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The role of intrinsic pathway in apoptosis activation and progression in Peyronie's disease

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Peyronie's disease (PD) is a connective tissue disorder where formation of fibrous plaques in tunica albuginea (TA) and erectile tissue can result in penile deformity, pain, and erectile dysfunction. Fibrosis, its major pathological manifestation, arises from fibroblast proliferation and accumulation of extracellular matrix; PD progresses with formation of plaques or even ectopic calcification having the appearance of scar tissue, which prevent TA expansion during erections. The mechanisms underpinning PD are unclear, and relatively little is known about the disease itself. To date corrective surgery is the sole effective treatment. A greater understanding of PD pathophysiology at the molecular level has the potential to help develop novel medical therapeutic approaches.

The aim of this study was to investigate the activation of the apoptotic intrinsic apoptotic pathway in plaques from PD patients. Tunica albuginea from either PD and control patients were assessed for the expression of bax, bcl-2, caspase 9 and 3 using immunohistochemistry, and by measurement of apoptotic cells using TUNEL assay. Bax overexpression was observed in metaplasic bone tissue, in fibroblasts and in myofibroblast of plaques from PD patients. Little or no bcl-2 immunostaining was detected in samples from either patients or controls. Caspase 3 immunostaining was very strong in fibrous tissue, in metaplasic bone osteocytes and in primary ossification center osteoblasts. Moderate caspase 9 immunostaining was seen in fibrous cells plaques and in osteocytes and osteoblasts of primary ossification centers from PD patients. Control samples were negative for caspase 9 immunostaining. In PD patients the TUNEL immunoassay showed intense immunostaining of fibroblasts and myofibroblasts, the absence of apoptotic cells in metaplasic bone tissue and on the border between fibrous and metaplasic bone tissue.

Apoptotic cell death occurs in stabilized PD plaques and is partly induced by the intrinsic mitochondrial pathway. The present findings can have clinical implications and may help devise improved treatment strategies. A therapeutic approach aimed at enhancing apoptosis-inducing molecules would at least help delay the progression of PD. Identification of target molecules for gene construct or biological or chemical reagent delivery to target sites could contribute to induce PD plaque stabilization.

References

[1] S. S. Gholami, T. F. Lue, "Peyronie's disease." Urol Clin North Am, vol. 28, pp. 377-390, 2001.
[2] N. F. Gonzalez-Cavid, J. Rajfer, "Mechanisms of disease: new insight into the cellular and molecular pathology of Peyronie's disease," Nat Clin Pract Urol, vol. 2, pp. 291-297, 2005.