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# Evidence of adenomyosis in fetuses: Another emerging piece in resolving the endometriosis puzzle

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## BACKGROUND

Endometriosis affects approximately 10% of the female population in their reproductive years and represents one of the most common human diseases. The most widely accepted theory of origin is Sampson's theory of reflux menstruation. Sampson's classification of heterotopic endometrial tissue is based on pathogenesis :

1) "direct or primary endometriosis" [adenomyosis];
2) "peritoneal or implantation endometriosis";
3) "transplantation endometriosis";
4) "metastatic endometriosis";
5) "developmentally misplaced endometrial tissue".

## METHODS

In order to test the hypothesis of congenital adenomyosis ("developmentally misplaced endometrial tissue"), we designed a prospective study of uteri in fetuses terminated spontaneously or for lethal malformations. Histology with systematic serial sections were performed in 420 fetal uteri.

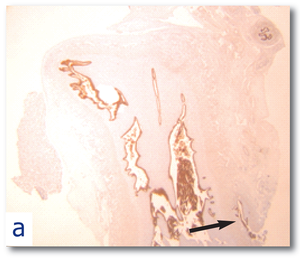
## FINDINGS

Adenomyosis was observed in a total of 10 (2,4%) fetuses aged from 19 to 37 weeks. There was no increase in the threshold toward adenomyosis in the fetuses presenting malformations of the uro-genital system.

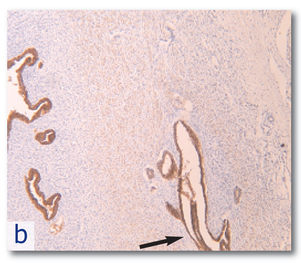
## INTERPRETATION

These data suggest that adenomyosis might be present from the fetal stage, with possible genetic backgrounds in some cases. Furthermore, our results enhance a novel etiopathogenetic concept of adenomyosis as a developmental defect of differentiation or migration of the mullerian duct system during embryogenesis.

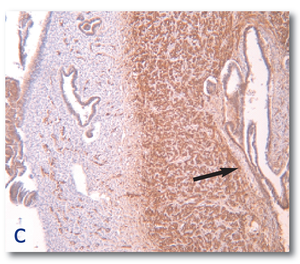
**Fig.1: Histological appearance of uterus in patient 5 (24 weeks).**




**a**: (EMA): presence of endometrial EMA + nests in the myometrium close to the posterior wall of the uterus.

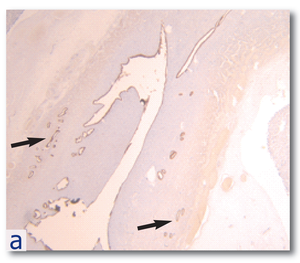



**b**: (EMA): ectopic endometrial cells at higher magnification

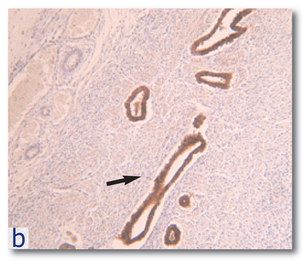



**c**: (SMA): strong actin positivity in the surrounding mesenchyme. Original magnification, X1,6 (a), X10 (b), X20 (c).

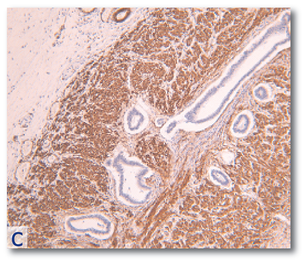
**Fig.2: Histological and immunohistological appearance of uterus in patient 9 (26,5 weeks).**



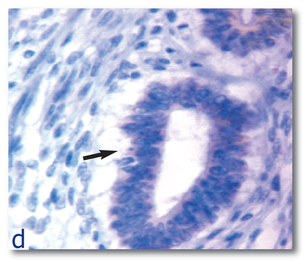

**a:** (EMA): presence of multiple ectopic endometrial EMA+ foci in the myometrium close to the posterior wall on both sides of the uterus.




**b:** (EMA): closer view to the ectopic epithelium strongly labelled by EMA.




**c:** (SMA): actin positivity in the surrounding mesenchyme.



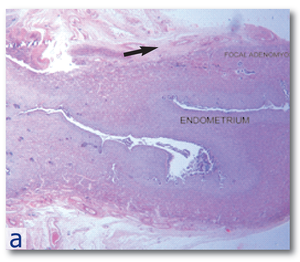

**d:** (RA): strong labelling of epithelial cells. Original magnification, X1,6 (a), X10 (b, c), X20 (d).

**Table 1: Clinical features of the 10 patients presenting focal adenomyosis**

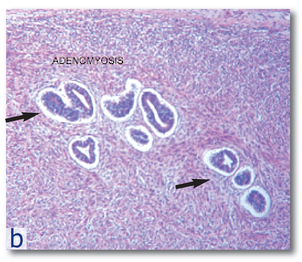
| PATIENT | GEST. AGE (wg) | IUFD/TOP | CARYOTYPE | CLINICAL FINDINGS | G/P |
|---|---|---|---|---|---|
| 1 | 19 | TOP | Trisomy 18 | Growth retardation, Facial dysmorphia, Camptodactyly | G1 |
| 2 | 25 | TOP | Normal | Bilateral renal agenesis | G1 |
| 3 | 18 | TOP | Normal | Osteogenesis imperfecta | G2P0 |
| 4 | 37.4 | Neonatal demise | Normal | Congenital Diaphragmatic Hernia | Non documented |
| 5 | 24 | TOP | Normal | Fetal Akinesia Deformation Sequence | G1 |
| 6 | 34 | TOP | Normal | Cerebral anomalies | G5P0 |
| 7 | 27 | IUFD | Normal | Pierre Robin, Adactyly / Syndactyly | G1 |
| 8 | 25.2 | IUFD | Non performed | Placental vascular pathology | G4P3 |
| 9 | 26.5 | TOP | Normal | Heart malformation, Clefting | G1 |
| 10 | 24 | TOP | Normal | Cerebral anomalies | G1 |

Legend: **IUFD**: in utero fetal demise, **TOP**: termination of pregnancy, **wg** : weeks of gestation, **G/P** : gestity/parity

**Fig.3: Histology of uterus in patient 2 (25 weeks).**




**a**: (H&E): presence of ectopic endometrial focus in the myometrium close to the posterior wall of the uterus.




**b**: (H&E): closer view with typical glandular appearence of adenomyotic foci. Original magnification, X1,6 (a), X20 (b).

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