

**Original contribution****Relationship between eosinophils and chronic endometritis**Patrick A. Adegboyega MD<sup>a,b,\*</sup>, Ying Pei MD<sup>a</sup>, Jerry McLarty PhD<sup>b</sup><sup>a</sup>Department of Pathology, Louisiana State University Health Science Center, Shreveport, LA 71130, USA<sup>b</sup>Feist Weiller Cancer Center, Louisiana State University Health Science Center, Shreveport, LA 71130, USA

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**Summary** The histopathologic diagnosis of chronic endometritis is based on the presence of plasma cells in the endometrial stroma. However, many conditions can mimic or interfere with the search for plasma cells, including the plasmacytoid stroma cells and predecidual changes of stroma cells. Eosinophils are another type of chronic inflammatory cells, which can be easily identified with routine hematoxylin and eosin stain by their characteristic eosinophilic granules. This study was conducted to investigate whether eosinophils can be used as diagnostic markers of chronic endometritis. The hematoxylin and eosin-stained glass slides of 422 consecutive endometrial biopsies were reviewed. The biopsies that have eosinophils were subjected to immunohistochemical staining with CD138, a marker for plasma cells. In all, 91 of 422 biopsies contained eosinophils with 72.5% (66/91) showing presence of plasma cells (positive staining with CD138). Of these 66 cases, only 4 cases were previously diagnosed as chronic endometritis. These results suggest the presence of eosinophils in endometrial biopsy specimen indicates a need to search for plasma cells (with immunohistochemical stain if needed) for the diagnosis of chronic endometritis.

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**1. Introduction**

Chronic endometritis is a persistent inflammation of the endometrium. Previous studies have indicated that chronic endometritis is diagnosed in between 3% and 10% of women who undergo endometrial biopsy for abnormal uterine bleeding [1]. Histologically, the diagnosis of chronic endometritis is based on the presence of plasma cells in the endometrial stroma [1]. However, many conditions can mimic or interfere with the search for plasma cells, including the plasmacytoid stromal cells and predecidual changes of stromal cells. Efforts to resolve this diagnostic difficulty have resulted in the use of ancillary diagnostic techniques

such as methyl green pyronin histochemical stain [2,3], immunohistochemical staining for immunoglobulin G [4], or syndecan [1], and in situ hybridization for  $\kappa$  and  $\lambda$  light chains [5]. Eosinophils are another type of chronic inflammatory cells, which can be easily identified with routine hematoxylin and eosin (H&E) stain by their characteristic eosinophilic granules. Just like plasma cells, eosinophils are normally absent in the endometrium during most of the menstrual cycle except immediately before menstruation [6]. There is a dearth of information regarding the relationship between chronic endometritis and the presence of eosinophils in the endometrium. This study was initiated as a result of personal observation over the years that some women with clinical diagnosis of abnormal uterine bleeding and endometrial biopsy specimens previously reported normal did not improve with hormonal treatment; and repeat biopsies showed eosinophils and plasma cells. Therefore, this study was conducted to

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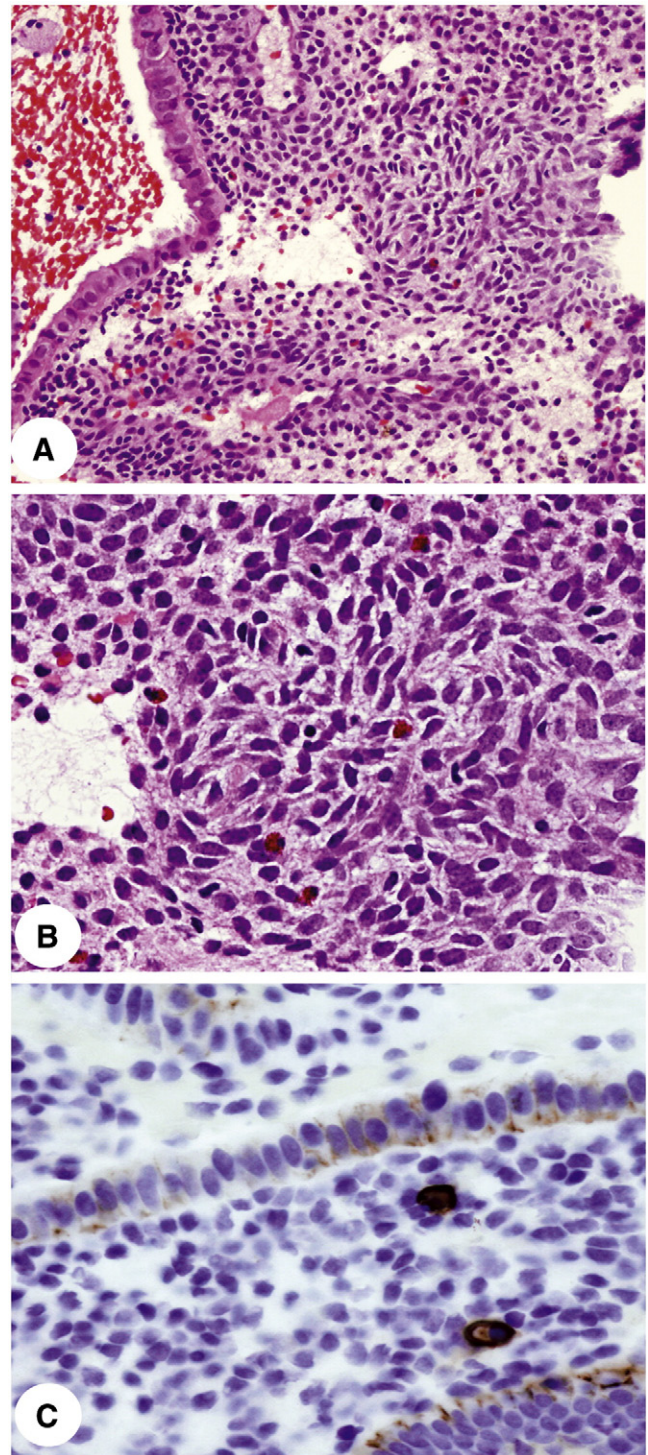
investigate whether eosinophils can be used as markers for chronic endometritis.

## 2. Material and methods

The H&E-stained glass slides of consecutive endometrial biopsies in Louisiana State University Health Science Center–Shreveport over a period of 5 months (06/01/2008 to 10/31/2008) were reviewed. The presence and frequency of eosinophils were recorded. The biopsies that have eosinophils were further studied for the presence of chronic endometritis by subjecting those cases to immunohistochemical staining with an antibody that has been shown to highlight plasma cells in routine formalin-fixed paraffin-embedded tissue sections (mouse antihuman CD138; Clone MI15, Dako, Carpinteria, CA) [7]. Immunohistochemical staining was done with a DAKO autostainer—using a modified avidin-biotin detection method as previously described [8]. The immunostained slides were reviewed and scored for the presence and frequency of plasma cells, using light microscopy. Eosinophils were counted using a high-power field (HPF) of an Olympus BX41 microscope (Center Valley, PA) at  $\times 400$  magnification with a cross-sectional area of  $0.229 \text{ mm}^2$ . The average number of eosinophils in 40 HPFs was calculated for each case. The results were then analyzed for correlation between number of eosinophils and the presence of plasma cells. Fisher exact test was performed with SPSS3 software (SPSS, Chicago, IL) and a statistical significance cut-off level of  $P < .05$ .

## 3. Results

In all, 422 cases of endometrial biopsy were reviewed and 91 biopsies (21.5%) showed eosinophils. Among those 91 cases, 66 (72.5%) revealed the presence of plasma cells (positive staining with CD138). Of those 66 cases, only 4 cases were previously diagnosed as chronic endometritis and one of them was diagnosed with the aid of immunohistochemistry using CD138 antibody ( $P < .0001$ ). As shown in Fig. 1, eosinophils can be easily identified in H&E-stained tissue sections. On the other hand, plasma cells are not so readily distinguishable among endometrial stromal cells. But with the aid of CD138 immunostain (as shown in Figs. 1 and 2), the plasma cells are highlighted by their characteristic staining with CD138. The relationship of the numbers of eosinophils and the presence of plasma cells (positive staining for CD138) is summarized in Table 1. The average number of eosinophils in the biopsies with positive plasma cell staining is 2.74/40 HPF, compared with 2.46 eosinophils per 40 HPF in cases that stain negative for plasma cells. Among the cases that stain positive for plasma cells, there is no statistically



**Fig. 1** A and B, Endometrium with eosinophils that are readily identified in routine H&E-stained tissue sections; C, CD138 confirms the presence of CD138-positive cells (plasma cells) in the stroma of the same case (original magnifications: A,  $\times 200$ ; B and C,  $\times 400$ ).

significant correlation between the number of eosinophils and the number of plasma cells identified by immunostaining ( $P = .099$  for 1 eosinophils per HPF compared with  $\geq 2$  eosinophils per HPF).

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