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A Rare and Aggressive Secondary Tumour of Vagina [Metastatic Choriocarcinoma]

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Abstract: This is a 38-year-old woman who initially presented to an outside emergency room with vaginal bleeding and abdominal pain for half a year. The pelvic ultrasound demonstrated suggestive features of molar pregnancy. Subsequently, she underwent to dilation and curettage with final pathology diagnosing choriocarcinoma. She was transferred to the hospital for further oncologic management with a recommendation for total abdominal hysterectomy. The same woman returned again to our emergency room with a vaginal mass measured 5× 4×3cm with a chest pain and coughing for a month. Vaginal biopsy with Immunohistochemistry proved it to be choriocarcinoma. Through the CT scan has showed multiple bilateral lung metastases and a vaginal mass with enlarged pelvic and inguinal lymph nodes. The Final diagnosis of Metastatic or Secondary vaginal choriocarcinoma stage III was made. BACKGROUND. This study aimed to assess the level of awareness and knowledge of vaginal metastatic cancer in the general population in Yemen. The value of vaginal excision biopsy in atypical metastatic malignant tumor to vagina remains limited due to the primary intrauterine choriocarcinoma is very rare. In the current study, the authors review the vaginal histology and cytology of carcinoma and identify common histological features that allow for the diagnosis of this uncommon chorionic malignancy. METHODS. A cross-sectional survey using a self-administered questionnaire was conducted to Yemeni adult women aged between15 to 49 years. The collected data were analyzed by microscopy evaluation of H&E-stained sections. The clinical history and all previous histological biopsy were reviewed. RESULTS. Choriocarcinoma is the most aggressive gestational trophoblastic neoplasia with a high incidence of women aged between 15 and 49 years. The vaginal metastasis comprises 30% of all metastatic incidences. Vaginal metastases are found in 20–30% of choriocarcinoma cases and are known to be a poor prognostic factor. We report a case of a patient with choriocarcinoma metastasized to the vagina. CONCLUSION. This study reports for the diagnosis of choriocarcinoma that is made by microscopy histological features. All tumors of choriocarcinoma are characterized by a mixture of two kinds of trophoblastic cells: mononuclear cytotrophoblast and syncytiotrophoblast. The typical arrangement pattern of inner mononuclear cytotrophoblasts surrounded by a peripheral rim of multinucleated syncytiotrophoblasts with a central core necrosis and completely absence chorionic villi.

Keywords: Metastases, Vagina, Choriocarcinoma, Primary, Secondary Vaginal Cancer

1. Introduction

Vagina is an organ of the female reproductive tract that extends from the vulva to the uterine cervix and

derived from paired Mullerian ducts. Histologically, the vagina is a fibromuscular tube lined by mucous membrane of stratified squamous epithelium with underlying fibro-cellular lamina propria. The second middle fibromuscular layer of smooth muscles encasing by third outer layer adventitia formed of fibrous tissue.

The primary cancer of the vagina is rare and is only 2% of all gynecological cancers less than 0.5% of all cancers in women [1]. Estimated new cases in the United States in 2017 are 4,810. Deaths from vaginal during the same time were 1,240 [2]. It is more common in older women [3].

In the UK, 254 cases of Vaginal cancer were identified in 2014. Deaths from vaginal cancer in this period were 110 [4]. Out of those with vaginal cancer, 53% are related to HPV infection [5].

There are two primary types of vaginal cancer: squamous cell carcinoma and adenocarcinoma [2]. Squamous cell carcinoma of the vagina arises from the squamous cells (epithelium) that line the vagina. This is the most common type of vaginal cancer. It is found most often in women aged 60 or older.

Vaginal adenocarcinoma arises from the glandular secretory epithelial cells in the lining of the vagina. Adenocarcinoma is more likely to spread to the lungs and lymph nodes.

The secondary cancer in the vagina is more common than primary vaginal cancer. This means the cancer has spread from another part of the body, such as the cervix, uterus, vulva, bladder, bowel or other nearby organs. The secondary type of vaginal cancer is metastatic choriocarcinoma with high metastatic potential to the vagina. The vaginal metastasis comprises 30% of all metastatic incidences [1]. Here we present a case of a 38-year-old woman who presented with a hard-vaginal mass six months after molar pregnancy and a total hysterectomy.

2. Materials & Methods

This present study is a retrospective study on vaginal metastatic choriocarcinoma that was conducted based on vaginal biopsy specimens retrieved from the archives of the Departments of Gynecology and Pathology, College of Medical Sciences, Taiz University, Taiz, Yemen, available from the year January 2016 through May 2019. The age and anatomical site of all cases were compiled from the clinical data sent together with the biopsy records. Histopathology slides stained with hematoxylin and eosin were selected and re-evaluated according to the current concepts outlined by the WHO.

Inclusion criteria involved the histological confirmation of vaginal metastatic choriocarcinoma. Lesions with histological findings that were not compatible with vaginal metastatic choriocarcinoma were excluded from the study. Some records that were sent with the biopsy material were inadequate and were omitted.

3. Result

A 38-year-old woman presented to an outside emergency room with a vaginal mass measured 5× 4×3cm with pain abdomen for one month. The mass was smooth, soft reddish and fixed to underlying structures. Multiple bilateral inguinal lymph nodes were enlarged. Vaginal biopsy with Immunohistochemistry proved it to be choriocarcinoma. CT scan thorax, abdomen, and pelvis showed multiple bilateral lung metastases. On the pelvic exam, she was found to have a 5cm fixed mass on the left labia extending up to encasing urethra with multiple enlarged pelvic and inguinal lymph nodes. All invasive components showed the same histomorphologic profiles. She had a history of molar pregnancy with final pathological diagnosing as choriocarcinoma and total hysterectomy was recommended half years previously. The cut section of the uterus showed diffuse, large, no masses and thick looking of the endometrium. It was provisionally diagnosed as disordered proliferative endometrium without invasion or metastases of choriocarcinoma to the uterine wall.

4. Histopathology

Choriocarcinoma is a gestational trophoblastic tumor in most cases arising in the uterus, although ectopic pregnancies provide extra-uterine sites of origin or metastases to vagina ass in this case. The diagnosis of choriocarcinoma was made by microscopy evaluation of H&E-stained sections. Histologically, it is differentiated from other gestational trophoblastic tumors by the absence of chorionic villi [figure 3], although it is composed of sheets of both anaplastic cytotrophoblast and syncytiotrophoblasts, which are cells types of the early embryo and gestational sac [figure 4].

Choriocarcinoma consists of a mixture of neoplastic syncytiotrophoblasts and cytotrophoblasts in a hemorrhagic and necrotic background [figure 1]. Syncyiotrophoblasts cells are giant cells with acidophilic cytoplasm, several pleomorphic and hyperchromatic nuclei and distinct nucleoli, while cytotrophoblasts cells are medium-sized with vacuolated basophilic cytoplasm and single eccentric hyperchromatic nuclei [figure 2]. This tumor was characterized by a mixture of two kinds of trophoblastic cells: mononuclear [including cytotrophoblast and intermediate trophoblast] and syncytiotrophoblast. The typical arrangement pattern of a central core of mononuclear cytotrophoblasts surrounded by a peripheral rim of giant multinucleated syncytiotrophoblasts.

5. Discussion

Metastatic choriocarcinomas might be a relatively common entity following molar pregnancy or abortion, but after normal pregnancy was often an infrequent event, if occurred, we should take highly malignant potential disease [7]. Generally, GC was in the neoplasm group with a high tendency to rapid spread and dissemination via lymphatic-hematogenous. So, potential risk extrapelvic metastases should be considered. Usually, most common sites of metastases outside of the pelvis were lung, and the second most common site of metastases inside the pelvis was a vagina. The involvement of the kidney was very infrequent [9]. Wang et al. believed that renal metastasis was often secondary to lung and vaginal metastasis. Successful control of retroperitoneal hemorrhage in bilateral renal metastasis of choriocarcinoma with angioembolization has reported and also the patient died due to life-threatening postoperative sepsis [10]. In this article, we have achieved unsuccessful management in our patients with chemotherapy.

Few cases of choriocarcinoma that developed after a long latent period from a previous pregnancy have reported [11,12]. However, due to the delayed diagnosis of choriocarcinoma, this patient has admitted in advance stage. We have also diagnosed our case in stage III of gestational choriocarcinoma GC. Therefore, our recommendation was considering the possibility of GC of different ages with different presentations.

We have kept in mind that for excision of vaginal metastasis of GC due to the risk of energetic hemorrhage, a deep caution should take continuously. Also because of the possibility of a diagnosis of GC, excisional biopsy has carried on for this case.

Cytotrophoblast cells are a new tissue to human biology. It was only in 1983 that this type of cell was mentioned for the first time in biology texts or medical journals. The physiology of these new cells is still being dissected [13,14,15]. It was discovered in 2006, that these cells produce hyperglycosylated hCG, and that this molecule drove cytotrophoblast growth and invasion [13,16].

As we now understand, cytotrophoblast cells produce hyperglycosylated hCG, which is an autocrine that functions through the TGFβ receptor [13,14,16], promoting cell growth and extreme cell invasion by the production of degradative enzymes, metalloproteinases, and collagenases [15,16].

In choriocarcinoma, decidual tissue can invade through the myometrium and into the lymphatic and hematic system, metastasizing possibly to the vagina, to the lungs, then to the liver, and finally to the brain.

6. Conclusion

The trophoblastic disease includes different types of pathologic events classified and divided by the WHO in 2003. It includes hydatidiform mole, invasive mole, gestational choriocarcinoma and placental site trophoblastic tumor. Most of those pathologies are chemosensitive and have an excellent prognosis, allowing preserving women's fertility because of the low relapse rate during further pregnancies. Hydatidiform moles have to be treated by suction rather than curettage. Placental site trophoblastic tumors are particularly chemoresistant, not secreting hCG which needs specific management. Gestational choriocarcinoma is the most aggressive form of trophoblastic disease with tumor cells morphologically recapitulating the trophoblast of the developing placenta at its previous stage. This tumor has a high propensity for hematogenous spread, and in fact, one of the most malignant tumors in humans if

untreated. This type of tumor we recommended treated by polychemotherapy methods to preserve the procreative ability of the woman who most of the time is young and desirous of maternity.

7. Declarations

7.1. Ethical Approval and Consent to Participate

This study was approved by the Ethical Committee of the Women's Hospital, Collage of Medicine, Taiz University.

7.2. Consent for Publication

We obtained consent to publish this manuscript.

7.3. Availability of Supporting Data

The data that support the findings of this study are not available.

7.4. Competing Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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7.6. Authors' Contributions

Fuad: conceived and designed the study, performed experiments. Mohammed: acquired and analyzed data, drafted the manuscript and figures.Both authors read and approved the final manuscript.

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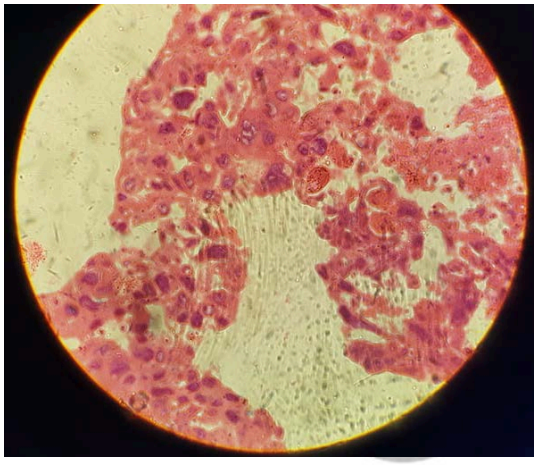

Figure 1. Histological section of vaginal GC showed malignant giant multinucleated cells of syncytiotrophoblasts, cytotrophoblasts with foci of hemorrhage (H&E 20x40x).

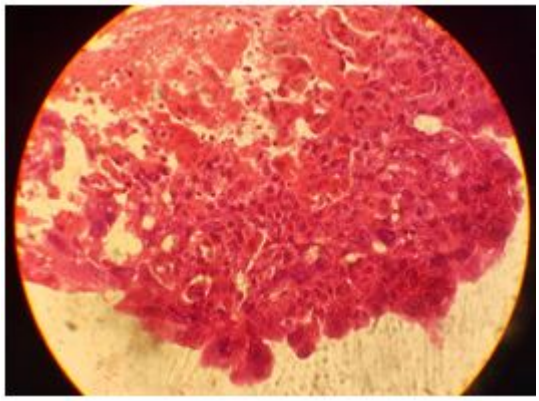

Figure 2. *Section showed malignant (giant multinucleated- syncytiotrophoblast and medium-size cytotrophoblasts with single eccentric nuclei) cells (H&E 20x80x).*

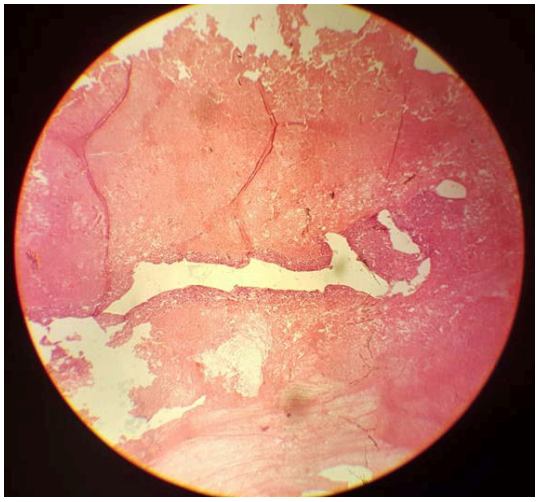

Figure 3. *The slide of the histological section showed malignant decidual tissue without chorionic villi [H&E 15x40x].*

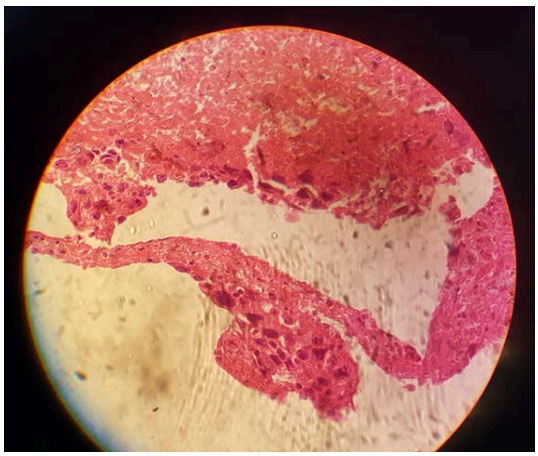

Figure 4. *The slide of vaginal GC showed malignant cells with large hyperchromatic nuclei and pleomorphism and no chorionic villi. (H&E staining 20x40x).*