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The concept of invasion in deep nodular endometriosis.

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Context
Deep nodular endometriosis is a complex and widespread pathology. However, its origin and progression have not yet been elucidated. Therefore, our laboratory created the first deep nodular endometriosis model in baboons. The model was found to efficiently recreate the pathology, showing nerve development, with glands and stromal cells invading adjacent organs. These invasive glands express a characteristic phenotype that resembles the collective cell migration process observed in some cancer types.
Objective
To study the mechanisms of invasion and innervation of human deep nodular endometriosis.
Methods
Morphological and immunohistochemical (IHC) analyses of human deep endometriotic biopsies (N=17).
Patients
Biopsies of endometriotic lesions were collected from patients undergoing surgery for deep nodular endometriosis.
Interventions
Human deep endometriotic samples were divided into two fragments: the most invasive area of the lesion colonizing the bowel (front) and less invasive area facing the posterior wall of the cervix (center).
Main outcome measures
Comparison of the collective cell migration markers between the center and front: IHC analysis for E-cadherin, ?-catenin (tight junction proteins) and Ki67 (mitotic activity); and morphological analysis (gland thickness). Nerve fiber density (NFD) in the lesions was also compared between center and front by IHC for the nerve growth factor (NGF) and the protein gene product 9.5 (PGP9.5).
Results
Glands in the front showed significantly reduced thickness and higher mitotic activity compared to glands in the center. Indeed, a significant correlation was found between gland thickness and mitotic activity (P< .0001; r= -0.82211). No difference was detected between the glands in the front and those in the center for the tight junction protein ?-catenin. The E-cadherin immunostaining intensity score was found to be significantly lower in the glands of the front.
NGF expression of epithelial and stromal cells was found to be significantly higher in the front than in the center of the lesions and a significantly higher NFD was encountered in the front.
Conclusion
The invasive process of human deep nodular endometriosis lesions displays similarities with the collective cell migration process, as observed in the baboon model. Our result also suggests that nerve

fibers may play a role in the development of lesions. This study contributes to better understand the mechanism of invasion in deep endometriosis.

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