse 142, 18057 Rostock, Germany. Tel: +49 381 494 8120, Fax: +49 381 494 8102, e-mail: volker.briese@uni-rostock.de

Key Words: Melanoma, fibrothecoma, ovarian tumor.

Figure 1. *Malignant melanoma and fibrothecoma of the left ovary.*

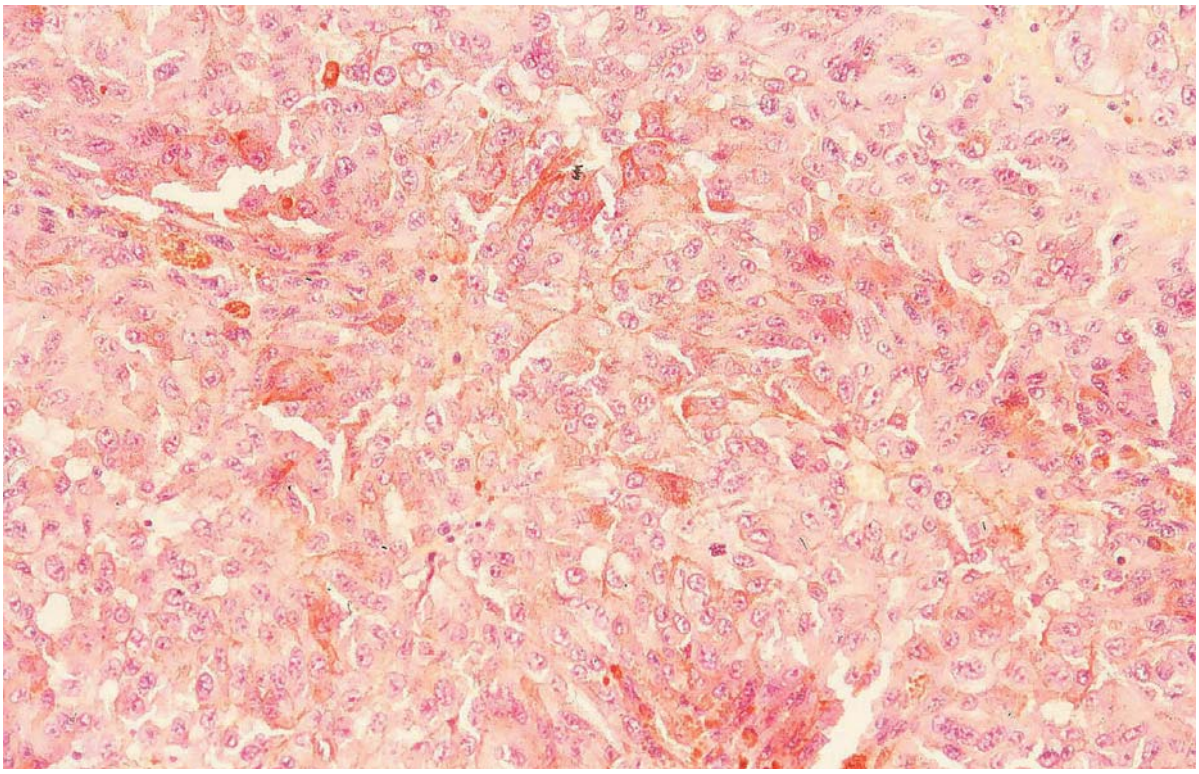

Figure 2. *Melanin pigment inside large tumor cells, H.E.*

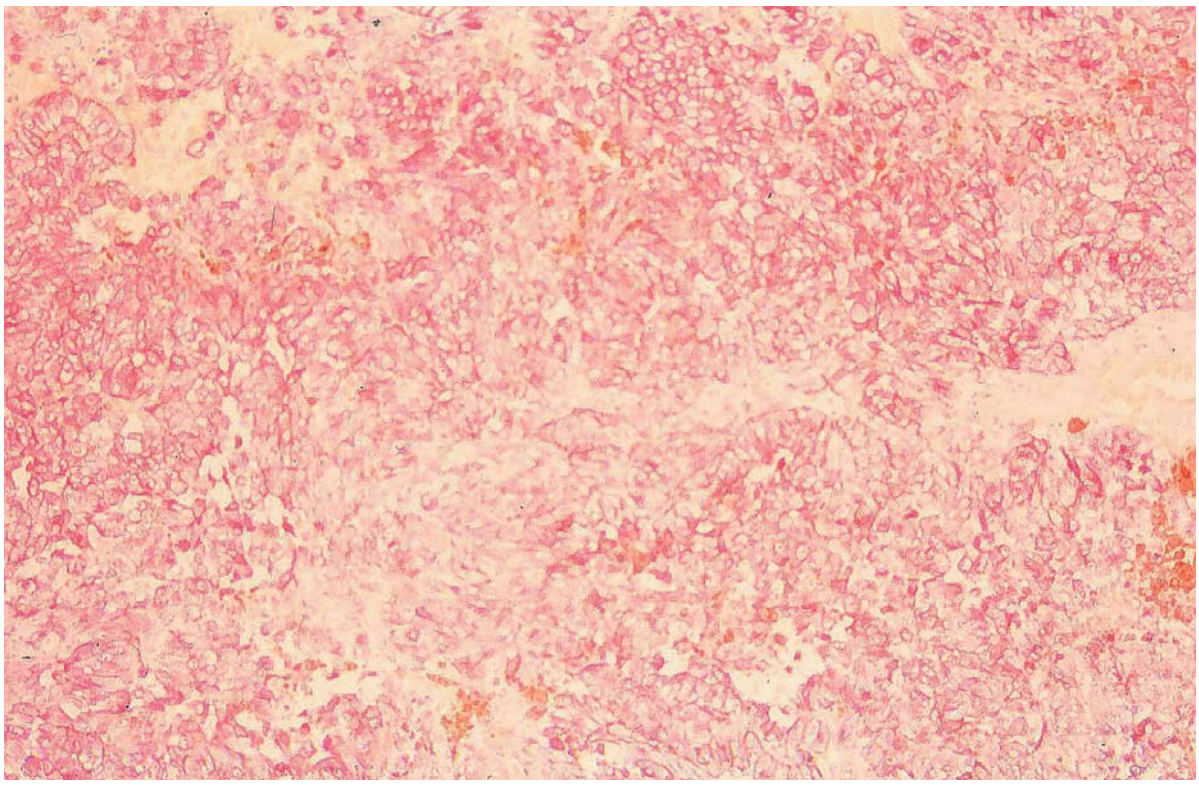

Figure 3. *HMB 45-positive tumor cells.*

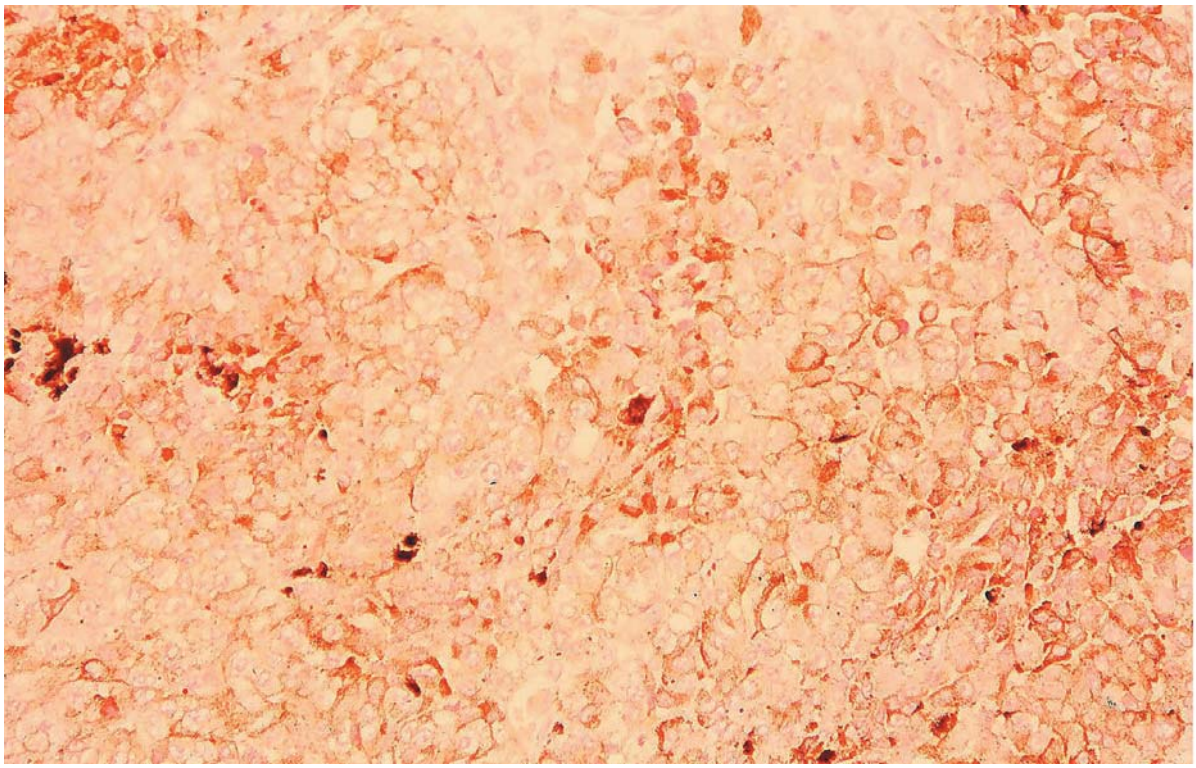

Figure 4. *Immunohistological staining of tumor cells with S-100.*

levels (CA 125, CA 72-4, CA 19-9) showed that only CA 125 was grossly elevated (129.53 U/ml) and all other markers were within normal limits. A transthoracical punction confirmed the mentioned pulmonary lesions as metastases.

Histology. The large white-yellow tumor was characterized by fibrocytes and fat story theca cells surrounded by fibers. Staining with Sudan III and Sudan-black revealed a positive reaction of the lipid content of theca cells. The macroscopically smaller brown-red tumor of the ovary (growing on top of the large one) consisted solely of atypical epithelioid cell formations enriched in melanin, which stained positive for fontana (Figure 2). Single epithelioid cells showed a light cytoplasm.

Immunohistochemical findings. The atypical epithelioid melanocytes stained positively for vimentin, S-100 and especially for HMB 45 (specific marker for melanocytes) (Figures 3 and 4). The tissue segments were negative for neuroendocrine markers (chromogranin, synaptophysin, NSE). Fibrocytes of the large tumor of the left ovary were positive for vimentin, but negative for S-100 and HMB 45. The results described here led to the diagnosis of a mixed tumor consisting of malignant melanoma and benign fibrothecoma of the left ovary.

Discussion

The evidence of pulmonary lesions in connection with a malignant melanoma of the ovary led to a first diagnosis of primary cutaneous malignant melanoma. Dermatological examination did not reveal any correlates of a primary cutaneous tumor. There is the possebility that these results are indicative of a malignant dermoid, developing from melanocytes of a germ cell tumor. Alternatively, tumor regression might have occurred in which a small primary tumor, already metastasized, dissociated through mechanical or other influences.

New diagnostic methods, such as expression of tyrosinase and S-100 protein, are available for the detection of a tumor mass and occult metastases (1, 6, 7). The interpretation of the results, however, may need further investigation.

Chemotherapy is the primary treatment strategy for metastasized melanoma. However, 70-80 percent of patients fail to respond to various regimens.

References

1 Battayani Z, Grob JJ and Xerri L: Polymerase chain reaction of circulating melanocytes as a prognostic marker in patients with melanoma. Arch Derm *131*: 443-447, 1995.

2 Das Gupta and Brasfield R: Metastatic melanoma a clinicopathological study. Cancer *17*: 1323-1339, 1970.

3 Dohan FC, Kornblith PL, Wellum GR, Pfeifer SE and Levins L: S-100 protein and 2',3'-cyclic nucleotide-nucleotide-3-phosphohydrolase in human brain tumor. Acta Neuropathol *40*: 123-128, 1977.

4 Garbe C: Epidemiologie des Hautkrebses und des malignen Melanoms in Deutschland in der Dermatologie. 38. Conference of the German Dermatological Association in Berlin, 29th April – 3rd May, 1995, pp. 201-204.

5 Gaynor C, Irle R, Morton D and Herschman HR: S-100 protein is present in cultured human malignant melanomas. Nature *286*: 400-401, 1980.

6 Guo HB, Stoffel-Wagner B and Bierwirth T: Clinical significance of serum S-100 in metastatic malignant melanoma. Eur J Cancer *31* : 924-928, 1995.

7 Isobe T and Okuyama T: The amino-acid sequence of S-100 protein (PAP1-b protein) and its relation to the calcium-binding proteins. Eur J Biochem *89*: 379-388, 1978.

Received April 27, 2004
Accepted February 31, 2005