

APPEARANCE OF HIGH ENDOTHELIAL VENULE-LIKE VESSELS IN BENIGN PROSTATIC HYPERPLASIA IS ASSOCIATED WITH BLADDER OUTLET OBSTRUCTION

Hypothesis / aims of study

Chronic prostatic inflammation has been implicated in the pathogenesis of benign prostatic hyperplasia (BPH)-associated lower urinary tract symptoms (LUTS). In previous studies, the degree of chronic prostatic inflammation has been evaluated by using histological scores. We previously demonstrated that the number of high endothelial venule (HEV)-like vessels was correlated with the magnitude of chronic inflammation in various chronic inflammatory gastrointestinal diseases [1]. The aim of this study is to evaluate the degree of BPH-associated chronic prostatic inflammation from the standpoint of appearance of HEV-like vessels, and to determine whether the magnitude of chronic prostatic inflammation is correlated with the severity of LUTS, particularly those evaluated by urodynamic study.

Study design, materials and methods

86 BPH tissue specimens with preoperative urodynamic study were immunostained for CD34 and MECA-79 to determine the number of HEV-like vessels. We scanned tissue sections immunostained with MECA-79 at x40 magnification and identified three tissue fragments with highest density of MECA-79+ vessels (a so-called "hot spot"). MECA-79+ vessels in these three fragments were then counted at x 200 magnification. In serial sections immunostained for CD34, the number of CD34+ vessels in the three tissue fragments was also determined, and the MECA-79+/CD34+ vessel ratio was calculated in each case. To demonstrate the validity of assessment of chronic prostatic inflammation by using the number of HEV-like vessels, we evaluated the extent of chronic inflammatory cell infiltrates in each of the three tissue fragments above was categorized into four grades: none (score 0), mild (score 1), moderate (score 2), and marked (score 3), and average score of the three tissue fragments was calculated in each case based on the criteria described by Nickel et al [2]. This histological grading is illustrated in Figure 1. Triple immunohistochemistry for either CD3 and CD20 or CD4 and CD8, together with MECA-79, was conducted to determine which lymphocyte subset is more closely associated with HEV-like vessels. Correlation analyses were carried out to determine whether the magnitude of chronic prostatic inflammation, as assessed by the number of HEV-like vessels, was correlated with the degree of LUTS.

Results

HEV-like vessels were induced in lymphoid aggregates formed frequently in BPH (Fig.1). The number of HEV-like vessels, that is, the MECA-79+/CD34+ vessel ratio, was positively correlated well with chronic inflammation score (correlation coefficient=0.6458; $P<0.0001$. see Fig.2). The magnitude of chronic prostatic inflammation, as assessed by the number of HEV-like vessels, was correlated with the degree of LUTS, particularly those associated with voiding functions, which was measured objectively by pressure flow study (Fig.3). On the other hand, the number of HEV-like vessels was not correlated with the prostatic volume.

Interpretation of results

The strong correlation between the number of HEV-like vessels and the extent of chronic prostatic inflammation indicates that the number of HEV-like vessels could be a surrogate for identifying the degree of chronic prostatic inflammation. Despite no correlation between the prostatic volume and the number of HEV-like vessels, voiding dysfunction was correlated with the number of HEV-like vessels. This result indicated that chronic prostatic inflammation could influence on the functional obstruction of lower urinary tract.

Concluding message

Chronic prostatic inflammation could be one of the factors that determine the association between BPH and voiding function. To the best of our knowledge, this is the first report demonstrating a correlation between chronic prostatic inflammation assessed by the HEV-like vessel count and the severity of voiding function evaluated objectively by urodynamic study. The number of HEV-like vessels could be a surrogate for the degree of chronic prostatic inflammation.

Fig.1

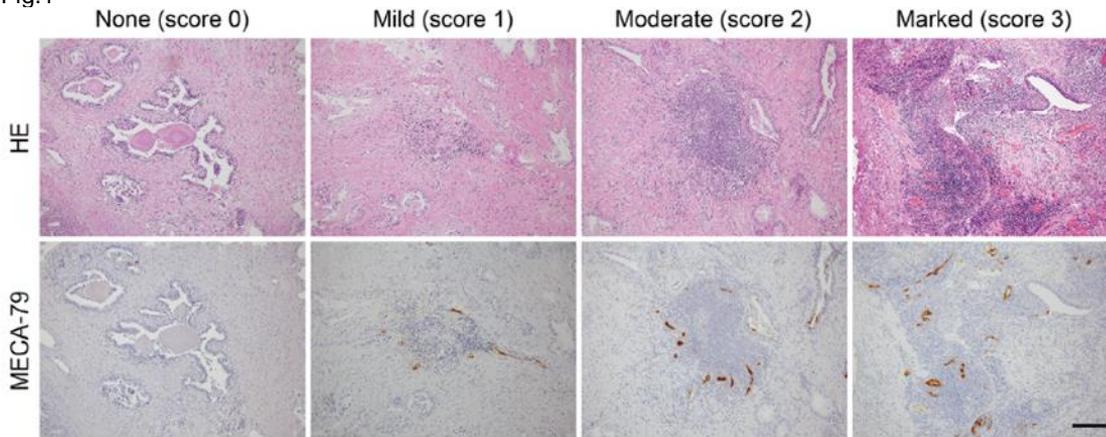


Fig.2

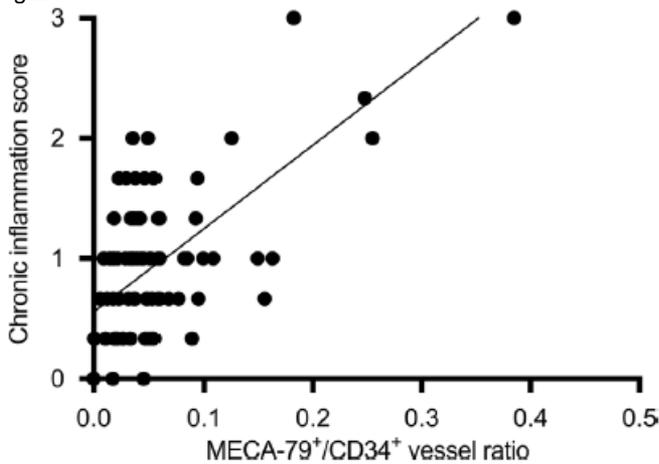
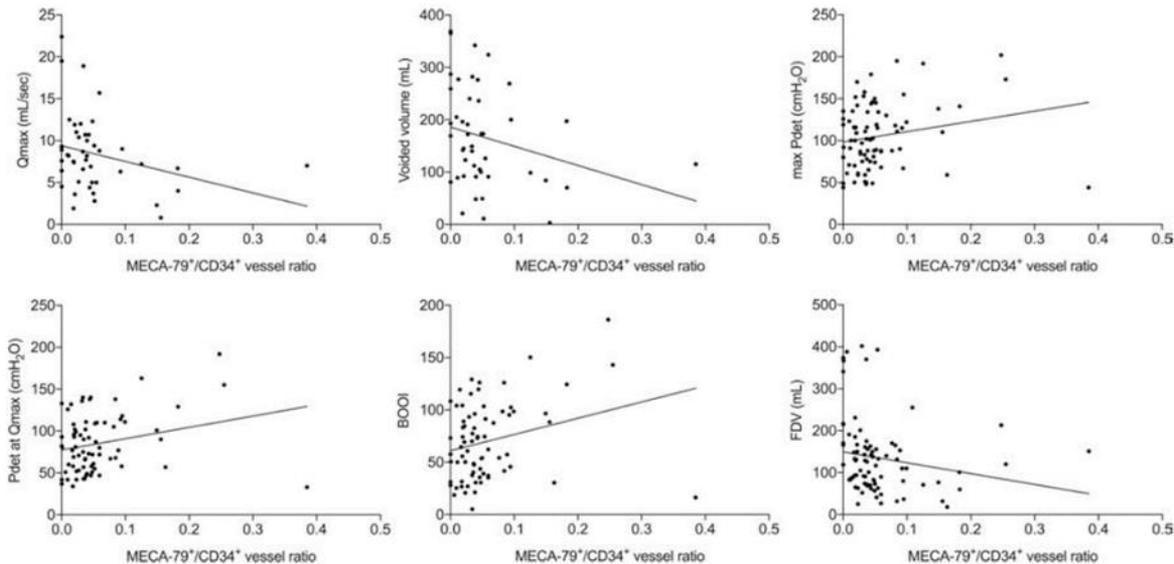


Fig.3



References

1. Suzawa K, Kobayashi M, Sakai Y, Hoshino H, Watanabe M, Harada O, Ohtani H, Fukuda M, Nakayama J. Preferential induction of peripheral lymph node addressin on high endothelial venule-like vessels in the active phase of ulcerative colitis. *Am J Gastroenterol* 2007;102:1499–1509.
2. Nickel JC, Roehrborn CG, O'Leary MP, Bostwick DG, Somerville MC, Rittmaster RS. The relationship between prostate inflammation and lower urinary tract symptoms: Examination of baseline data from the REDUCE trial. *Eur Urol* 2008;54:1379–1384.

Disclosures

Funding: NONE **Clinical Trial:** Yes **Public Registry:** No **RCT:** No **Subjects:** HUMAN **Ethics Committee:** the Ethics Committee of the Faculty of Medical Sciences, University of Fukui **Helsinki:** Yes **Informed Consent:** Yes