

Letter to Editor

Extensive squamous metaplasia (morules) of the otherwise normal endometrium: a case report with immunohistochemical studies

Tadashi Terada

Departments of Pathology, Shizuoka City Shimizu Hospital, Shizuoka, Japan

Received October 2, 2012; Accepted December 17, 2012; Epub February 15, 2013; Published March 1, 2013

Squamous (morules) metaplasia of the endometrium is usually seen in endometrial hyperplasia and endometrial carcinoma [1]. Morular metaplasia of normal endometrium is very rare. In addition, immunohistochemical studies of the morules of the endometrium have not been performed [2-5].

A 32-year-old woman consulted to our hospital because of abnormal uterine bleeding. Various imaging modalities showed endometrial thickening. The clinical diagnosis was suspected endometrial carcinoma. The endometrial curettage biopsy was performed.

The biopsy shows numerous morulus (**Figure 1A**). The morules consisted of round and spindle cells. Central necrosis (comedo necrosis) was scattered. Cells of the morules were free from atypia (**Figure 1B**). The endometrium is normal proliferative phase in which buds of small morules were scattered (**Figure 1C**). No apparent endometrial hyperplasia was seen. No malignancy was recognized.

An immunohistochemical study was performed with the use of Dako's EnVision method, as previously described [6, 7]. The results are shown in **Table 1**. The morules were positive for pancytokeratins (AE1/3 and CAM5.2), cytokeratin (CK) 34BE12, CK5/6, CK8, CK19, Ki-67 (labeling=1%) and p63, but were negative for CK7, CK14, CK20, p53, vimentin, CA125, S100 protein, desmin, CEA, α -smooth muscle antigen (ASMA), EMA, CD34, estrogen receptor (ER), and progesterone receptor (PgR). In contrast,

the endometrial glands were positive for pancytokeratin (AE1/3 and CAM5.2), CK7, CK8, CK18, CK19, p53, Ki-67 (labeling=7%), p63, CA125, EMA, ER and PgR, but were negative for CK34BE12, CK5/6, CK14, CK20, vimentin, S100 protein, desmin, CEA, ASMA, and CD34.

Morules are mostly seen in the premenopausal women [1-5]. The current case is a 32-year-old woman. Morules are mainly associated with endometrial hyperplasia and endometrial carcinoma [1-5]. The current case showed normal endometrium. The etiology of morule formation is unclear, but estrogen and progesterone may be responsible for morule formation [1]. Endometrium with morular metaplasia must be differentiated from adenoacanthoma [4]. The present case is not adenoacanthoma because endometrial glands lacked significant atypia. Clinical features of endometrial morules are not clear. In the present case, the clinical features are abnormal uterine bleeding and endometrial thickening. The clinical diagnosis was suspected endometrial carcinoma. Thus, extensive morule formation may clinically simulate endometrial carcinoma.

Immunohistochemical study of endometrial morular metaplasia has not been performed. The present study revealed CK profile of the morules. The morules showed a wide range of CK expression, indicating that morules have high and low molecular weight CKs. In contrast, endometrial glands had low molecular weight CKs. P53 was negative in morules, while it was positive in endometrial glands. This suggests

Numerous morules in the endometrium

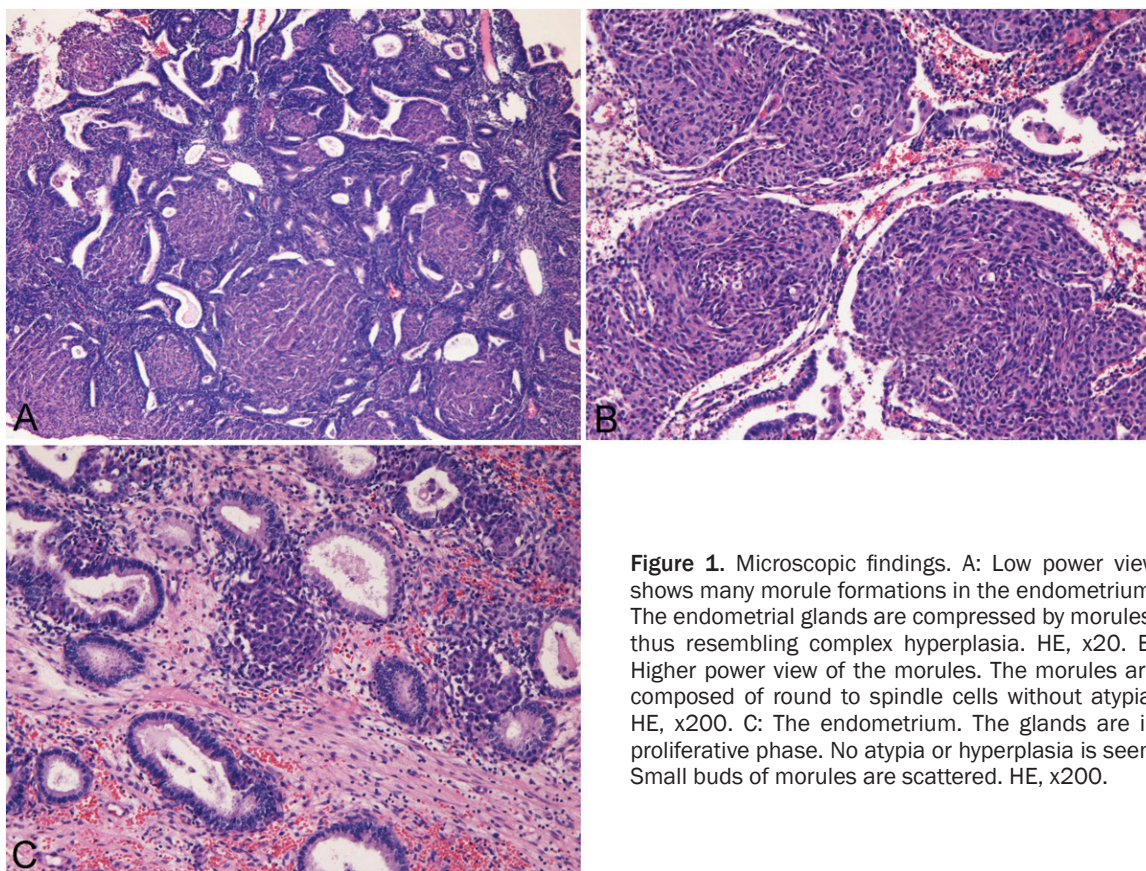


Figure 1. Microscopic findings. A: Low power view shows many morule formations in the endometrium. The endometrial glands are compressed by morules, thus resembling complex hyperplasia. HE, x20. B: Higher power view of the morules. The morules are composed of round to spindle cells without atypia. HE, x200. C: The endometrium. The glands are in proliferative phase. No atypia or hyperplasia is seen. Small buds of morules are scattered. HE, x200.

Table 1. Immunohistochemical findings

| | Morules | Glands |
|-----------|---------|--------|
| CK AE1/3 | +++ | +++ |
| CK CAM5.2 | +++ | +++ |
| 34BE12 | ++ | - |
| CK5/6 | ++ | - |
| CK7 | - | + |
| CK8 | + | + |
| CK14 | - | - |
| CK18 | +++ | +++ |
| CK19 | ++ | ++ |
| CK20 | - | - |
| P53 | - | + |
| Ki67 | 1% | 7% |
| P63 | + | + |
| Vimentin | - | - |
| CA125 | - | + |
| S100 | - | - |
| Desmin | - | - |
| CEA | - | - |
| ASMA | - | - |
| EMA | - | + |
| CD34 | - | - |
| ER | - | +++ |
| PgR | - | +++ |

CK: cytokeratin. ASMA: alpha-smooth muscle actin. EMA: epithelial Membrane antigen. ER: estrogen receptor. PgR: progesterone receptor.

that the morules are free from activation of this anti-oncogene. Ki-67 labeling (1%) in morules was very low, indicating that the morules show little proliferative activity. P63 was positive in morules, suggesting that morules show some features of squamous epithelium. ER and PgR were negative for morules while they were positive in the endometrial glands, suggesting that morules are not influenced by estrogen and progesterone. CA125 and EMA were negative in morules while they were positive in endometrial glands, indicating that morules are different from endometrial glands. Mesenchymal antigens were negative in both morules and endometrial glands.

In conclusion, the author reported a case of extensive morular metaplasia of the endometrium in a 32-year-old woman. Immunohistochemical studies were also performed.

Conflict of interest statement

The author has no conflict of interest.

Address correspondence to: Dr. Tadashi Terada, Department of Pathology, Shizuoka City Shimizu

Numerous morules in the endometrium

Hospital, Miyakami 1231 Shimizu-Ku, Shizuoka 424-8636, Japan. Tel: +81-54-336-1111; Fax: +81-54-334-1173; E-mail: piyo0111jp@yahoo.co.jp

References

- [1] Rosai J. Metaplasia of endometrium. In Rosai J ed. Rosai and Ackermann's Surgical Pathology. Volume 2, Ninth Edition. Mosby, New York 2004, pp: 1675-1577.
- [2] Dutra FR. Intraglandular morules of the endometrium. *Am J Clin Pathol* 1959; 31: 60-65.
- [3] Crum CP, Richart RM, Fenoglio CM. Adenoacanthosis of endometrium: a clinicopathologic study in premenopausal women. *Am J Surg Pathol* 1981; 5: 15-20.
- [4] Blaustein A. Morular metaplasia misdiagnosed as adenoacanthoma in young women with polycystic ovarian disease. *Am J Surg Pathol* 1982; 6: 223-228.
- [5] Miranda MC, Mazur MT. Endometrial squamous metaplasia: an unusual responses to progestin therapy of hyperplasia. *Arch Pathol Lab Med* 1995; 119: 458-460.
- [6] Terada T, Kawaguchi M, Furukawa K, Sekido Y, Osamura Y. Minute mixed ductal-endocrine carcinoma of the pancreas with predominant intraductal growth. *Pathol Int* 2002; 52: 740-746.
- [7] Terada T, Kawaguchi M. Primary clear cell adenocarcinoma of the peritoneum. *Tohoku J Exp Med* 2005; 206: 271-275.