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Case Report

Primary Malignant Melanoma of the Vagina and Cervix Uteri

Report of a Case with Ultrastructural Study

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Summary. This report concerns a very rare case of primary malignant melanoma involving the vagina and cervix uteri occurring in a 45-year-old woman. The clinical, light-microscopic and ultrastructural findings are presented and discussed.

Key words: Malignant melanoma of the vagina – Malignant melanoma of the cervix – Malignant melanoma – Ultrastructure

Malignant melanoma is a relatively common cutaneous tumor but primary melanoma of the female lower genital tract, especially that of vagina and cervix, is exceedingly rare. Norris and Taylor (1966) reported only three vaginal melanomas per 1,000 cutaneous melanomas at the A.F.I.P. Perez et al. (1973) found only two melanomas among the 118 primary malignant tumors of the vagina they reviewed. Puri et al. (1976) in their comprehensive review of the literature found only 9 previously reported melanomas originating primarily in the uterine cervix. In only 5 cases was the documentation of the primary site well established.

The purpose of this report is to present and discuss the clinical, light-microscopic and ultrastructural findings in a recently observed case of primary malignant melanoma involving the vagina and cervix uteri.

Case Report

A 45-year-old woman, para 3, with unremarkable past history was admitted to the hospital because of recurrent vaginal spotting during the preceeding three months. The patient was in good physical condition and examination revealed no pathological findings, in particular, there were no significant changes in the skin. On speculum examination a soft, polypoid and livid tumor was seen in the upper third of the vagina on the right side. Bimanual gynaecological examination revealed no other pathological findings. Laboratory data were unremarkable. Chest roentgenogram, urogram, cystoscopy, renal ultrasound scanning and curettage were performed to exclude the presence of another primary tumor such as carcinoma of the urinary tract or endometrium, or choriocarcinoma. All these

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investigations were negative, and a tumorectomy was performed. The first histological diagnosis was anaplastic carcinoma. Because the results of further investigations such as liver-scan and bone-scan were normal and the CT-scan showed no enlarged retroperitoneal lymphnodes, the clinical diagnosis of a primary vaginal carcinoma Stage I was made. Nine weeks after tumorectomy a radical hysterectomy with pelvic lymphadenectomy and partial vaginectomy was performed. The post-operative course was uneventful.

Pathology

Macroscopically the tumor was polypoid, bluish, measured $3 \times 2.5 \times 1.5$ cm and was broadly inserted on the vaginal mucosa. Its surface was focally ulcerated and haemorrhagic. The cut surface revealed a poorly demarcated solid tumor tissue, white to grayish in color and obviously infiltrating the vaginal wall. Most of the tumor was fixed in formalin for conventional light microscopy. Tiny blocks of tumor tissue were immediately fixed in cold buffered glutaraldehyde and further processed for electron microscopy.

Microscopically the tumor tissue consists of broad sheets of round to polygonal cells with an epithelial appearance (Fig. 1). The nuclei are large, occasionally indented, polymorphic, and have one or more prominent acidophilic nucleoli. Mitosis are present in great number. The cytoplasm is faintly eosinophilic and rarely contains a few brown granules that remain negative with iron and melanin stains, suggesting that they possibly represent lipofuchsin. The tumor tissue invades the vaginal wall without lymphocytic reaction but lymphatic permeation is present. This tumor was first diagnosed as an anaplastic carcinoma. The possibility of an

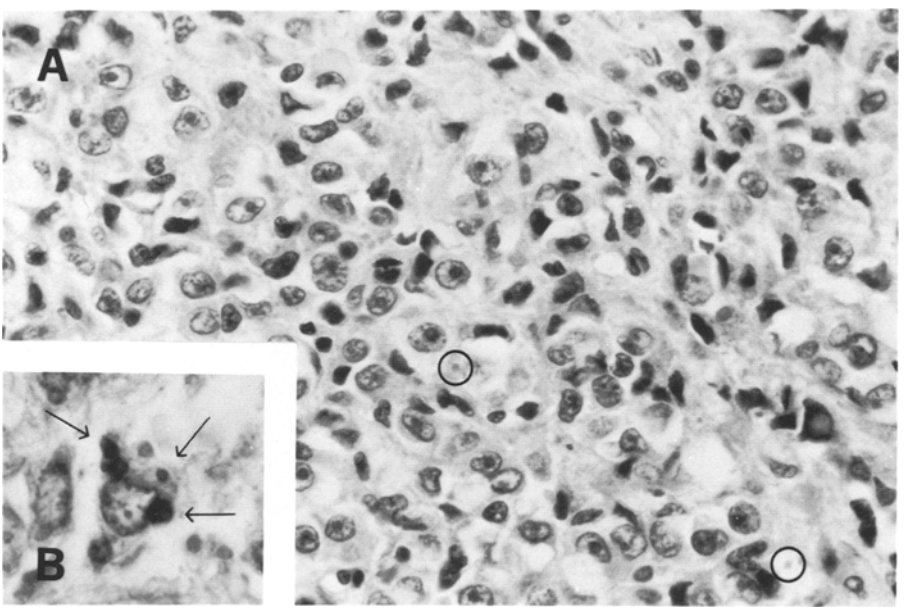

Fig. 1. A Tumor tissue with carcinomatous appearance. The tumor cells have irregular nuclei with a prominent eosinophilic nucleolus. Some lipofuchsin granules are present (*circles*). HE, ×400. **B** Rare tumor cell with obvious melanin granules (*arrows*). Schmorl, ×1,000

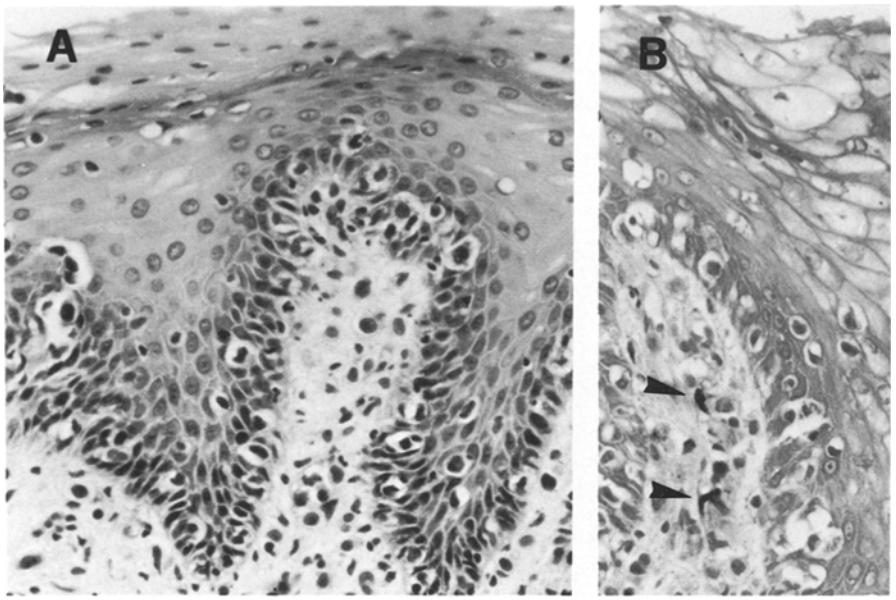

Fig. 2. A Cervical epithelium displaying strong junctional activity. HE, ×250. **B** Same area with melanin-laden cells in the stroma (*arrowheads*). Schmorl, ×250

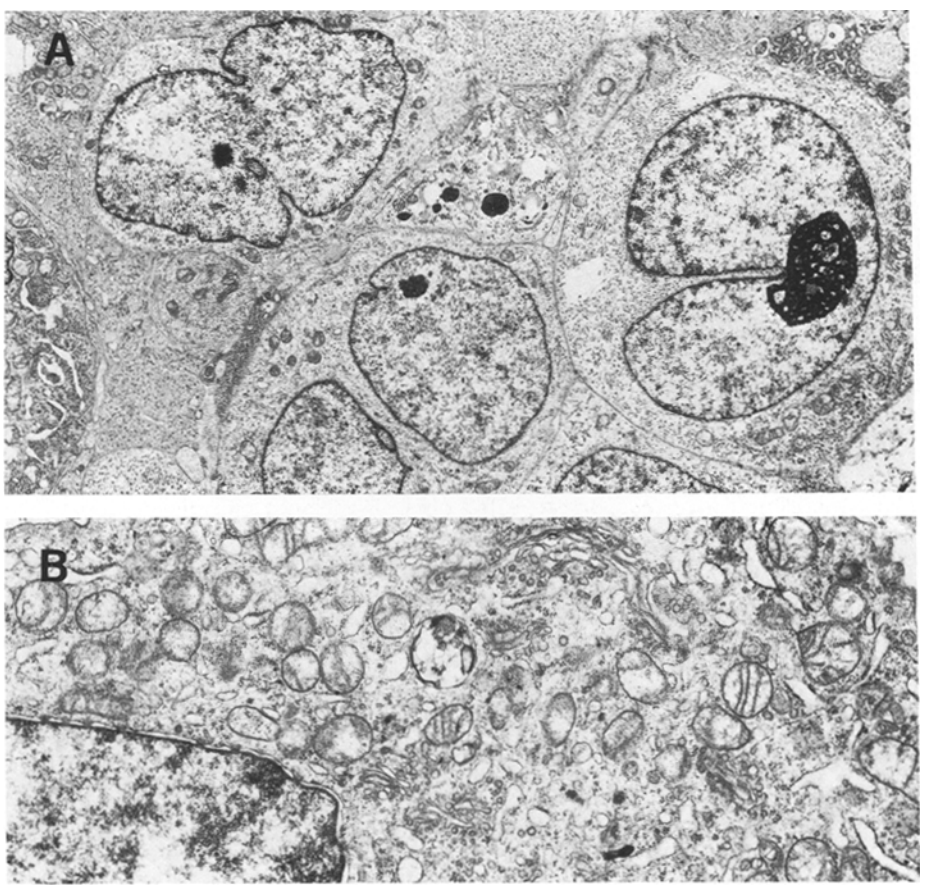

Fig. 3. A Low magnification electron micrograph showing the polygonal tumor cells with their partly deeply indented nuclei. Cell attachments are rare. In the cytoplasm of one cell a few electron dense bodies and lipochrome granules. ×4,200. **B** Cytoplasmic detail of a tumor cell with strongly developed Golgi apparatus. Numerous mitochondriae with sparse cristae are present as well as some free ribosomes. ×13,800

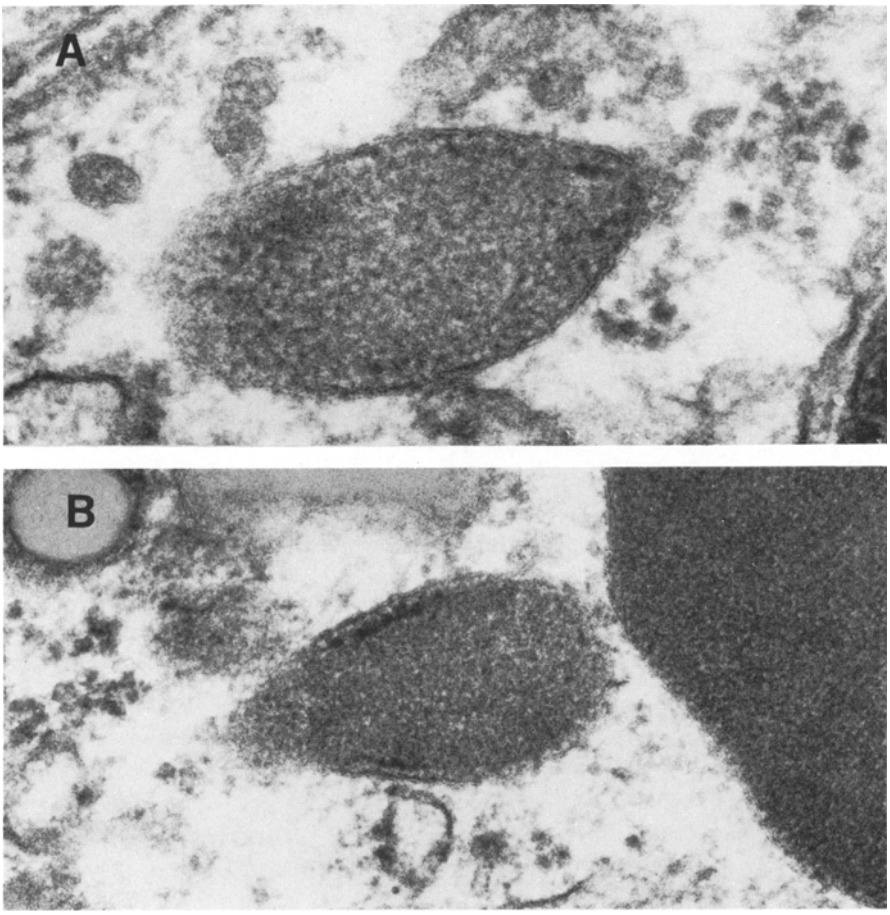

Fig. 4A and B. Two granules somewhat reminiscent of premelanosomes. A: ×127,000, B: ×88,600

amelanotic melanoma was not excluded and further tumor tissue was examined. These additional investigations revealed obvious melanin granules in some rare cells (Fig. 1B).

On examination of the vaginal mucosa in the second operation specimen the site of prior tumorectomy showed a few thickenings which were white to grayish in color and reached down to the resection plane. Similar nodules were also found on the right side of the ectocervix. Macroscopic examination of the endocervix, parametria, uterus and pelvic nodes revealed no pathologic findings.

Histologically several types of lesions were found in both vaginal and cervical mucosa. Extensive areas of the epithelium covering the vaginal and cervical mucosa exhibit intense junctional activity (Fig. 2). In such areas melanin-laden cells can be readily identified. The invading tumor tissue displays two different patterns. At some locations the tumor cells are spindle-shaped and invade the stroma in a diffuse sarcomatous fashion. At other places they grow in broad sheets and exhibit the

same carcinoma-like features as found in the previously resected vaginal tumor. In such areas melanin-containing cells are very sparse. Only one of the 22 pelvic lymph nodes examined proved to be metastatic.

At *ultrastructural level* the tumor cells are polygonal, irregular in size and shape (Fig. 3A). Some tight junctions are present but no desmosomes could be found. The nuclei are often deeply indented and contain one or more prominent heterogenous nucleoli. In many cells the Golgi apparatus is well-developed and multicentric (Fig. 3B), the granular endoplasmic reticulum is sparse. Mitochondria are present in small numbers and unevenly distributed throughout the cytoplasm. Lipochrome granules can be readily found. Very few granules, somewhat reminiscent of premelanosomes, are occasionally found (Fig. 4) but no typical melanosome could be identified. This last finding is not surprising as the tumor proved to be predominantly amelanotic. Many cells contain aggregates of glycogen as well as autophagosomes of various aspect.

Discussion

As recently as 1962, Novak and Woodruff questioned the existence of primary vaginal melanoma. Whatever the origin of melanocytes, it is now well established that they do occur in the vagina of a limited number of subjects. Nicholson (1936) reported a case of "epidermal heteromorphosis", a lesion in the upper third of the vagina containing two pigmented naevi and other epidermal structures. Intraepithelial melanocytes were found to be present in 3 % of vaginas (Nigogosyan et al. 1964) thus providing a theoretic histogenesis for melanomas in this location. Benign melanosis of the vagina and cervix has also been described (Tsukada 1976). It is still uncertain how the melanocytes arrive in the vagina but migration from the neural crest seems to be a reasonable assumption at present.

Vaginal melanoma occurs predominantly in postmenopausal women with an average age of 55 years. The symptoms are usually vaginal bleeding, as in our patient, foul vaginal discharge or the discovery of a lump by the patient. The tumor may arise anywhere in the vaginal canal but seems to have a predilection for the anterior wall and lower half (Morrow and DiSaia 1976). Vaginal melanoma is most often described as polypoid with ulceration and necrosis.

Treatment should be based on the location and extent of the disease. DasGupta and d'Urso (1964) recommend wide excision of the primary lesion and radical hysterectomy for those of the upper third of the vagina. The value of radiation and chemotherapy is still under discussion but as a whole both methods seem to be quite ineffective. The prognosis is poor, especially in patients who present with metastasis (Daw 1972; Fenn and Abell 1973; Ragni and Tobon 1974).

The demonstration of junctional activity seems to be regarded as an important factor in determining whether a melanoma was a primary or not. Norris and Taylor (1966) proposed the following criteria for ascertaining primary malignant melanoma of the vagina: presence of junctional change, histochemical identification of melanin granules, absence of involvement of the skin or other predisposed site, and distribution of metastatic lesions in a pattern expected from primary vaginal neoplasm. All these criteria are fulfilled in our case. Whether the tumor nodules on the ectocervix represent further primary tumors or are due to local

invasion and seeding could not be definitively proven but it is noteworthy that junctional activity was present at both sites.

There are very few reports of electron microscopic evaluation of malignant melanoma of the vagina. Yamada et al. (1978) described the presence of a prominent Golgi apparatus often occupying several sites within a single tumor cell. They also observed nuclear inclusion bodies, sparse glycogen, cytoplasmic autophagosomes with aggregated melanosomes and some rare premelanosomes. Unfortunately no typical melanosomes could be found in our tumor which was predominantly amelanotic, but the histochemical identification of melanin granules was successful, in particular in the areas suggestive of lentigo maligna.

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References

DasGupta T, D'Urso J (1964) Melanoma of female genitalia. Surg Gynecol Obstet 119:1074–1078

Daw E (1972) Primary melanoma of the vagina. Am J Obstet Gynecol 112:307–308

Fenn ME, Abell MR (1973) Melanomas of vulva and vagina. Obstet Gynecol 41:902–911

Morrow CP, DiSaia PJ (1976) Malignant melanoma of the female genitalia: a clinical analysis. Obstet Gynecol Surv 31:233–271

Nicholson GW (1936) An epidermal heteromorphosis of the vaginal vault. J Pathol Bacteriol 43:209–221

Nigogosyan G, De La Pava S, Pickren JW (1964) Melanoblasts in vaginal mucosa. Origin for primary malignant melanoma. Cancer (Philad) 17:912–913

Norris HJ, Taylor HB (1966) Melanomas of the vagina. Am J Clin Pathol 46:420–426

Novak ER, Woodruff D (1962) Gynecologic and obstetric pathology. 5th Ed. WB Saunders Co., Philadelphia

Perez CA, Arneson AN, Galakatos A, Samanth HK (1973) Malignant tumors of the vagina. Cancer (Philad) 31:36–44

Puri S, Yoonessi M, Romney SL (1976) Malignant melanoma of the cervix uteri. Obstet Gynecol 47:459–462

Ragni M, Tobon H (1974) Primary malignant melanoma of the vagina and vulva. Obstet Gynecol 43:658–664

Tsukada Y (1976) Benign melanosis of the vagina and cervix. Am J Obstet Gynecol 124:211–212

Yamada M, Yamamoto H, Terada S, Yasoshima A, Nishida E (1978) Primary malignant melanoma of the vagina. Gynecol Oncol 6:515–526

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