CD10 Is Helpful in Detecting Occult or Inconspicuous Endometrial Stromal Cells in Cases of Presumptive Endometriosis

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Background.—Previous studies have shown that CD10 is a marker for normal, ectopic, and neoplastic endometrial stromal cells. However, its value in confirming a diagnosis of presumptive endometriosis has not been extensively studied.

Objective.—To assess the reactivity of CD10 in a series of cases of presumptive endometriosis and to establish the potential usefulness of this antibody in confirming the diagnosis.

Design.—We studied hematoxylin-eosin sections and immunoreactivity of CD10 in 20 cases diagnosed as “suspicious for,” “suggestive of,” or “compatible with” endometriosis as well as in 12 cases of lesions that may be confused with endometriosis (3 endosalpingioses, 3 mesothelial hyperplasias, 3 ovarian follicular cysts, and 3 hemorrhagic corpora lutea).

Results.—Routine sections from cases of presumptive endometriosis showed glands lacking a distinct cuff of endometrial stromal cells because of atrophy or because of changes secondary to hemorrhage, inflammation, fibrosis, and/or cystic dilatation. In a few cases, the distinction between endometrial and ovarian stroma could not be assessed with certainty. CD10 immunostaining confirmed the diagnosis in 17 (85%) of the cases, as it strongly stained endometrial stromal cells that were not apparent on hematoxylin-eosin sections. All sections from lesions that may simulate endometriosis were CD10−.

Conclusion.—CD10 is helpful in detecting occult or inconspicuous ectopic endometrial stromal cells and in distinguishing endometriosis from its potential mimickers. We recommend its use to confirm or exclude the presence of endometrial stromal cells in cases of presumptive endometriosis and in lesions that may be mistaken for this entity.

CD10, also known as enkephalinase, is a human membrane-associated neutral peptidase widely used in lymphoma phenotyping. In addition, it has been shown to stain normal, ectopic, and neoplastic endometrial stromal cells. CD10 immunostaining in endometriosis has been previously evaluated in 2 studies, which mostly included cases of typical endometriosis. To our knowledge, this is the first series to be exclusively composed of cases in which the diagnosis of endometriosis was not conclusive on hematoxylin-eosin sections. Our purpose was to evaluate the potential utility of CD10 in identifying occult endometrial stromal cells in cases of presumptive endometriosis and in distinguishing endometriosis from its potential mimickers.

MATERIALS AND METHODS

Patients, Specimens, and Tissue Preparation

Twenty cases diagnosed between 1995 and 2002 as “suspicious for,” “suggestive of,” or “compatible with” endometriosis were retrieved from the surgical pathology files of the Hillel Yaffe Medical Center (Hadera, Israel). The original slides were reviewed, and the diagnosis was confirmed. Clinical data and macroscopic details were obtained from the surgical pathology reports. They included 10 cases from the ovary, 5 cases from the tubal peritoneum, 2 cases from cesarean section scars, and 1 case from each of the following locations: the broad ligament, the rectovaginal septum, and the umbilical skin. For comparison, we examined representative sections from 12 cases of lesions that may be misdiagnosed as endometriosis: 3 of endosalpingiosis, 3...
of mesothelial hyperplasia, 3 of ovarian follicular cysts, and 3 of hemorrhagic corpora lutea. All the specimens were fixed in formalin and embedded in paraffin. Further 4-μm-thick sections were stained for CD10 immunohistochemistry.

**Immunostaining With CD10 and Pathologic Evaluation**

Sections were placed on positively charged glass slides, deparaffinized, and subjected to high-temperature antigen unmasking with an electric pressure cooker set at 120 degrees for 5 minutes. Endogenous peroxidase activity was quenched with hydrogen peroxide. Detection for the binding of CD10 (clone 56C6, dilution 1:20; Novocastra, Newcastle upon Tyne, United Kingdom) was achieved by a labeled streptavidin-biotin peroxidase complex method (Zymed Histostain Plus Kit, Zymed Laboratories, South San Francisco, Calif). The formed complexes were visualized with aminoethyl carbazole chromogen/substrate. Sections were then counterstained with hematoxylin, dehydrated, cleared, and permanently mounted. Slides with normal endometrium represented positive controls. Negative controls were performed without the primary antibody. All sections were evaluated by one of us (G.M.G.). CD10 immunostaining was recorded as negative, weakly positive, and strongly positive.

**RESULTS**

Hematoxylin-eosin sections showed glands lined with an endometrial, Müllerian, or flattened epithelium, lacking a well-defined cuff of endometrial stromal cells (Figure 1, A) or cysts, sometimes lacking an epithelial lining, surrounded by numerous macrophages and inflammatory cells without evident endometrial stromal cells (Figure 2, A). In some ovarian cases, when glandular structures lay next to fascicles of ovarian stromal cells, it was difficult to assess whether small amounts of endometrial stromal cells were also present (Figure 3, A).

CD10 immunostaining showed endometrial stromal cells that remained unnoticed on hematoxylin-eosin sections in 17 of the cases. The staining was cytoplasmic, strong, and diffuse. The reactive cells formed thin cuffs around glands (Figure 1, B) or were scattered among macrophages and inflammatory cells (Figure 2, B). In cases of ovarian endometriosis, CD10 helped distinguish positive endometrial stromal cells from negative ovarian stromal cells (Figure 3, B). No reactivity was observed in endometrial glands or in other tissues. In 3 cases (1 from the broad ligament, 1 from the rectovaginal septum, and 1 from the ovary), no CD10-reactive cells were present. All sections from lesions that may be confused with endometriosis were CD10− (Figures 4 and 5).

**COMMENT**

In this study, CD10 immunostaining helped confirm the diagnosis in 17 of 20 cases of presumptive endometriosis. CD10 is a human 100-kd membrane-associated neutral endopeptidase, also known as enkephalinase or nephrilysin, which is identical to the common acute lymphoblastic lymphoma antigen. First regarded as a marker of acute
lymphoblastic leukemia, it was subsequently identified in a variety of lymphoid and nonlymphoid malignancies. The major clinicopathologic application of CD10 immunoreactivity has been in the diagnosis of precursor B-cell leukemia, follicular lymphoma, and Burkitt lymphoma. In addition, it has been proven that CD10 has a wide distribution on the surfaces of various normal cell types and that it may play specific roles in the control of cell growth and differentiation in both hemopoietic and epithelial systems. CD10 is normally expressed on the bile canalicular surface of hepatocytes and is useful for identifying hepatocellular carcinoma. Likewise, surface membrane staining with CD10 may be used to confirm a diagnosis of suspected clear cell or papillary renal carcinoma. In normal small bowel enterocytes, CD10 stains the brush border, whereas an abnormal cytoplasmic staining pattern is diagnostic of microvillous inclusion disease. CD10 functions as a cell surface peptidase that regulates the biologic activity of peptide substrates such as peptide hormones by reducing the local concentrations and their corresponding neoplasms express CD10 antigen, including normal, ectopic, and neoplastic endometrial stromal cells.

CD10 has been shown to be a reliable marker of endometrial stromal differentiation. Imai et al. were the first to report CD10 expression in endometrial stromal cells, which included endometriosis and adenomyosis. However, they used the indirect immunofluorescence technique. Recently, a CD10 monoclonal antibody (clone 56C6) became commercially available for paraffin immunohistochemistry, allowing further investigation of this topic. Chu and Arber studied CD10 expression in a large variety of normal and neoplastic tissues and found reactivity in normal endometrial stromal cells and in 5 of 5 cases of endometrial stromal sarcoma (ESS). These findings were confirmed in 2 studies in which strong and diffuse CD10 immunoreactivity was found in normal endometrial stroma and in 100% of low-grade ESSs and in 77% of high-grade ESSs. In both studies, focal and weak CD10 reactivity was also reported in 30% to 66% of uterine leiomyomas and in 60% of uterine leiomyosarcomas. A few other reports that evaluated antibody panels including CD10 and diverse smooth muscle markers found strong and diffuse CD10 reactivity in 90% to 100% of low-grade and high-grade ESSs but also focal and weak CD10 expression in 10% to 40% of cellular leiomyomas and in 90% of leiomyosarcomas. Conversely, smooth muscle markers such as actin, desmin, caldesmon, calponin, and smooth muscle myosin heavy-chain stain were reported to stain 28% to 70% of ESSs. The shared conclusion was that dependence on the results of staining for a single antibody can be unreliable and that CD10 is helpful in distinguishing ESSs from smooth muscle tumors when used in conjunction with smooth muscle markers. The immunophenotypic overlap between endometrial stromal and smooth muscle uterine tumors is explained by their common embryologic derivation from the Müllerian duct. Endometrial stromal cells have been reported to have myofibroblastic properties and a potential to differentiate into smooth muscle cells.

Following the original report by Imai et al., only 2 studies evaluated CD10 expression in endometriosis. Toki et al. and Sumathi and McCluggage reported strong and diffuse CD10 reactivity in stromal cells from 21 of 21 and 22 of 25 cases of endometriosis, respectively. The former study included only cases of typical endometriosis. In the series of Sumathi and McCluggage, 3 of the cases were presumptive endometriosis, but no specific results or documentation regarding these cases was provided. Our study included only cases of presumptive endometriosis in which stromal cells could not be clearly identified on hematoxylin-eosin sections. CD10 immunostaining helped confirm the diagnosis in 17 of 20 cases (85%).

Figure 4. A, This figure shows several Müllerian-type glands. The appearance is compatible with endosalpingiosis (hematoxylin-eosin, original magnification ×200). B, The diagnosis of endometriosis is excluded, as no CD10+ cells are identified around the glands (immunohistochemistry, original magnification ×100).

Figure 5. A, This figure shows the wall of a hemorrhagic ovarian cyst. A resolving corpus luteum was seen in other sections (hematoxylin-eosin, original magnification ×100). B, The CD10 stain is negative, excluding the diagnosis of endometriosis (immunohistochemistry, original magnification ×100).
tential mimickers. It should be remembered, however, that CD10 is not specific for endometrial stromal cells and that, as discussed previously, it can be expressed by a wide variety of normal and pathologic cells and tissues. Therefore, the findings should be carefully interpreted in the context of the overall clinicopathologic picture to avoid confusion or misdiagnosis.

We conclude that CD10 is helpful in detecting occult or inconspicuous ectopic endometrial stromal cells and in distinguishing endometriosis from its potential mimickers. We recommend its use to confirm or exclude the diagnosis in cases of presumptive endometriosis and in lesions that may be mistaken for this entity.

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References