EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 4
Issue: 7
181-184
Year: 2017

SCC CERVIX OF ISTHIMUS EXTENDING INTO ENDOMETRIUM MIMICKING SQUAMOUS MORULE IN ENDOMETRIAL CARCINOMA IN SITU

Nirupma Lal[1*], Neema Tiwari[1], Parul Gupta[1], Ramis Khan[1], Osman Musa[2]

[1]Department of Pathology Eras Lucknow Medical College and Hospital.
[2]Department of Surgery Eras Lucknow Medical College and Hospital.

***Corresponding Author: Dr. Nirupma Lal**
Department of Pathology Eras Lucknow Medical College and Hospital.

Article Received on 25/04/2017 **Article Revised on 15/05/2017** **Article Accepted on 05/06/2017**

INTRODUCTION

Carcinoma cervix is one of the most common causes of post menopausal bleeding and shows a strong correlation with HPV infections. It is the most common gynecological malignancy in India. Recognized patterns of the local tumor spread include direct invasion of the parametrium and endometrial cavity, but a superficial upward spread without invasion of the underlying myometrium is uncommon[1] A common differential to carcinoma cervix extending into the uterus is the Squamous differentiation/squamous metaplasia often associated with endometrial adenocarcinoma and benign lesions, such as endometrial hyperplasia and chronic endometritis. These squmaous morules have distinct histological characteristics, and are referred to as squamous metaplasia or squamoid metaplasia.[2] Another entity that should be discussed here is the double malignancies of uterus and cervix co existing. Synchronous double cancer was defined as additional cancer developing within 6 months of the first cancer and metachronous double cancer was defined as additional cancer developing after an interval of 6 months or longer.[3] We report an interesting cases of squamous cell carcinoma of the cervix in the isthmus extending upwards into the endometrium with moderate cervical stenosis resulting in pyometra, which mimicked a focal islands of epithelial squamous morule with surrounding glands showing reactive atypia due to intense inflammation which mimicked a Endometrial In-situ Neoplasia. This is a very rare phenomenon, with fewer than 30 cases reported so far in the literature hence this case report is important in highlighting the mimickers as well as a possibility of double malignancy in such type of tumors.[4]

CASE

A 65-year-old female, ten-year post-menopausal presented with mild cervical stenosis with pyometra. Wertheim's hysterectomy was performed and sent for histopathological examination to the department of Pathology ELMCH. The uterus weighed revealed cervical stenosis, but no obstruction. On gross examination, the uterus and cervix measured 8 × 5 × 4 cm. The cervix showed some grey white homogenous firm areas. The endometrial cavity was dilated and the endometrial surface had a gray–white corrugated appearance. Microscopically, the first time a diagnosis of EIN with squamous morule was given. On regross minute foci of the cervical lesion consisting of nests of intraepithelial squamous cell carcinoma, moderately differentiated and extending up and over the endometrial surface of the lower uterine segment as carcinoma in situ, without involvement of the underlying myometrium was seen. The adjacent endometrium show dense mixed inflammatory infiltrate and endometrial glands showed marked degenerative atypia. Rest of endometrium and endocervix was unremarkable. Ectocervix showed hyperplasia and koilocytosis. A final diagnosis of squamous cell carcinoma cervix extending into the isthmus was made. [FIGURE 1-6]

IMAGES

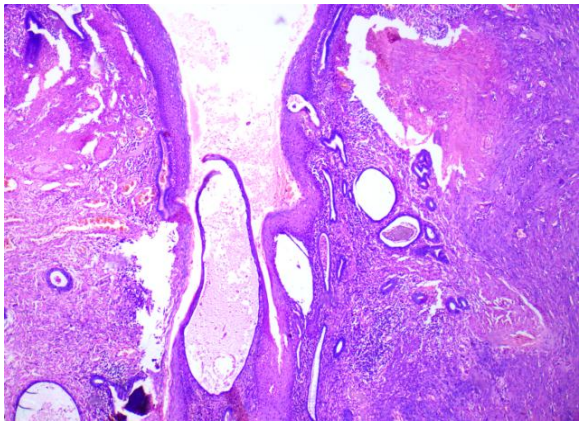


FIGURE 1-4 X[OBJECTIVE] VIEW OF THE OVERLYING COLUMNAR ENDOMETRIAL EPITHELUEM BEING REPLACED BY SQUAMOUS EPITHELIUM WITH DYSPLASTIC ENDOMETRIAL GLANDS BELOW IT IN THE STROMA

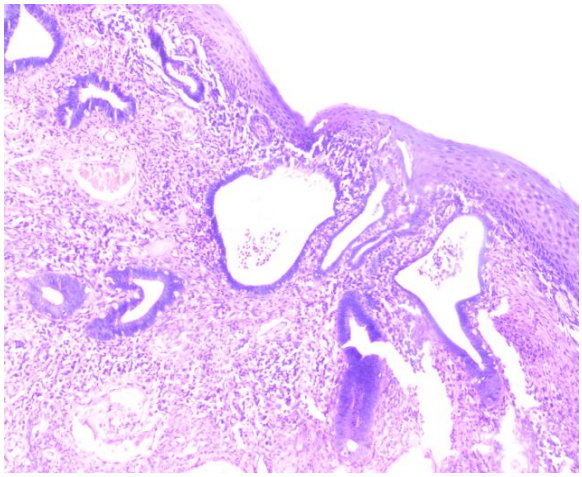
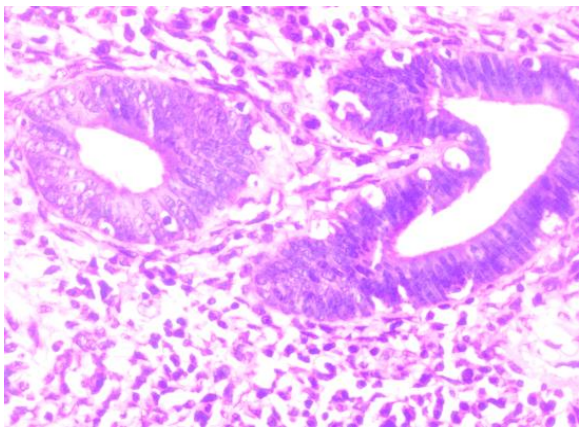


FIGURE 2-10X[OBJECTIVE] VIEW SHOWING THE OVERLYING COLUMNAR ENDOMETRIAL EPITHELUEM BEING REPLACED BY SQUAMOUS EPITHELIUM WITH DYSPLASTIC ENDOMETRIAL GLANDS BELOW IT IN THE STROMA



FOGURE 3-40X[OBJECTIVE[VIEW SHOWING DYSPLASTIC ENDOMETRIAL GLANDS IN STROMA

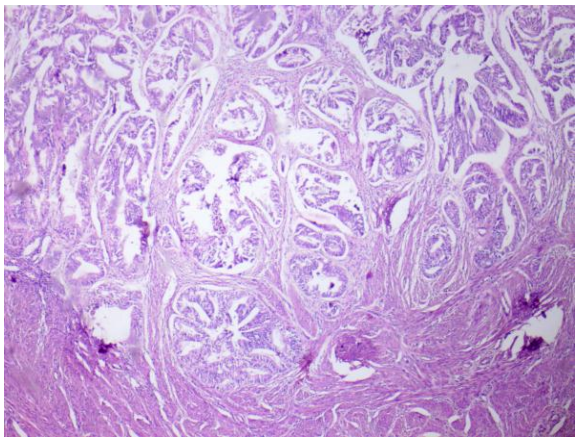


FIGURE 4- 10X[OBJECTIVE[VIEW SHOWING FOCUS OF COMPLEX ENDOMETRIAL HYPERPLASIA WITH ATYPIA WHICH LEAD TO THE DIAGNOSTIC CONFUSION IN THE FIRST ATTEMPT.

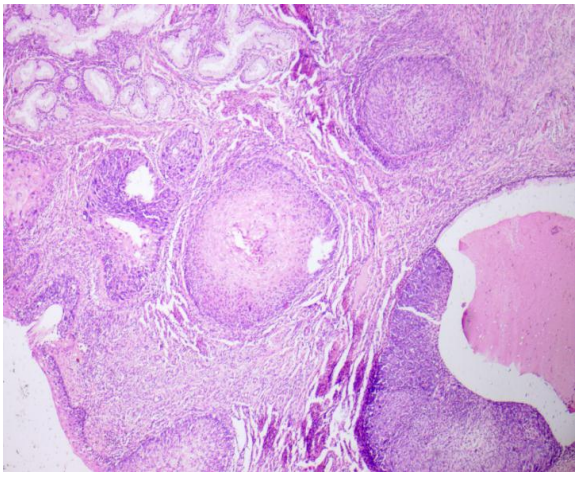


FIGURE 5-10X [OBJECTIVE[RGROSSING THE CERVIX REVEALED NESTS OF MICROINVASIVE SQUAMOUS CARCINOMA IN THE CERVIX.HENCE CLEARING THE DOUBT THAT THE SQUAMOUS EPITHELUM IN ENDOMETRIUM WAS FROM THE CERVIX DUE TO INVOLVEMENT OF THE ISTHIMIC AREA RATHER THAN A SQUAMOUS MORULE.

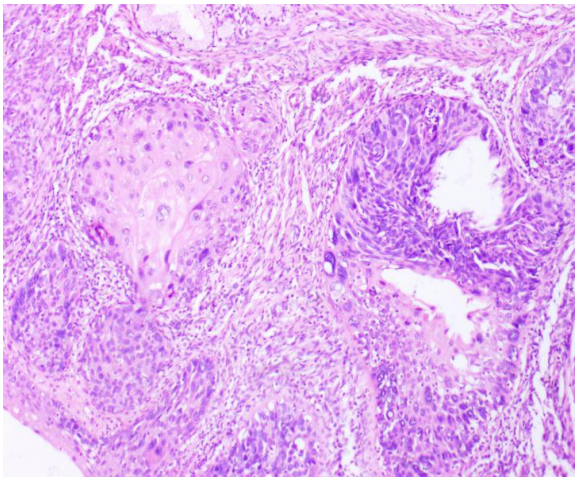


FIGURE 6- 40X [OBJECTIVE] VIEW OF MICROINVASIVE SCC CERVIX.

DISCUSSION

Squamous cell carcinoma of cervix is the most common tumor of the female genital tract, comprising 70-78% of the cervical malignancies.[2] It is one of the most common cause of cancer deaths occurring in elderly female population especially in Indian subcontinent. Carcinoma of the cervix generally spreads upward to the parametrium, and through the lymphatic invasion to the uterine wall. The presence of invasive squamous cell carcinoma of the cervix, associated with squamous cell carcinoma in situ in the endometrium, suggests a superficial spread or a concomitant carcinoma in the endometrium hence double malignancy has to be ruled out too. Primary squamous cell carcinoma may arise through the process of squamous metaplasia..[3]

To be accepted as primary carcinoma of the endometrium, the tumor must satisfy the criteria

established by Fluhmann and modified by Kay.[4,5] These criteria are: No coexistent endometrial adenocarcinoma, no demonstrable connection between the endometrial tumor and the stratified squamous epithelium of the cervix, and no primary cervical carcinoma. Pyometra, non-specific and specific endometritis, tuberculosis, syphilis, vitamin A deficiency, irradiation, foreign body, including intrauterine devices (IUDs), chemical agents, and exogenous and endogenous estrogens have been mentioned as being associated with or as precursors of this type of lesion.

The common pattern of uterine corpus involvement by cervical cancer is through deep myometrial penetration or via lymphatic dissemination. Superficial spread of in situ or invasive squamous cell carcinoma of the cervix over the contiguous endometrial surface may occur in rare instances. The intrauterine spread of cervical carcinoma in the endometrium may be evident as whitish patches, on gross inspection, a condition called 'cake icing' or 'Zukerguss' carcinoma, wherein the superficial squamous tumor sweeps over or replaces the entire endometrium.[6] Such an involvement was seen in all of our cases. Such a lesion may involve the entire endometrial cavity and may extend into the tubal mucosa, fimbria, and ovary.

The tumor appeared more often in the older age group. Various predisposing factors, such as, early marriage, early first sexual intercourse, and multiparity were seen in one of our patients as well. Cervical stenosis and subsequent pyometra could have a promoting effect for surface propagation of cervical cancer.[7]

An extensive survey of the literature revealed 26 reported cases of cervical carcinoma with endometrial surface involvement; of these 26 cases presented by various authors, nine cases were of carcinoma in situ,[8,9] two cases of microinvasive carcinoma,[10,11] and 15 cases were of invasive cervical carcinoma.[12,13] In three cases, the fallopian tube was also involved, in direct continuity with the cervical and endometrial lesions.[14,15,16] In four cases, the bilateral ovaries were also involved.[17,18] In addition, two cases showed an extensive superficial spread to almost the entire genital tract, with associated endometrial stromal sarcoma.[19] A study. reported a case of superficial endometrial spread and pointed out that this condition may be followed by radiation therapy.[20] These studies suggested a need for more cytological and histological studies on patients receiving radiation therapy previously. However, there was no such past medical or surgical history in the present cases. The present cases showed the endometrium with infiltrating nests of Cervical SCC with dense endometrial inflammation and endometrial glands showing reactive and degenerative atypia.

Another important aspect to keep in mind is the double malignancy. In Japan, synchronous double cancer involving cervical cancer has an incidence of 0.46-2.94%; the additional cancer is most often uterine cancer, followed by ovarian cancer, breast cancer, and then gastric cancer.[12] Metachronous double cancer involving cervical cancer has an incidence of 0.82-1.33%; the additional cancer is most often gastric cancer, followed by breast cancer, colon cancer, and then lung cancer.[21] In the cited source, the histologic type of cervical cancer was most often squamous cell carcinoma, and adenocarcinoma was rare.[12] Based on that source, synchronous double cancer in the form of cervical cancer and endometrial cancer is somewhat likely to occur, as is metachronous double cancer in the form of cervical cancer and breast cancer [double malignancy].

A important differential of our case is the squamous morule with EIN which can be confused with a carcinoma especially if SCC is present with endometrial glandular atypia. Some foci of squamous differentiation resembled morules and could easily be confused with them, although detailed examination revealed certain morphological differences between morules and squamous differentiation tissue. The nuclei of tissue with squamous differentiation are more atypical and slightly larger than those found in the morules, and prickle cell differentiation was also found in some places. Diffuse staining (varying in strength) for NSE was found in the morules, but not in squamous differentiation tissue.[22] It is still difficult to determine the optimal treatment; whether squamous morules associated with endometrial lesions can be safely treated by simple hysterectomy or they require radical hysterectomy and pelvic lymphadenectomy, still needs to be resolved. As reports on unusual forms of superficial spreading squamous cell carcinoma of the cervix have been primarily limited to case series, and the data are limited, the prognostic significance is uncertain.[23]

Superficial spreading squamous cell carcinoma of the cervix is a rare phenomenon, with fewer than 30 cases reported in the literature, and guidelines for the management of these cases have not been determined yet. The International Federation of Gynecology and Obstetrics (FIGO) staging system has ignored such an entity, leading to the fact that all these cases will be in stage 1B or higher.[24]

CONCLUSION

We felt the need to discuss this case as squamous cell carcinoma cervix can mimic an EIN with squamous morule specially when extending up to the isthmus. Hence one can not only sign out a wrong report but also miss the staging of carcinoma cervix as it extends into the endometrium.So it is important to bring to notice such mimickers which lead to confusing diagnosis.

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