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Case Report

Extensive morular metaplasia in an endometrial polyp – A rare occurrence - creating a diagnostic dilemma

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ABSTRACT

Morular metaplasia is an unusual type of metaplastic change, often observed in numerous endometrial lesions. It has been considered a variant of squamous metaplasia and has a mulberry-like appearance. Morular metaplasia lacks the characteristic histopathological features of conventional squamous differentiation and hence their relationship with each other has not been clearly defined. These lesions are usually seen along with pre-malignant and malignant glandular lesions of endometrium. Their presence in normal endometrium or benign endometrial polyps is rare, however it can cause a diagnostic dilemma. We present a case of a 39-year-old female who underwent hysteroscopic removal of an endometrial polyp. On gross examination it was a well-defined tan white lesion. Microscopy showed cystically dilated glands along with foci of extensive morular metaplasia. There was no evidence of any atypia/ dysplasia or malignancy in the material studied. It is important to report morular metaplasia in benign localised endometrial lesions due its usual association with endometrial hyperplasia/ atypical hyperplasia or endometrial endometrioid carcinoma. The patient requires regular follow up with clinico-radiological correlation in view of risk of presence of other coexisting lesions in these cases.

1. Introduction

Morular metaplasia (MM) is an unusual type of metaplastic change, observed in numerous benign and malignant endometrial lesions.[1] The term 'morular metaplasia' is derived from its mulberry-like appearance.[2] These morules have a nodular appearance, they are seen in endometrial-type glands.[3] Although MM is considered to be a type of squamous metaplasia, it does not show classical keratinized cells with prominent intracellular membranes and intercellular bridges. In MM bland cells with ovoid to spindle shaped nuclei usually form a syncytium filling the lumen of the glands. The origin of squamous cells is postulated to be the reserve cells between glands and stroma, however the exact nature of these cells remains uncertain.[2] Similar histopathological structures have been observed in neoplasms of lung, thyroid, pancreas, stomach and colon.[3] Endometrial morular metaplasia has also been described in normal endometrium and other benign lesion like submucosal myoma, chronic endometritis, lesions resulting from prolonged use of intrauterine contraceptives, radiation and endometrial hyperplasia without atypia.[4,5] With extensive literature search we found that endometrial polyp with morular metaplasia has been seldom reported and may lead to diagnostic dilemma.

2. Case Presentation

A 39-year-old female presented with abnormal uterine bleeding. On ultrasound examination the possibility of benign endometrial polyp was suggested. Hysteroscopic polypectomy was done and the sample was sent to our

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laboratory. On gross examination the polyp was well defined with smooth borders, and the cut section was homogenous tan white. The polyp was processed entirely and slides were stained with Hematoxylin and Eosin. On microscopic examination the polyp was lined by columnar epithelium of three sides.

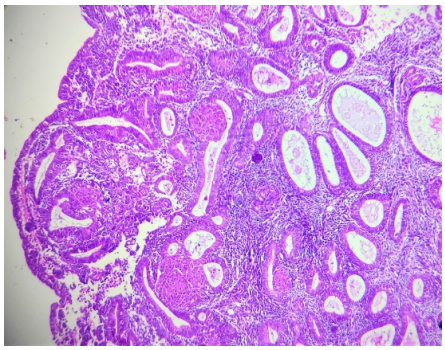

Fig. 1: Endometrial polyp with dilated glands with morular metaplasia and clustering vessels (HE x100).

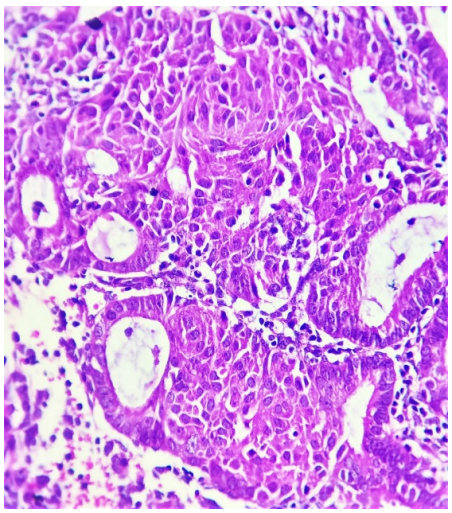

Fig. 2: Endometrial glands with morular metaplasia (HE x400).

There were numerous cystically dilated glands [Figure 1]. Glands were lined by cuboidal to columnar epithelium with some eosinophilic debris in the lumen [Figures 1, 2, 3, 4 and 5]. Numerous glands showed presence of intra-glandular morules, there was abrupt transition from columnar epithelium to a peculiar circumscribed proliferation of oval to spindle shaped cells [Figures 2, 3, 4 and 5]. These cells had indistinct cell borders, moderate amounts of dense eosinophilic cytoplasm. The nuclei were ovoid and bland. There was no evidence of mitotic activity in the morules. The stroma was dense and showed numerous vessels. Features of endometritis or endometrial hyperplasia were not seen. There was no atypia/ dysplasia or malignancy in the sample

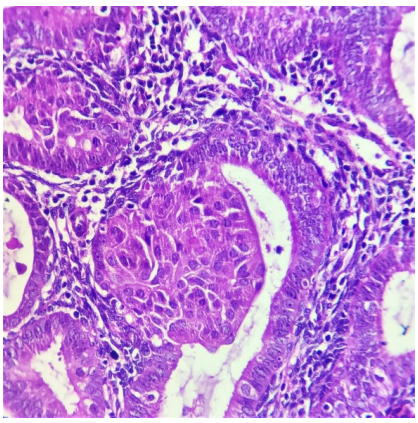

Fig. 3: Morular metaplasia in gland lumen, in continuity with the glandular columnar epithelium (HE x400).

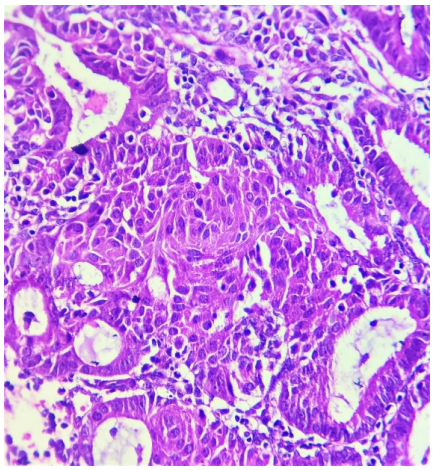

Fig. 4: Morular metaplasia, showing syncytial pattern of cells with bland nuclei (HE x400).

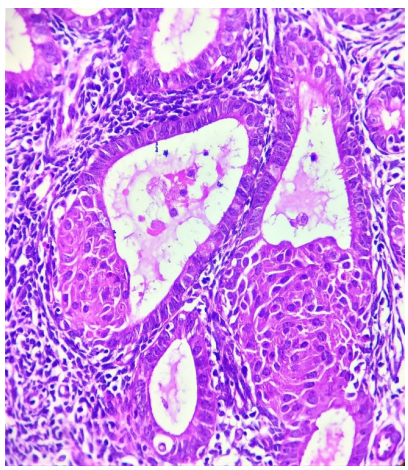

Fig. 5: Morular metaplasia in gland lumen, showing sharp demarcation of knob like morular structures from stroma (HE x400).

studied. The patient was followed up and did not show any recurrence.

3. Discussion

Most of the patients who showed endometrial morules were premenopausal, the current case also belongs to the same age group.[5] In a study by Chiarelli et al the morules were associated with endometrial hyperplasia with or without atypia, in various uterine and ovarian lesions such as atypical polypoid adenoma, polyps, ovarian adenofibroma, and endometrial carcinomas.[3] Our case showed an endometrial polyp with morular metaplasia and there was no evidence of atypia/ dysplasia or malignancy. The exact etiopathogenesis of morule formation remains unknown, however there might be role of aberrant levels of estrogen and progesterone.[5] Some studied have described that MM is an immature type of squamous metaplasia, while other consider it be a peculiar kind of non- squamous differentiation.[1]

Histopathological description of morular metaplasia was elaborated in detail by Dutra in 1959.[6] As per study, the cells of the morule originated from glandular epithelium.[6] In the beginning of the lesion, the glands may have an intact columnar cell lining and lumen shows projections of small rounded morule cells. These morules are separated from endometrial stroma by a basement membrane, similar to that of columnar cells.[6] These morules appear to have a 3-dimensional arrangement with whorls at places.[6]

All previous morphological studies have shown the differences between MM and classical squamous differentiation.[2] As per previous studies, electron microscopy findings, immunohistochemistry findings and molecular studies; the classical features of squamous differentiation are not seen in MM.[7]

Few studies have postulated MM might have differentiation towards hair matrix/ hair, on the basis of ghost cell keratinization and nuclear b-catenin accumulation.[8] Travaglino et al have also considered the possibility of relation of MM to odontogenic differentiation.[9] In their study they compared endometrioid carcinoma with MM to odontogenetic tumors and there was a histopathological and immunohistochemical overlap of MM with whorl-like formations of adamantinomatous craniopharyngiomas, which are similar to enamel knots of teeth development.[9] Houghton et al described that morules express diffuse nuclear positivity for intestinal transcription factor CDX2.[10] In a study by Kujdowicz the immunohistochemistry showed positivity for AE1/ AE3, HMWCK, EMA CD10, B-Catenin in glandular epithelium while ER and PR receptor were negative in morules and positive in glands.[2]

As per Chinen et al the morules in endometrial lesions do not have squamous differentiation and they are not infected by human papilloma virus like squamous epithelium of other areas.[4] They also found B-Catenin gene mutation in morules. B-Catenin mutation has been noted in similar morular structures in hair follicle tumor and lung tumors.[4] The morules of lung, thyroid and colon also have oncofetal expression of blood group antigens but it was not observed in endometrial morules.[4] The expression of neuropeptides was also not common in endometrial morules.[4]

Endometrial morular metaplasia is considered to an atypical response to hormones.[2] MM itself is a benign inert change; however due its association with endometrial endometrioid carcinoma and endometrial hyperplasia with atypia, careful examination of glandular component is mandatory.[11] It is also important to differentiate MM from solid areas of endometrioid carcinoma to avoid the upgrading of the tumor[2] and the benign cases should be examined meticulously to rule out any atypical changes elsewhere.

4. Conclusion

Endometrial polyp is benign and a very common entity, however the presence of morular metaplasia has not been described in previous studies. The presence of morules may cause a diagnostic dilemma if meticulous histopathological examination is not done. The syncytial sheets of morules might appear as solid areas of endometrial neoplasms. The bland appearance of morular cells and presence of intact basement membrane are important distinguishing factors. These are usually associated with atypical glandular lesion, hence the finding of extensive morular metaplasia without any epithelial abnormality should be carefully examined and the patient requires regular close follow up.

5. Conflicts of interest

There are no conflicts of interest.

6. Source of Funding

None.

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