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Macrophages and Leydig cells in testicular biopsies of infertile patients: friends or enemies?

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One of the most severe forms of male infertility is a non-obstructive azoospermia (NOA) [1]. NOA is frequently characterized by a heavy damage of seminiferous tubules. Much less is known on the changes of the interstitial testicular tissue, where macrophages and Leydig cells reside [2].

We assumed that, in infertile patients, macrophages exert a negative influence on Leydig cells and their androgen production. Therefore, the aim of the current survey was to investigate the above mentioned cells types within the testicular interstitium of infertile men.

In total, 120 testicular biopsies from infertile patients with azoospermia were analysed. According to their histological appearance, the biopsies could be divided into the control group (n=12, normal morphology of the testicular parenchyma) and NOA group (n=108, damaged seminiferous tubules). From paraffin and Durcopan /plastic/ embedded tissue, standard paraffin and semithin sections have been made. For the identification of macrophages, two immunohistochemical markers have been applied: CD68 (DAKO, Denmark) and KiM1P1 (Univ. of Kiel, Germany). Testosterone-producing cells also were identified by immunohistochemistry (anti-testosterone, Biogenex, USA). Leydig cells morphology (the presence of heavy vacuolated cells) was evaluated in semithin sections. Quantification of both macrophages and Leydig cells has been done using stereological methods.

Quantitative and qualitative (stereological) analysis of testicular biopsies pointed out the following changes in the infertile group: a) a significant increase in the number of macrophages; apart from the interstitial compartment, these cells could be found within seminiferous tubules; b) a significant increase in the number of Leydig cells with irregular morphology (abundant vacuolization of the cytoplasm); c) a significant decrease in the number of testosterone-producing cells; d) a negative correlation between the number of macrophages and the number of testosterone-producing cells (the more macrophages, the less testosterone-producing cells).

Based on the above-mentioned results of the histological analysis, it seems that the increased presence of macrophages has a negative impact on Leydig cells morphology and testosterone production.

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2. S.C. Esteves, A. Agarwal, Int Braz J Urol. 37 (2011), pp. 5-15.

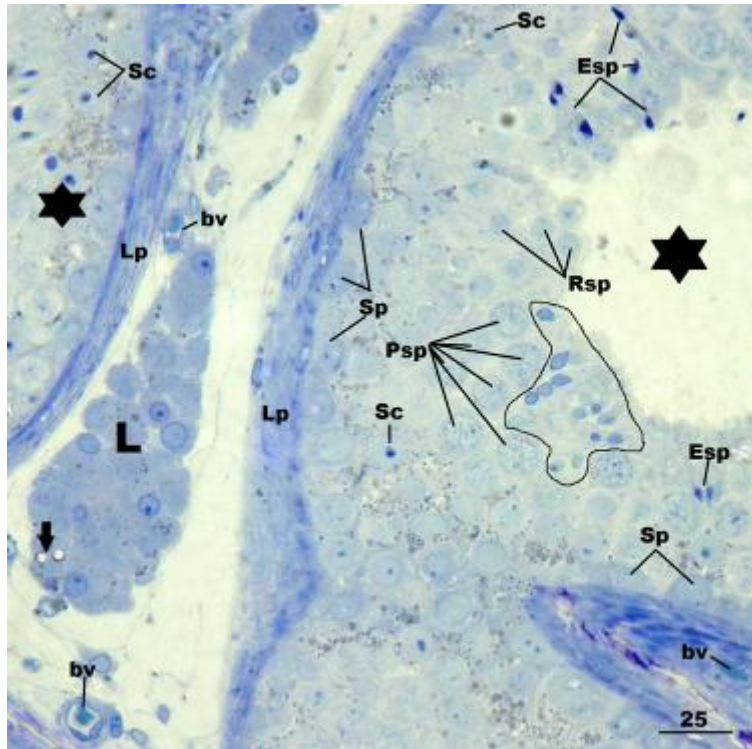


Figure 1. Control testicular biopsy with regular morphology of Leydig cells (L). Some of these cells have occasional lipid droplets (↓). Within seminiferous tubules (★) cells of seminiferous epithelium are seen: Sertoli cells (Sc), spermatogonia (Sp), primary spermatocytes (Psp), round (Rsp) and elongated spermatids (Esp, encircled area). (Lp-lamina propria; bv-blood vessels). Toluidine blue, x400, scale bar = 25 μm

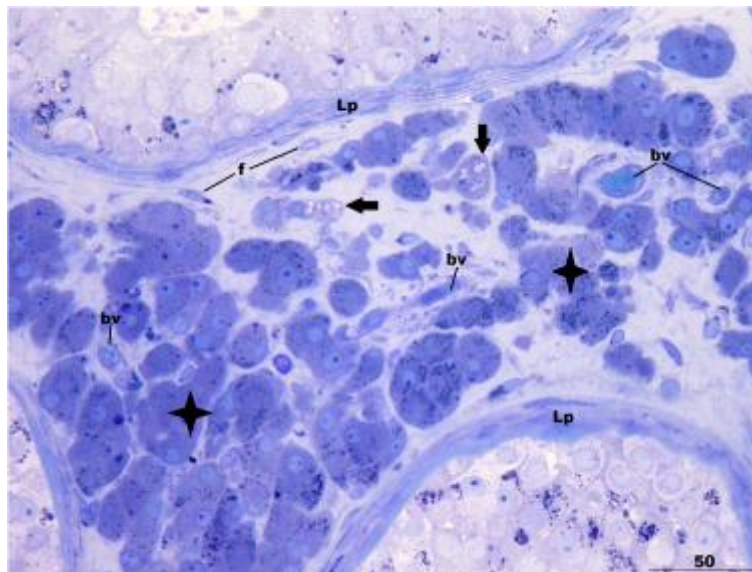


Figure 2. Hypertrophic and hyperplastic Leydig cells (★) in the biopsy of an infertile patient. In the cytoplasm of some Leydig cells, many vacuoles and lipid droplets (↓) are visible. (bv-blood vessels; f-fibroblasts; Lp-lamina propria). Toluidine blue, x200, scale bar = 50 μm