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Primary malignant melanoma of the female genital tract

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Abstract: *The primary malignant melanoma of the female genital tract is an extremely rare tumor, it is less than 2 % of all melanomas. This tumor is frequently observed at the vulva but rarely in the cervix and vagina. The diagnosis is often initially unknown and is late during bleeding or tumor mass stage. Its histogenesis has long been debated. The pathological diagnosis is necessary for use with immunohistochemical study. Its management is not coded with several therapeutic proposed including metastatic melanomas. His prognosis is disastrous, associated with a high recurrence rate and a shorter survival. We report in our study five cases of primary melanoma of the female genital tract. Our objective is to analyze the epidemiological, clinical, therapeutic and evolutionary factors of this pathology.*

Keywords: **Malignant melanoma; female genital tract; Surgery, chemotherapy ; Prognosis**

Introduction

Malignant melanoma is an aggressive tumor of the skin and mucous membranes that develops in melanocytes.
Mucosal melanoma is an extremely rare tumor. It represents 0.03% of all cancers. Its location in the female genital mucosa represents less than 2% of all melanomas. In this case, it occurs in the vagina and vulva, more rarely in the cervix.
We report in our study five cases of primary melanoma of the female genital tract :1 case of vulvar melanoma, 3 cases of vaginal melanoma, and 1 case of cervical melanoma. Our objective is to analyze the epidemiological, clinical, therapeutic and evolutionary factors of this pathology.

Results

Our patients were aged 76 years, 75 years, 64 years, 46 years and 45 years respectively.
The main reason for consultation was metrorrhagia. One of the patients consulted for the discovery of a vulvar mass.
The diagnosis was vulvar melanoma in one case, vaginal melanoma in three cases, cervical melanoma in one case All patients benefited from a biopsy confirming the histological diagnosis of melanoma.

An evaluation of tumor extension was performed in all patients, and showed metastatic lesions in 60% of cases.
Only one patient received surgical treatment which consisted of a vulvectomy with bilateral inguinal curage; while the other patients were referred for chemotherapy.

One patient was lost to follow-up before treatment.

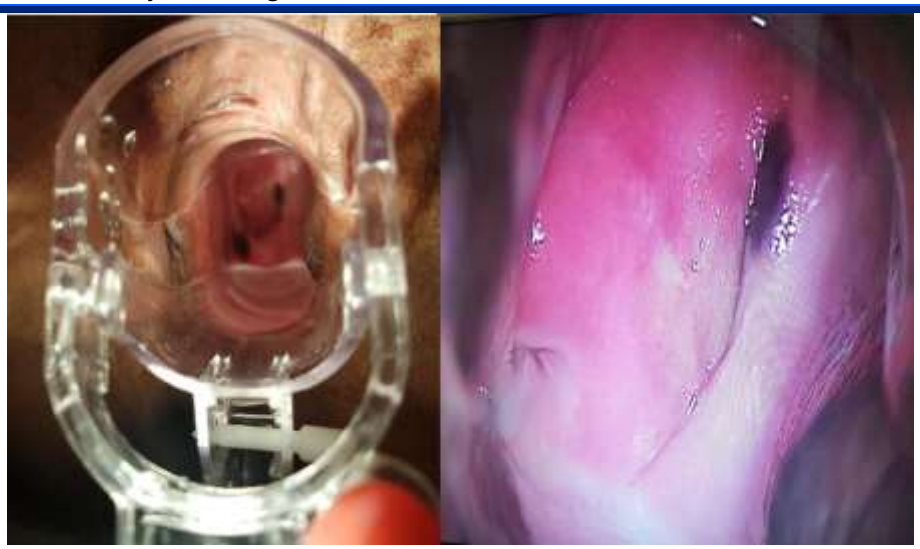

Figure 1: first lesion in the posterior wall of the vagina, second lesion in the posterior wall of the vagina in the upper third.

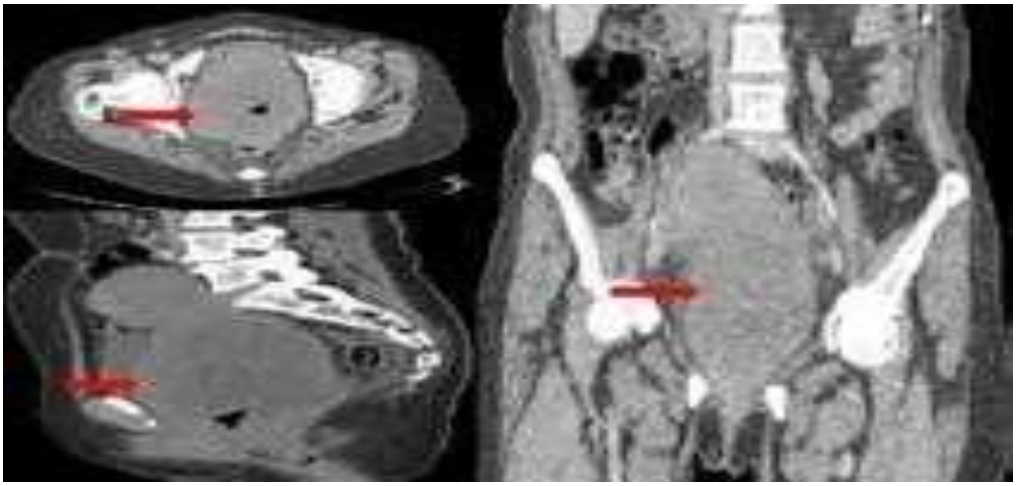

Figure 2 : Axial sections of a pelvic scan with reconstruction in the coronal and sagittal plane showing a bilobed mass centered in the uterus, containing calcifications. The mass is well limited moving the bladder forward and the sigmoid posteriorly.

Figure 3: Marking of neoplastic cells with MELAN A

Figure 4: Marking of neoplastic cells by CD117

Discussion

Melanoma is a malignant tumor developed from melanocytes (cells which synthesize melanin which is the source of skin pigmentation), appearing most often on the skin and rarely on the mucous membranes.
Primary malignant melanomas of the female genital tract are rare tumors whose prognosis is more severe than that of cutaneous melanoma.

Primary mucosal melanomas of the female genital tract represent 18% of all mucosal melanomas and 3% of melanomas diagnosed in women. The vulva is the most common site for gynecologic melanoma (1-2-3).
Melanoma is the second most common cancer of the vulva after squamous cell carcinoma, it represents 2 to 9% of melanomas in women (4-5); it was first described in 1861.Around 85% of cases arise in the labia minora, clitoris, or inner side of the labia majora. However, primary melanomas of the uterine cervix are extremely rare.

Primary malignant melanoma of the vagina is a very rare cancer, with approximately less than 300 cases described in the literature (1-3). This cancer represents 4% of vaginal cancers, and represents 1% of melanoma locations in the female genital tract, and 0.3 to 1% of all malignant melanomas.It is often located in the lower third representing half of cases, followed by the middle third in 27% of cases and the upper third in 24% of cases.

Cervical melanoma represents 3% of primary malignant melanomas of the genital tract, approximately 80 cases reported in the literature (7). Since the uterine cervix rarely contains melanocytes, a cervical origin of melanoma has been debated. Therefore, before a diagnosis of primary cervical melanoma is made, it is of utmost importance to exclude primary melanomas at other sites.

The cervix is usually involved secondarily, either by recurrent vaginal or vulval tumors or by hematogenous metastases from primaries elsewhere in the body. However, owing to the relatively limited blood supply and the presence of a fibrous stroma, which is not suitable for growth of a metastatic neoplasm, some controversy remains regarding metastases to the cervix (8).

The symptomatology is uncharacteristic, thus causing a diagnostic delay and therefore an increase in the vigilance of practitioners with regard to this pathology seems to be the key to reduced morbidity (9-10).
The anatomopathologist plays a vital role in the diagnosis, the latter can however be difficult especially when the morphological aspect is not very suggestive, hence the importance of the immunohistochemical study which makes it possible to address the diagnosis by the use of melanocyte antibodies.

Surgery is the optimal treatment of choice. For vulvar melanoma, the trend is toward more conservative surgery as there is no difference in overall survival between wide local excision and radical vulvectomy. The benefit of lymphadenectomy is also questionable. Complete regional lymphadenectomy does not seem to have any beneficial role in patients with vulvar melanoma, and should be avoided if the sentinel lymph node biopsy is negative (11-12). However, this decision showed be made with caution.
For cervical melanomas, radical hysterectomy with or without pelvic lymphadenectomy is the optimal technique (13-14).
The contribution of radiotherapy is not admitted by all authors. Systemic adjuvant treatment of melanoma is disappointing.
Interferon immunotherapy does not increase overall survival and is associated with significant impairment.

Conventional chemotherapies such as dacarbazine (Deticene®), fotemustine (Muphoran®) oreven cisplatin can be used with poor results, particularly in melanomas of gynecological origin (15,16).
At the metastatic stage, treatment of melanoma has until now been palliative using chemotherapy with modest reported response rates without any evidence of significant prolongation of survival.
The prognosis remains generally very unfavorable.
In recent years, better knowledge of the biology of melanoma has revealed several genetic alterations at the origin and maintenance of the cancer cell (17).
In the context of primary melanomas of the genital tract, the search for C-Kit, B-raf, N-ras mutations is essential because treatment by targeted therapy will be favored if a mutation is present.

Somatic mutations in mucosal melanomas more likely involve c-KIT unlike cutaneous melanomas, which are often BRAF mutated. The particular genetic profile of MVu and MVa justifies the search for mutations in the c-KIT and NRAS genes in addition to BRAF. The presence of c-KIT mutations could justify the use of c-KIT-specific tyrosine kinase inhibitors, and that of NRAS mutations the use of MEK inhibitors.

Poor prognostic factors are advanced age, lymph node invasion and the presence of distant metastases (19). Other factors have been highlighted in different studies, such as the presence of ulceration, tumor thickness, high mitotic index as well as vascular and lymph node invasion.

Conclusion

Primary malignant melanoma of the female genital tract is an extremely rare location. The diagnosis is often initially unknown and is made at a late stage. Its management is not codified, with several therapies proposed, particularly for metastatic melanoma. Its evolution is unfavorable with frequent visceral metastases and a very short survival.
The discovery of a c-Kit mutation suggests that c-Kit inhibitors, such as imatinib or sunitinib, may improve survival.

References

1. Tcheung WJ, Selim MA, Herndon JE 2nd, Abernethy AP *et al*.

Clinicopathologic study of 85 cases of melanoma of the female genitalia

2. Boel K. Ragnarsson Olding., Kanter-Tewensohn LR., Lagerlof FB., Nilsson BR., RINGBORG UK. Malignant melanoma of the vulva in a nation wide, 25 year study of 219 swedish females. Predictors of survival. Cancer,1999, 86 (7) : 1285-93.

3. Valerie E. Sygiyama , John K. Chan, Jacob Y.Shin, Jonathan S.Berek, Kathryn Osann and Daniel S. Kapp. Vulvar Melanoma. Obstet Gynecool 2007; 110:296- 301

4. N B Séguin, N Soufir. Cancérologie fondamentale. Cancers cutanés. Edition John Libbey 2005. P: 270-275.

5. referential élaboré par un groupe de travail pluridisciplinaire de professionnels des réseaux régionaux de cancérologie de Lorraine (ONCOLOR),d'Alsace (CAROL),de Bourgogne(ONCOBOURGOGNE), de Champagne-Ardenne (ONCOCHA) et de Franche-Comté (ONCOLIE), en tenant compte des recommandations nationales, et conformément aux données acquises de la science au**17 mai 2013**.

6. Pinedo F., Ingelmo J.M., Miranda P., Garcon A., Lopez J.I. Primary malignant melanoma of the uterine cervix : case report and review of the literature. Gynecol Obstet 1991 ; 31 : 121-124

7. Uzum N, Kose F, Ataoglu O. Metastatic malignant melanoma of the uterine cervix: first diagnosed on liquid-based cytology. *Diagn Cytopathol* 2008;36:769–72.

8. Duggal R, Srinivasan R. Primary amelanotic melanoma of the cervix: case report with review of literature. *J Gynecol Oncol* 2010;21:199–202.

9. Boel K. Ragnarsson Olding., Hemming J., Ringborg U.K., Rutqvist LE. Malignant melanoma of the vulva and vagina : trends in incidence, agedistribution and long-term survival among 245 consecutive coss i Sweden 1960-1984. Cancer, 1993, 71 (5) : 1893-97

10. Breslow A . : Pronostic factors in the treatnt of cutaneouxmelanoma. J. Cutan. Pathol., 1997,6 : 208-12

11. Piura B. Management of primary melanoma of the female urogenital tract. *Lancet Oncol*2008;9:973–81

12. Sugiyama VE, Chan JK, Kapp DS. Management of melanomas of the female genital tract. *Curr Opin Oncol* 2008;20:565–9.

13. Myriokefalitaki E, Babbel B, Smith M, et al. Primary malignant melanoma of uterine cervix FIGO IIa1: a case report with 40 months ongoing survival and literature review. *Gynecol Oncol Case Rep* 2013;5:52–4.

14. Berger JL, Samrao D, Huang M, et al. Primary gynecologic melanoma: a report of two unusual cases. *Gynecol Oncol Rep* 2015;11:31–3.

15. Liu Z, Wang H, Zhang X, et al. Primary malignant melanoma of the cervix: a case report. *Oncol Lett* 2014;8:2661–3.

16. Ives NJ, Stowe RL, Lorigan P, et al. Chemotherapy compared with biochemotherapy for the treatment of metastatic melanoma: a meta-analysis of 18 trials involving 2,621 patients. *J Clin Oncol* 2007;25:5426–34.

17. BouwhuisMG, Suciu S,Testori A, et coll. Phase III trial comparingadjuvant treatmentwith pegylated interferon Alfa-2b versus observation:prognostic significance of autoantibodies--EORTC 18991. JClin Oncol 2010;28:2460-6.

18. Kennedy C, ter Hurne, J, Berkhout M et al. Melanocortin 1 Receptor MC1R gene variants are associated with an increased risk for cutaneous melanoma wich is largely independent of skin type and hair color. J Invest Dermatol 2001; 117: 294- 300.

19. Blanc Francois, Phillipe Saiag : à propos des mélanomes de la vulve :20 cas rapportés et une revue de la littérature. Rev. Press, 2004,n°156.