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CAN MATURATION ARREST OCCUR AT THE STAGE OF SPERMIOGENESIS?

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This article attempts to clarify the pathological condition during which the maturation of the germinal epithelium is unable to evolve beyond a certain stage and is characterized as maturation arrest. Emphasis is given to the histological entity named spermiogenic arrest.

Keywords male infertility, nonobstructive azoospermia, spermiogenesis arrest

Maturation arrest is the pathological condition wherein the development of germ cells is arrested and therefore mature spermatozoa are not formed [1, 2, 7]. However, the stage where this arrest of development will occur has not yet been specified. Some scientists believe that it can occur at any level of spermatogenesis [3], whereas others believe that spermatogenesis can be halted only at specific stages [2, 7]. This debate has recently acquired clinical importance since round cells with haploid set of chromosomes from azoospermic men are now used to

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fertilize oocytes, with the methods of round spermatid injection (ROSI) or round spermatid nucleus injection (ROSNI) [5, 6].

The past few years two opposing theories regarding this debate have been developed. According to the first theory spermatogenesis can stop even at the stage of spermiogenesis [5, 6]. In this case round spermatids exist but cannot develop into elongated spermatids or spermatozoa. These immature germ cells are injected into oocytes based on the methods of ROSI or ROSNI. However, recent data suggest that this might not be the case. The second theory was proposed by Silber and Johnson in 1998 [4]. Based on the study of testicular biopsies of men with nonobstructive azoospermia they observed that maturation arrest occurred only at stages before the formation of spermatids. If round spermatids were present in the biopsy then it was rather certain that elongated spermatids or even spermatozoa would also exist in another site of the same biopsy specimen [4]. This means that maturation arrest cannot occur at the stage of spermiogenesis and therefore questions the use of ROSI and ROSNI, which is based on the presence of round spermatids without the presence of elongated ones or spermatozoa.

The aim of the present study was to determine (1) the frequency of spermatogenic arrest in men with nonobstructive azoospermia–severe oligozoospermia (OTA) and (2) the stage where maturation arrest can occur and the histological picture that is observed.

MATERIALS AND METHODS

A total of 87 men with azoospermia or severe OTA (number of spermatozoa $<1 \times 10^6$/mL, motility <10%) participated in the study. In all 142 testicular biopsies that were performed the testicular tissue was fixed in Bouin's or Steive's solution, embedded in paraffin, and then cut into 3 sections, 5–8 μm thick. One section was stained with hematoxylin–eosin, the second with PAS, and the third with Masson. There were at least 100 seminiferous tubules per biopsy and the histological evaluation was done according to the Levin method [2].

RESULTS

The histological diagnosis of 87 men with azoospermia–severe OTA that participated in the study was as follows: normal spermatogenesis (n = 20), hypospermatogenesis (n = 31), germinal epithelium aplasia (n = 15), tubular sclerosis (n = 3), and maturation arrest (n = 18). The clinical diagnosis of the 18 men with maturation arrest was as follows: idiopathic azoospermia (n = 13), cryptorchidism (n = 3), varicocele (n = 1), and hypogonadotropic hypogonadism (n = 1).

Regarding the stage where maturation arrest has occurred it was observed in the majority of cases (17 out of 18 cases: 94.4%) at the level of primary spermatocytes. In 11 men the maturation arrest was complete and only spermatogonia and primary spermatocytes were found in the testicular biopsy, whereas in the remaining 6 the maturation arrest was incomplete with round spermatids, elongated spermatids and spermatozoa only occasionally found in some tubules. In only 1 out of the 18 cases (5.6%) the maturation arrest was at the level of round spermatid. The testicular biopsy of this patient presented the following histological picture: in all of the seminiferous tubules spermatogonia were able to mature to round spermatids, and cellular types from all stages of spermatogenesis were present. However, elongated spermatids and spermatozoa were rarely found even after extensive search of the biopsy.

DISCUSSION

The frequency of maturation arrest in our patient population with nonobstructive azoospermia or severe OTA is 20.6%. There is no consensus in the literature regarding this percentage. It was reported by Wong et al. that the percentage of maturation arrest of the subfertile male population was 22.9% [7]. On the contrary in his original study in 1979 Levin reported that only 4% of subfertile men were diagnosed to have maturation arrest [2]. More recently the differences in the percentage of maturation arrest were attributed to the difficulty that exists in separating hypospermatogenesis from maturation arrest [1]. As a result, the histological picture of a biopsy can be considered to represent hypospermatogenesis, whereas other scientists may characterize it as maturation arrest. Therefore, in this study we were particularly careful in the evaluation of the testicular biopsies, especially in cases of hypospermatogenesis and maturation arrest. The sum of both conditions was reported to be 55% in a recent study [1]. In our patient population 35.6% exhibited hypospermatogenesis and 20.6% maturation arrest. The sum of both conditions in our study is, therefore, 56.2%, which is similar to the percentage reported in the literature.

We diagnosed 17 out of 18 men with maturation arrest at the stage of primary spermatocyte and only one case with arrest of spermiogenesis even in a partial form. In this particular case, round spermatids were present, whereas elongated spermatids or spermatozoa were rarely found in some tubules. This is in accordance with the findings of Silber and Johnson [4], who studied the testicular biopsies of a large population of subfertile men and reported that maturation arrest never occurred at stages beyond meiosis. Based on their results they concluded that arrest of spermiogenesis must be a very rare condition. Our findings are in accordance with this theory and it seems from our data that arrest of spermiogenesis is rare in azoospermic patients with maturation arrest. It should be noted, however, that our patient population is relatively small and definite conclusions can be reached only with the study of larger patient populations.

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