HYALURONAN AND MYELOPEROXIDASE IN HUMAN PERITONEAL FLUID DURING GENITAL INFLAMMATION

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Abstract—The changes in concentration of hyaluronan (HYA) and myeloperoxidase in the peritoneal fluid (PF) were studied during genital intraperitoneal inflammation. PF were collected from 111 women undergoing laparotomy for adhesiolysis and reconstructive surgery of the fallopian tubes or laparoscopy in search of causes of infertility or low abdominal pain. When the number of leukocytes in the PF had been counted, the fluid samples were centrifuged and the supernatants analyzed for the concentrations of HYA and myeloperoxidase. During genital inflammation, whether postoperative or postinfectious, leukocytosis and elevated levels of HYA and myeloperoxidase were found in the PF. Concentrations of these substances in the PF may be usable as clinical markers for genital inflammation.

INTRODUCTION

Hyaluronan (hyaluronic acid, HYA), a major glycosaminoglycan in the extracellular matrix of connective tissue, is a linear polysaccharide, consisting of repetitive disaccharide units of N-acetyl glucosamine and glucuronic acid and having a molecular weight in the range of $10^6$-$10^7$ daltons (1). It is abundant in mesenchymal tissue and is synthesized by fibroblasts and other cells at the cell surface (2). Accumulation of HYA has been observed in tissues and organs during inflammatory conditions, and it is known that various inflammatory mediators such as interleukin-1, growth factors, and prostaglandins can stimulate

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HYA synthesis in fibroblasts (3). In wound healing there is an increased HYA production that may be of importance for phagocytosis, cell proliferation, and cell migration during the process of repair (4). A participation in the inflammatory process has been suggested, e.g., through angiogenesis induced by HYA of low molecular weight (5), while high-molecular-weight HYA prevents development of new capillaries (6), and through effects on lymphocytes and other cells where the human homing receptor CD-44 binds to HYA (7).

Infertility and low abdominal pain are often reasons for performing laparoscopy; this in many instances leads to a diagnosis, but there are patients with these symptoms in which few pathological changes are found. One way of extending the usefulness of diagnostic laparoscopy is to aspirate PF from the Douglas pouch for various analyses (8).

Previously, in animal experiments with rabbits, we have induced aseptic peritonitis that generated large amounts of HYA in peritoneal lavage fluid. The turnover rate of HYA was also investigated in rabbits and a surprisingly short half-life was found (9). Furthermore, we have found increased amounts of HYA in biopsies from adhesions in women with infertility due to pelvic adhesive disease, and we concluded that it might represent an ongoing inflammatory and/or connective tissue proliferative process (10). Thus, in this study we set out to investigate whether the concentration of HYA in the PF could be of help in diagnosing genital inflammation and causes of infertility, and if the presumed ongoing inflammatory and/or proliferative process in pelvic adhesive disease was reflected in increased amounts of HYA also in the PF. To confirm the diagnosis of pelvic inflammation, the concentration of myeloperoxidase (MPO, a granule protein secreted by the neutrophilic granulocytes), leukocytes, and neutrophilic granulocytes were registered.

**MATERIALS AND METHODS**

*Patients.* Samples of blood and PF were collected at 10 laparotomies for adhesiolysis and at 101 laparoscopies on women with low abdominal pain or infertility or on healthy women who were to be sterilized. The cases were randomly selected among patients at a gynecology ward. All samples were taken after permission from the patients, and the sampling procedure was approved by the Ethical Committee, Faculty of Medicine, Uppsala University.

The patients were divided into six different groups. The reference patients (*N* = 22; mean age, 30 years) were women going through laparoscopic sterilization or women with unclear low abdominal pain that was not caused by any intraperitoneal disease. The reference cases had laparoscopic findings considered as normal with anatomically normal uterus and fallopian tubes.

Women undergoing laparoscopy in search of the cause of infertility or low abdominal pain (without desiring pregnancy), were divided into two groups: endometriosis (*N* = 13; mean age, 32 years) or adhesions and/or sactosalpinx (*N* = 33; mean age, 33 years). Patients with any visible endometrial implant (stage I-III) (11) were included in the endometriosis group, while both endometriosis and adhesions (stage III–VI) (11) were included in the adhesion group. Patients with