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Inflammasomes on, Male Infertility Out

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Introduction

The major and common condition in infertile men is the inflammation of genital tract, although it has been often underestimated in the clinical practice. Specific mechanisms such as impaired secretion of the accessory glands, obstruction of the seminal ducts, development of an inflammatory microenvironment lead to a dysregulation of spermatogenesis. Thus, it's clear that the association between inflammation of the male reproductive system and oligozoospermia has been established in the clinical practice of male infertility. In a recent study, the role of inflammasome components and the end-product cytokines has been investigated in the semen of patients with spinal cord injury (SCI) [1]. Based on previous scientific data concerning the abnormal motility of seminal plasma from spinal cord injured men, the authors hypothesized that this effect could be due to elevated semen concentrations of specific inflammatory cytokines such as IL-1b, IL-18, caspase-1 and ASC (apoptosis-associated speck-like protein containing a caspase activation and recruitment domain). This study confirmed elevated concentration of these cytokines and caspases in the seminal plasma of SCI patients compared with healthy control subjects, and also immunocytochemistry revealed the ASC localization in the acrosome, equatorial segment and midpiece of spermatozoa. Il-1b and IL-18 are activated by high-molecular-weight platforms called inflammasomes. Inflammasomes are activated by intracellular nod-like receptors (NLRs) that change their conformation and recruit proteins for platform assembling during preliminary phases of inflammation. The NLR family comprises 20 members and plays a pivotal role in the recognition of intracellular ligands [2]. The activation of inflammasomes allows the autocatalytic cleavage of procaspase 1 that modulates the proteolytic maturation of a set of inflammatory cytokines. This pivotal role of inflammasomes during inflammatory processes prompt us to investigate the role of specific NLRsin the semen of infertile patients with disorders related to reproductive system, compared to healthy control subjects. Our preliminary results show a significant increased expression of NLRP3, NLRP4, NLRP9 and NAIP in the sediment of semen samples, compared to controls suggesting an involvement of inflammasomes in male infertility. In literature it is well known that inflammation of the male genital tract reduces concentration, motility and the number of morphologically normal spermatozoa. Nevertheless, the diagnosis of male genital tract inflammation is very difficult because affected patients are frequently asymptomatic and semen samples are often free from bacteria [3]. Several works associated increased expression of pro-inflammatory cytokines with poor semen quality and infertility. On this regard, Milardiand coworkers evaluated if the treatment with prednisolone, a steroid anti-inflammatory drug, might be useful both in reducing inflammation and improving sperm parameters and sofertility outcome [4]. A total of 90 infertile patients with different degrees of oligozoospermia and gland inflammation, underwent prednisone treatment at a daily dose of 12.5 mg for one month. Results demonstrated that prednisone treatment significantly improves sperm parameters such as concentration, total count and motility of spermatozoa. They hypothesized that this treatment probably reduced edema and leukocyte infiltration of ejaculatory ducts, thus improving sperm output and quality.In the light of these considerations, it is determinant to find specific molecular markers that improve the evaluation of underestimated inflammatory status and the choice of therapies with anti-inflammatory drugs.

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Competing Interests

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