Images in Medicine

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# Unveiling Morular Metaplasia of Endometrium: A Pathological Enigma

Pathology Section

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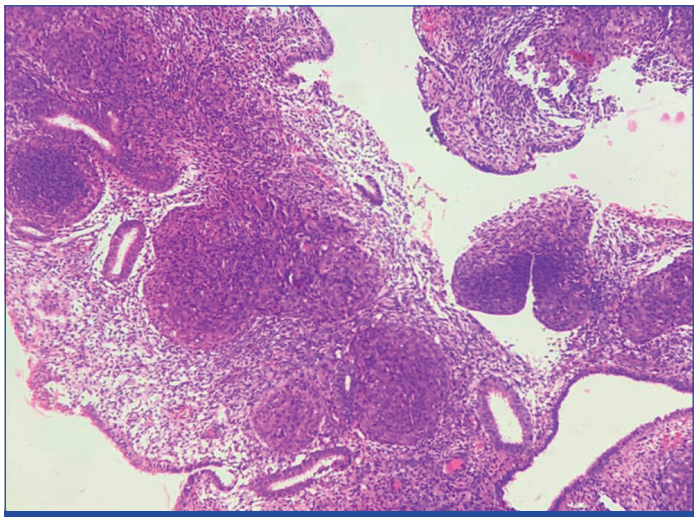
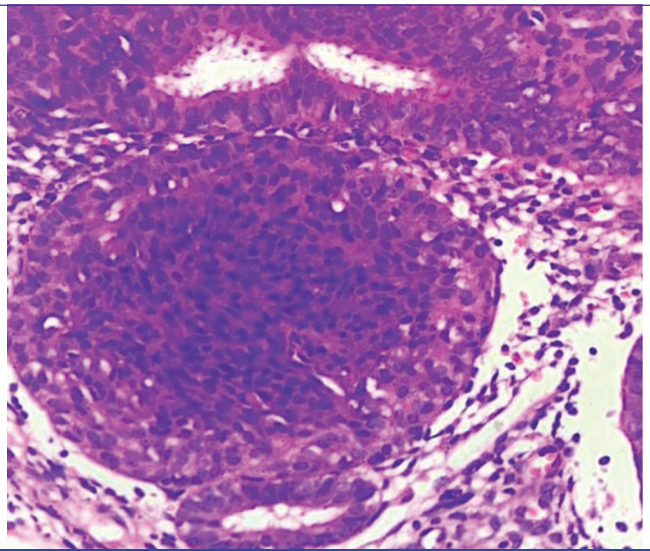
A 46-year-old female came to the Gynaecology Outpatient Department (OPD) with complaints of amenorrhoea for one month associated with abdominal pain on and off. Ultrasonography revealed multiple well-defined heteroechoic lesions with largest measuring 1×1 cm, uterus measuring 9×6.2×4.5 cm and endometrial thickness 8 mm. A clinical diagnosis of uterine fibroids was made. Following this, endometrial curettage was done and sent for histopathological examination. Microscopy showed fragments of endometrial tissue with glands in disordered proliferative pattern and stroma showed extensive morules of squamous metaplasia [Table/Fig-1]. The morules consisted of round and spindle cells. Cells of the morules showed no atypia [Table/Fig-2]. There were no endometrial hyperplasia or malignancy in the specimen received.



**[Table/Fig-1]:** Photomicrograph showing fragments of endometrium with glands in disordered proliferative pattern and extensive squamous morules (H&E, 100x).



**[Table/Fig-2]:** Photomicrograph showing squamous morules composed of round to spindle cells without atypia (H&E, 400x).

Morular Metaplasia (MM) is an unusual metaplastic change that is rarely seen in endometrial lesions, and is characterised by the absence of obvious squamous characteristics and a distinct immunophenotype [1]. The majority of premenopausal women exhibit morules. This is most typically encountered in hyperplastic endometrium but can also be seen in association with leiomyoma or uterine cysts [2]. The term "morula," which was first used in 1959 by Dutra, describes the histological similarity between this type of endometrial metaplasia and a mulberry [3,4]. Morules are round in shape, consisting of spindle- or round-shaped cells arranged regularly and well-circumscribed; these cells have eosinophilic cytoplasm and inactive uniform nuclei without prominent nucleoli [3]. It seldom demonstrates keratinisation, mitoses and central necrosis. They are cytologically bland but can obscure examination of the normal glandular framework of endometrium. Morular borders are not well-defined. This change is distinguished from well-differentiated endometrioid adenocarcinoma with squamous metaplasia because of the benign appearance of the glandular structures, without glandular crowding or atypia [2]. The morules represent a functionally inert tissue, in the sense of being devoid of sex hormone receptors and having an extremely low proliferation rate [5]. They are immunoreactive for the intestinal transcription factor Caudal Type Homeobox 2 (CDX2) [2]. The endometrium in the present instance was proliferative and normal. Although the exact cause of morular development is unknown, progesterone and oestrogen may play a role. Adenoacanthoma and endometrium with MM need to be distinguished from one another. Since there was no atypia in the endometrial glands, the present case was not adenoacanthoma [6,7]. According to studies conducted by Litta P et al., the formation of morules is secondary to a mutation in the beta-catenin gene (CTNNB1) [3]. Since beta-catenin is thought to be a transcriptional activator of the Wingless-related Integration Site (WNT) signaling pathway, which encourages cell division and proliferation, CTNNB1 is regarded as a protooncogene. When this gene changed, beta catenin was abnormally localised within nuclei as opposed to where it normally is on the cell membrane. Since these morules usually show higher nuclear beta-catenin antibody, Immunohistochemistry (IHC) is particularly helpful. From a prognostic perspective, then, the beta-catenin mutation and the creation of morular formation may be the beginning of a continuum of oncogenic pathway leading to low grade endometrial cancer, which has a greater recurrence rate and necessitates close monitoring, if not early surgical intervention [8].

As an uncommon, benign, and hormonally inactive condition, MM is almost always linked to premalignant or malignant endometrial glandular proliferations, which can result in low-risk endometrial carcinomas. Because Endometrial MM (EMM) is uncommon, developing treatment routes has never been simple. As a result, management options range from conservative measures to hormone therapy and surgical excision, depending on the patient's condition and the woman's preference [8]. Therefore, it is a diagnostic challenge for the pathologists to rule out malignancy.

The conservative suitable for those needs uterine preservation for fertility needs or unsuitable for major pelvic surgery. They are managed by repeated endometrial sampling or hysteroscopy. Major pelvic surgery is not appropriate for patients with glandular subtypes of EMM; instead, hormonal treatment is suggested. Surgical hysterectomy is appropriate for people with squamous subtypes of EMM, menopausal women, women who have finished having children, women who have a significant family history of endometrial cancer, women who have associated endometrial hyperplasia, or women for other gynaecological reasons that require a hysterectomy in order to avoid repeat endometrial sampling [8].

The EMM is an uncommon, benign, proliferative, hormone-inert disease that can lead to both precancerous and malignant neoplastic alterations [8]. The gold standard study for these patients is a histopathological examination, and careful monitoring is necessary to prevent unnecessary hysterectomies [3]. Utilising recent developments in molecular biology, IHC technologies can facilitate clinical treatment by streamlining and improving the diagnostic and prognostication procedures [8].

## REFERENCES


[1] Travaglino A, Raffone A, Saccone G, Migliorini S, Maruotti GM, Esposito G, Mollo A, Martinelli P, Zullo F, D'Armiento M. Placental morphology, apoptosis, angiogenesis and epithelial mechanisms in early-onset preeclampsia. European Journal of Obstetrics & Gynecology and Reproductive Biology. 2019;234:200-6.

[2] Goldblum JR, Lamps LW, McKenney JK. Rosai and Ackerman's Surgical Pathology E-Book. Elsevier Health Sciences; 2017 Oct 25.

[3] Litta P, Codroma A, D'Agostino G, Breda E. Morular endometrial metaplasia: review of the literature and proposal of the management. European Journal of Gynaecological Oncology. 2013;34(3):243-47.

[4] Dutra FR. Intraglandular morules of the endometrium. American Journal of Clinical Pathology. 1959;31(1):60-65.

[5] Miranda MC, Mazur MT. Endometrial squamous metaplasia. An unusual response to progestin therapy of hyperplasia. Archives of pathology & laboratory medicine. 1995;119(5):458-60.

[6] Blaustein A. Morular metaplasia misdiagnosed as adenoacanthoma in young women with polycystic ovarian disease. Am J Surg Pathol. 1982;6:223-28.

[7] Terada T. Extensive squamous metaplasia (morules) of the otherwise normal endometrium: a case report with immunohistochemical studies. Int J Clin Exp Pathol. 2013;6(3):543-45. Epub 2013 Feb 15. PMID: 23413394; PMCID: PMC3563190.

[8] Kotigala DSK,Adedipe TO. Morular Metaplasia of the Endometrium: A Case Report and Literature Review: Care Pathways based on Molecular Biology. Clin J Obstet Gynecol. 2024;7:059-63.



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