The contribution of cavernous body biopsy in the diagnosis and treatment of male impotence

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Summary. This study concerns the results of penile biopsies in 50 patients aged 27 to 80, with secondary impotence removed with a biopty gun or during penile surgery. The biopty gun specimens were equally representative as the open biopsy ones. The cause and the degree of erectile dysfunction were determined by clinical and laboratorial investigation. The histological study of the cavernous bodies in the patients with psychogenic impotence revealed normal erectile tissue. In patients with organic impotence, histological lesions were graded as mild, moderate or severe. The most severe lesions were observed in the erectile tissue and in particular in the smooth muscle of the trabeculae and the helicine arteries, which had been reduced and replaced by connective tissue. Histological lesions were found not only in the arterial but also in the venous leak cases. There was a correlation between their severity and the degree of impotence, although of no statistical significance. The penile biopsy determines the condition (state) of the functional cavernous smooth muscle tissue, the integrity of which is essential for the erectile mechanism as well as for the action of the vasoactive drugs and the results of vascular surgery. Its important role is evident as it contributes not only to the diagnosis of the cause, but also to the choice of treatment of male impotence.

Key words: Male impotence, Penile biopsy, Erectile tissue, Histological lesions

Introduction

Although there are a number of established clinical diagnostic methods for the assessment of the functional integrity of the blood vessels of the penis, a test to assess the functional integrity of cavernous smooth muscle tissue is still lacking (Krane et al., 1989). Atrophy and

loss of function of cavernous smooth muscle cells may cause erectile dysfunction. The success rate of reconstructive vascular surgery and/or pharmacological treatment depends on the presence of sufficient functional muscle tissue. The important role of the biopsy in the diagnosis, pathogenesis and treatment of male impotence, therefore becomes, clear, since histological examination may define not only lesions of the cavernous muscle tissue, but also lesions of all other tissues that contribute to the erectile mechanism.

Materials and methods

This study is based on the biopsies of 50 patients with secondary impotence aged 27 to 80. The specimens were removed from both cavernous bodies with a biopty gun or during penile surgery. The histological findings of the cavernous bodies were evaluated in correlation with the type and degree of impotence, as determined by the clinical investigation, cavernography, cavernometry and ultrasonography after the injection of vasoactive-relaxative substances, such as papaverine, prostaglandin E_1 and phentolamine. Of 50 patients, 3 had psychogenic and the remaining 47 organic impotence with a history of diabetes mellitus, hypertension and/or arteriosclerosis in the majority of the cases. The cause of organic impotence was arteriogenic in 17 cases, venogenic in 15 cases, mixed vasculogenic in 12 cases and neurogenic in 3 cases. Peyronie's disease coexisted in 8 cases with arteriogenic or mixed vascular disease.

Histological specimens were fixed in buffered formalin solution 10%, were embedded in paraffin, cut in 4 μm sections and stained with Haematoxylin-Eosin, Masson's Trichrome for the identification of smooth muscle tissue (red colour) and the fibrous skeleton of the corpora cavernosa (green colour) and Elastica for the identification of the elastic fibre network. In addition, an immunohistochemical study with the avidin-biotin method (ABC) was performed, using monoclonal antibodies against desmin to differentiate smooth muscle from collagen fibres.

Results

Histological examination of the cavernous bodies of patients with psychogenic impotence revealed normal erectile tissue, the percentage of the smooth muscle tissue in the trabeculae ranging between 70 and 90% (Fig. 1). On the contrary, in patients with organic impotence, histological changes graded as mild, moderate or severe were observed.

The most impressive lesions were found in the erectile tissue, mainly in the smooth muscle tissue of the trabeculae. Disturbance of normal architecture, reduction, atrophy and degeneration of smooth muscle and its replacement by connective tissue were noted (Fig. 2). As a consequence of the above, the sinusoids were obliterated. In mild lesions the percentage of smooth muscle of the trabeculae was 50-70%, in the moderate lesions 30-50% and in the severe ones <30%.

Table 1. Correlation of the histological lesions with the pathogenetic mechanism and the grade of male impotence.

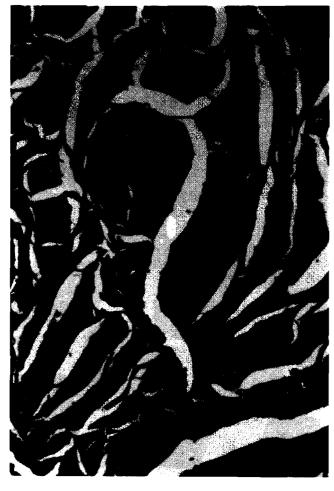| HISTOLOGICAL LESIONS	PATHOGENETIC MECHANISM AND GRADE OF MALE IMPOTENCE												Neurogenic	
	Arteriogenic				Venogenic				Mixed vasculogenic					TOTAL
	Grade I	Grade II	Grade III	Total	Grade I	Grade II	Grade III	Total	Grade I	Grade II	Grade III	Total		TOTAL
Mild	3		1	4	1	2	3	6	2			2	3	15
Moderate	5	2	1	8	1	1	5	7	1	5	1	7		22
Severe		2	3	5			2	2		1	2	3		10
TOTAL	8	4	5	17	2	3	10	15	3	6	3	12	3	47

Fig. 1. Normal erectile tissue in psychogenic impotence. Masson's Trichrome, x 100

Fig. 2. Moderate smooth muscle reduction in organic impotence. Masson's Trichrome, x 100

Similar changes were observed in the valvular mechanism of the helicine arteries. The elastic fibres of the trabeculae were slightly reduced. Another characteristic change was the appearance of elastic fibres in the tunica albuginea and an architectural disturbance of its collagen fibre (Fig. 3).

There was a correlation between the severity of the histological lesions and the grade of impotence, although it was not statistically significant (Tables 1, 2). The

Table 2. Correlation of the histological lesions with the grade of male impotence.

HISTOLOGICAL LESIONS	GRADE OF MALE IMPOTENCE						
	Grade I		Grade II		Grade III		Total
	No.	%	No.	%	No.	%	
Mild	8	53.3	2	15.4	5	26.4	15
Moderate	7	46.7	8	61.6	7	36.8	22
Severe			3	23	7	36.8	10
Total	15		13		19		47

Fig. 3. Elastic fibres in the tunica albuginea in organic impotence. Elastica, x 200

histological changes were mild in the great majority of cases with grade I impotence (arterial, venous or mixed), moderate in those with grade II impotence and moderate or severe in those with grade III impotence.

Histological lesions were observed not only in the arterial but also in the venous leak cases. Additional lesions were found in the cases with Peyronie's disease, i.e. lymphocytic vasculitis and fibrous plaque formation.

Discussion

Open biopsy of the cavernous bodies at the time of insertion of a penile prosthesis is routinely performed and contributes to the evaluation of the degree of male impotence, the diagnosis of which has already been made by other diagnostic methods (Meuleman et al., 1990; Wespes et al., 1990c). Biopsy with the biopty gun before deciding the method of treatment, presents great interest (Wespes et al., 1990d). In the absence of sufficient functional smooth muscle tissue, the patient can be spared aimless reconstructive vascular surgery or unsuccessful pharmacological treatment and be managed with a prosthesis implantation (Meuleman et al., 1990). In our series, as well as in other studies, biopty gun biopsy was equally representative as open biopsy and so it is our feeling that it can replace the open method (Wespes et al., 1990c,d).

Today, erection is considered to be a neurovascular function, accomplished by a succession of three phases: the neurological-psychogenic phase; the arterial phase; and the venous phase (veno-occlusive mechanism) (Fournier et al., 1987; Junemann, 1989; Krane et al., 1989). The first phase is accompanied by simultaneous relaxation of the smooth muscle tissue, situated in the trabeculae and the subendothelial valvular mechanism of the helicine arteries (Goldstein and Padma-Nathan, 1990). These are arteriovenous anastomoses that remain closed during the flaccid state of the penis, and most of the blood passes through shunt vessels (Conti et al., 1988; Fugleholm et al., 1989; Banya et al., 1990a,b; Fernandez et al., 1991). During tumescence the helicine arteries open and blood flows into the sinuses (Banya et al., 1990b). Relaxation of the functional smooth muscle tissue is achieved through neurotransmitters, released locally by nerves, and therefore erection is totally dependent on intact innervation (Goldstein et al., 1984; Shirai et al., 1990; Crowe et al., 1991). It is believed that apart from cholinergic and adrenergic mechanisms there are also noncholinergic-noradrenergic mechanisms responsible for the contraction and relaxation of penile smooth muscle (Krane et al., 1989; Lue, 1990). Such dilator substances are the vasoactive polypeptide (VIP), the calcitonin gene-related peptide, histamine and prostaglandin E_1 (Lue, 1990; Shirai et al., 1990; Alaranta et al., 1991; Crowe et al., 1991). Acetylcholine and nonadrenergic-noncholinergic dilator agents probably act indirectly by stimulating the vascular endothelium to release the endothelium-derived relaxing factor (EDRF) or nitric oxide (NO) (Azadzoi et al.,

1990; Knispel et al., 1992).

The arterial phase is characterized by dilatation of the sinusoids, that are filled with blood, so that tumescence is achieved (Lue, 1990; Fernandez et al., 1991). Through the veno-occlusive mechanism in the tunica albuginea, tumescence and rigidity of the penis are maintained (Fournier et al., 1987).

In organic impotence, we found histological changes corresponding to the tissues involved in the three phases of erection (Krane et al., 1989). In all types of organic impotence the most affected tissue was the smooth muscle tissue of the trabecualae and the subendothelial valvular mechanism of the helicine arteries (Jevtich et al., 1990; Wespes et al., 1990a). Thus, atrophy, degeneration and replacement of the smooth muscle tissue by connective tissue were observed (Persson et al., 1989; Jevtich et al., 1990; Meuleman et al., 1990; Wespes et al., 1990a, 1991). These changes, correlating with the degree of impotence, can justify erectile dysfunction, as tumescence and penile rigidity are only obtained after the relaxation of integral erectile tissue (Persson et al., 1989; Jevtich et al., 1990). Several studies agree with our findings, with the exception of Vickers et al. (1990) who support the contention that no remarkable histological lesion is observed in such cases.

Through image analysis method assisted by computer the quantity of smooth muscle tissue can be exactly defined as can its proportion in relation to the connective tissue of the trabeculae (Wespes et al., 1990a, 1991). Otherwise, this can be subjectively done with simultaneous evaluation of the architecture and the integrity of the smooth muscle bundles.

Studies performed with electron microscopy have shown ultrastructural alterations not only in the smooth muscle cells but also in the vascular endothelia (Bossart et al., 1980; Kano et al., 1987; Khawand et al., 1987; Persson et al., 1989; Jevtich et al., 1990; Fernandez et al., 1991; Mesdorf et al., 1991; Tamaki, 1992). Persson refers to an increase of the mitochondria and cyto-plasmic vacuoles in smooth muscle cells, the presence of pleomorphic nuclei, irregular border, loss of basement membrane and deplacement of the myo-filament to the periphery (Persson et al., 1989).

The insufficient blood supply of the smooth muscle tissue in arterial disease could be the pathogenetic mechanism leading to the histological changes. However, the existence of lesions in patients with venous leak as well, makes it possible that the problem in such cases is also inside the corpora (Wespes et al., 1990a,b).

The observed arteriosclerotic lesions of the penile vessels, as well as sinusoidal fibrosis, theoretically justifies the disturbance of the arterial phase (Hanju, 1988). The changes of the tunica albuginea and the underlying vasculoconnective tissue could be responsible for the disturbance of the venous phase (Goldstein et al., 1985; Bitsch et al., 1990). The relatively non-expansible tunica albuginea acquires elasticity with the appearance of elastic fibres and is

unable to compress the efferent venous network in order to maintain the final tumescence and rigidity of the penis (Bitsch et al., 1990).

The combination of different histological lesions may contribute to the dysfunction of different phases of the complex erectile mechanism. The degree and type of these lesions must be carefully and reciprocally coestimated before the correct choice of treatment is made (Jevtich et al., 1990; Meuleman et al., 1990). With mild histological changes self-injection therapy is perhaps enough. In cases with severe reduction of the functional smooth muscle of the trabeuale and helicine arteries, it is clear that the sole solution is implantation of a prosthesis, since the target organ of the vasoactive substances has been destroyed. The results of vascular sugery also depend on the condition (state) of the functional smooth muscle tissue as well as of the penile vessels.

The important role of penile biopsy is evident, as it contributes not only to the diagnosis, but also to the correct choice of treatment for male impotence, thus making the future management of such cases more optimistic.

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