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Male Fertility as a Bull's Eye for Mastocytosis

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Abbreviations: MC: Mast Cell; ICs: Immune Cells; ROS: Reactive Oxygen Species

Opinion

Mast cell (MC) as a free cell type can be found in connective and epithelial tissues throughout the body as well as peritoneal and thoracic cavities in rodents [1].The MCs are located in subepithelial areas in connective tissue surrounding blood cells, smooth muscle, mucous and hair follicles and have been detected in all vascularized tissues except for the central nervous system and the retina [2]. The cytoplasm of MC contains 50-200 large granules storing a variety of substances with potent physiological activities including histamine, heparin, serotonin, cytokines, chondroitin sulfate and neutral proteases [3-5]. It is well-established that these multi-functional master cells are involved in a wide spectrum of functions including vasodilation, angiogenesis, bacterial and parasite elimination, immune system, vascular and bronchial homeostasis and bone growth, remodeling and mineral homeostasis along with inflammatory, hypersensitivity and fibrotic disorders [2, 6-8].Three populations of MCs have been identified based on protease content. The mucosal MC (MCT) only containstryptase, the connective tissue MC (MCTC) contains tryptase, chymase, carboxypeptidase and cathepsin and the third MC type (MCC) has chymase and carboxypeptidase [9].

A growing body of evidence indicates association between mastocytosis and male infertility [10-12]. It has been reported that increased number of MCs is ascribed to idiopathic male infertilities and spermatogenic disorders [13-15]. Accordingly, it has been revealed that number of MCT and MCTC increases in the testes of patients with spermatogenic arrest and Sertoli-cell-only syndrome, confirming MCs roles in the male infertility pathogenesis [16-18]. It has also been shown that increased numbers of MCs are associated with different types of spermatological abnormalities including asthenospermia, oligospermia, azoospermia and sperm DNA damages [19-21]. It has been suggested that paracrine factors from myoid, Sertoli and spermatogenic cells can play crucial roles in testicular mastocytosis [19]. Myoid cells may also trigger MCs activation through formation of membrane-to-membrane connections [16]. It is well-known that MC products can stimulate fibroblast migration, proliferation and synthesis of extracellular matrix compounds leading to tissue fibrosis [22]. On the other hand, increased depositions of fibrous connective tissue in the peritubular layers and thickening of the tubular wall have been attributed to several testicular pathological patterns resulting in male infertilities [23].

Additionally, MCs degranulation in response to biochemical stresses can lead to release of histamine and chemotactic factors causing increased vascular permeability and immune cells (ICs) infiltrations [24]. It is noteworthy to mention that ICs are sources of reactive oxygen species (ROS) production and excessive ROS generation induced oxidative stress is one of the major causative factors of reproductive dysfunctions [25-27]. Moreover, it was found that testicular mastocytosis is associated with blood-testis barrier malfunction [28]. In line with that, previous reports have shown the beneficial effects of MC blockers in improvement of male fertility impairments. Recently, it has been demonstrated that Ketotifen can improve sperm motility in asthenospermic infertile men and sperm quality, chromatin integrity and pregnancy rate after varicocelectomy [20]. Furthermore, it has been suggested that tranilast is clinically useful for the treatment of severe idiopathic oligozoospermia [29]. On the whole, mastocytosis in reproductive tract can result in male fertility disturbance through fibrotic changes and oxidative stress inductions as well as inflammatory responses formation and medicinal strategies such as administration of MC blockers may be beneficial in treatment of idiopathic male infertilities (Figure 1).

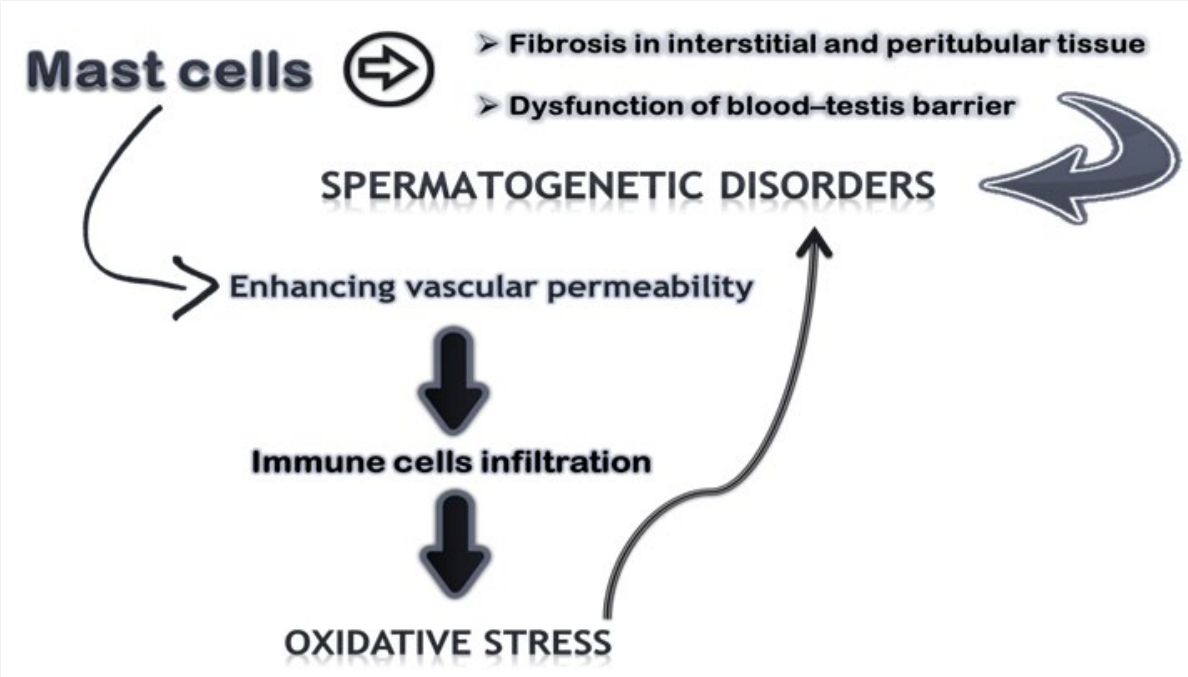

Figure 1: Role of mast cells in spermatogenic disorders.

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