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Balance of Apoptosis and Proliferation of Germ Cells Related to Spermatogenesis in Aged Men

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To clarify whether germ cell apoptosis is related to a decrease of germ cells in the aged testis with impaired spermatogenesis, we investigated the apoptotic rate of each germ cell type. Testicular specimens were obtained by orchiectomy from 36 men with advanced prostate cancer and by testicular biopsy from 21 men with obstructive azoospermia, which served as controls. The terminal deoxynucleotidyl transferase-mediated nick end labeling (TUNEL) technique was used to identify apoptosis. As a marker of cellproliferation activity, the expression of Ki-67 was immunohistochemically evaluated. Expression of Bcl-xl, which regulates apoptosis of germ cells, was also immunohistochemically examined. Histologically, except for spermatogonia, the ratios of primary spermatocytes, round spermatids, and elongated spermatids to Sertoli cells were significantly decreased in aged testes. The apoptotic rate in spermatogonia was significantly lower in aged men than it was in controls (0.11% ± 0.06% vs 0.34% ± 0.21%). Expression of Ki-67 in spermatogonia was decreased in aged men (18.6% ± 6.0%) compared with that of controls (24.9% ± 3.3%), suggesting that germ cell proliferation diminished with aging. Consequently, the balance of spermatogonial proliferation and apoptosis showed no difference between the two groups. This was believed to be one of reasons why spermatogonial numbers in aged testes was similar to those of controls. The apoptotic rate of primary spermatocytes in aged men was significantly elevated compared with that of controls (0.60% ± 0.54% vs 0.22% ±0.12%), resulting in a decrease of the number of primary spermatocytes per Sertoli cell. The expression of Bcl-xl was inversely correlated with the apoptotic rate in primary spermatocytes, suggesting that Bcl-xl may be related to the regulation of primary spermatocyte apoptosis. Based on these findings, we conclude that accelerated apoptosis of primary spermatocytes might account for a part of the mechanism of germ cell loss in aging men.

Key words: Apoptosis, proliferation, Bcl-xl, aging, spermatogenesis

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