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RESEARCH ARTICLE

HISTOPATHOLOGIC CHANGES IN PENIS IN ORGANIC ERECTILE DYSFUNCTION DUE TO SYSTEMIC DISEASE

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ABSTRACT

Penile Corpora Cavernosa have a complex histology and blood supply that may mirror systemic illnesses and provide an insight into the pathogenesis and pathology of various systemic disorders leading to Organic Erectile Dysfunction. The present study aims to investigate the extent and nature of pathologic changes in penile corpora cavernosa in patients with erectile dysfunction due to systemic illness.

INTRODUCTION

Penile corpora cavernosa have a complex anatomy and histology which undergo a series of programmed changes during physiologic erection, the cornerstone of which is a prompt and sustained vasodilation and engorgement of cavernosal sinusoids leading to a rigid erection.[1,4]

A large number of systemic diseases that affect vascular integrity like Diabetes, Hypertension, Hyperlipidemia, Chronic heavy smoking, Alcohol abuse and Veno-occlusive disease affect the structure and histology of corpus cavernosum tissue and blood vessels leading to Erectile Dysfunction. [2,3]. We present the morphologic findings in Penile Corpus Cavernosum Biopsies of 35 patients with one or several systemic diseases leading to Erectile dysfunction with a special emphasis on smooth muscle to collagen ratio and histology of penile vessels in these conditions. [1, 3]

MATERIALS AND METHODS

- Bilateral Corpus Cavernosum biopsies were obtained from 35 men with complaints of Erectile dysfunction and associated co-morbidities undergoing evaluation for the purpose of suitability of Penile Prosthetic Implants.
- During the process of Penile Implant surgery open biopsies were obtained from bilateral (Right & left) corpora cavernosa (a minimum of 0.5 cm in aggregate) and immediately transferred to appropriately prelabelled containers with 10% neutral buffered formalin.[13]
- Bilateral penile biopsy specimens received in the histology laboratory in barcodedlabelled containers were processed routinely and separate numbered paraffin embedded blocks made of both Right & Left Corpus Cavernosum in each patient.
- Both the right & left corpus cavernosum biopsy blocks were then sectioned to produce.
- 3-4 µm thick sections. A minimum of 6 sections were taken per block in three slides at different levels.
- Two slides (A minimum of 4 sections) were stained with Hematoxylin and Eosin.
- (H&E) stain as per standard routine protocol & 1 slide (2 sections) were stained with Masson Trichrome connective tissue stain for the identification of smooth muscle (Fuchsinophilic) and fibrous tissue (blue in color). The percentage of smooth muscle in trabeculae of corpora cavernosa is normally between 70 and 90%. The histologic changes observed in our patients were graded based on smooth muscle percentage as Mild (50 to 70%); Moderate (30 to 50%) and Severe (<30%).
- Each of these 6 sections were evaluated by light microscopy for the following parameters :

  - ❖ Precentage of smooth muscle and collagen.
  - ❖ Presence of perisinusoidal fibrosis.
  - ❖ Patency of Sinusoids /Cavernous veins
  - ❖ Histology of Helic ine arteries-Intima and media.
  - ❖ Status of small caliber arterioles
  - ❖ Nerve fibres and
  - ❖ Interstitium

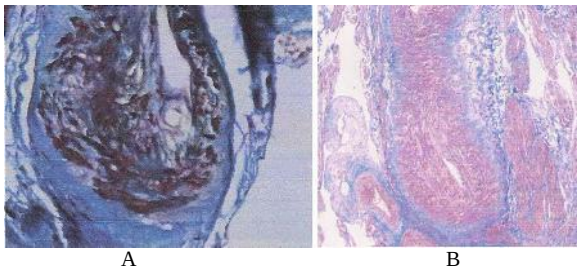
RESULTS AND DISCUSSION

The histologic parameters evaluated were correlated with history of Diabetes and Hypertension with or without Hyperlipidemia, chronic smoking and Alcohol abuse. [3,4]

30 of the 35 patients studied had a history of Diabetes Mellitus for a minimum of 5 years with or without other co-morbidities.

The following findings were noted in all the 60 biopsies evaluated in patients with diabetes:

- Dilation of Cavernosal sinusoids with Perisinusoidal fibrosis.
- Moderate to Marked hyaline arteriolosclerosis with vacuolation of smooth muscle fibres.
- Dilation of sinusoids with perisinusoidal fibrosis.
- Marked hyaline arteriolosclerosis with vacuolation of smooth muscle fibres.



A B

Figure 1A: M arked Arteriosclerosis in hy p ertension &diabetes – M assonTrichrome stain –M agnification × 400
Figure 1B: Perisinusoidal fibrosis and arteriosclerosis in hy p erlip idemia & diabetes – M asson trichrome stain –M agnification × 100

- Fibrointimal hyperplasia with thickening of media.
- Average smooth muscle to collagen ratio – 0.4 (Smooth muscle percentage –
- 40% - Moderate) [4,5]
- Edema and splaying of nerve fibres.

The following findings were observed in 27 patients (54 biopsies) with Hypertension with or without associated Diabetes.

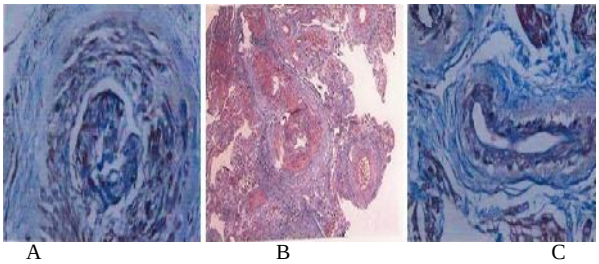
- Decreased smooth muscle to collagen ratio – 0.4 to 0.5 (smooth muscle 40 to
- 50% - Moderate) [5,6]
- Fibrointimal hyperplasia with mucoid intimal change and fibrosis of media.
- Perisinusoidal fibrosis.
- Moderate hyaline arteriolosclerosis.

Hyperlipidemia (16 patients – 32 biopsies) – all with associated hypertension and / or diabetes [6, 7]

- Perisinusoidal fibrosis [Figure 1B]
- Reduced smooth muscle to collagen ratio – 0.6 (60% Smooth muscle – Mild)
- Atherosclerosis
- Vascular changes with interstitial fibrosis [8,9]

Chronic Heavy smoking (7 patients – 14 biopsies) – 4 with associated hypertension.

- Vasospasm
- Atherosclerosis
- Fibrointimal and mucoid intimal hyperplasia. [Figure 2A, 2B & 2C]



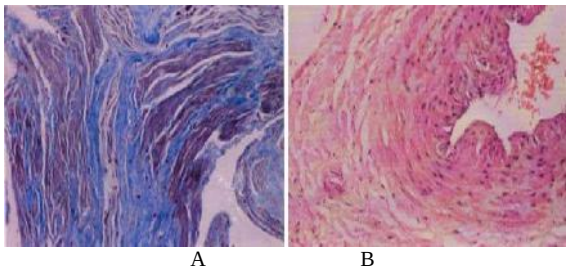
A B C

Figure 2A: Mucoid intimal hyperplasia in artery in chronic heavy smoking –Masson trichrome stain –Magnification × 400
Figure 2B: Severe arteriosclerosis in chronic heavy smoking – Masson trichrome stain –Magnification × 100
Figure 2C: Fibrointimal hyperplasia in chronic heavy smoking – Masson trichrome stain –Magnification × 400

- Interstitial and perisinusoidal fibrosis and hyalinization.

Alcohol Abuse (5 patients – 10 biopsies) all with associated Diabetes and / or Hypertension.

- Fibrosis and decrease in smooth muscle to collagen ratio (0.5 to 0.6-50 to 60% smooth muscle - Mild) [Figure 3A & 3B]



A B

Figure 3A Interstitial fibrosis in alcohol abuse &chronic heavy smoking –Masson trichrome stain – Magnification × 400
Figure 3B Severe mucoid intimal hyperplasia in alcohol abuse & chronic heavy smoking – Hematoxylin & Eosin stain – Magnification × 400

- Vascular changes
- Luminal narrowing

Summary of observed histopathologic changes in 35 cases analyzed

1. Increased interstitial fibrosis and hyalinization. [8,9,10]
2. Reduction in smooth muscle content and increase in collagen content (Normal trabecular smooth muscle content is 70-90%. Reduction in smooth muscle content was observed in all cases ranging from mild to moderate.
3. Fibro elastic hyperplasia of arterial / arteriolar wall, fibrosis hyalinization and thickening of arterial wall.
4. Fibro intimal hyperplasia, intimal hyalinization, mucoid changes in intima, endothelial cell apoptosis.
5. Peri arterial, peri arteriolar and peri sinusoidal fibrosis.
6. Oedema and splaying of nerve bundles (Observed only in Diabetic cases).

CONCLUSIONS

- Penile Corpus Cavernosum Biospies provide important in sights into pathobiology of erectile dysfunction associated with systemic diseases.
- All systemic ill-ness producing Erectile dysfunction show similar changes in corpora cavernosa including reduced smooth muscle, interstitial fibrosis and vascular changes
- This is probably due to the common etiologic pathway producing erectile dysfunction in all these conditions – namely vascular compromise and vascular dysfunction leading to hypoxemia and a cascade of Histomorphologic changes triggered by Hypoxia - namely smooth muscle injury and loss fibrosis due to increased collagen and extracellular matrix deposition. [7,8,9]
- The morphologic evaluation and grading of changes observed Penile Corpus Cavernosum biopsies may provide Prognostic information in patents with erectile dysfunction. [10,12]
- Estimation of smooth muscle to collagen ratio and percentage of smooth muscle and semi-quantitative evaluation of degree of vascular changes may help to stratify and estimate risk of progression to end stage Erectile Dysfunction.
- The importance of Penile Biopsy evaluation lies in the possible contribut ion it may make in terms of choice of therapy. [7,8,9]
- The absence of sufficient smooth muscle tissue on histologic evaluation may preclude the use of reconstructive surgery or medical treatment and indicate a subset of patients wherein a Penile Prosthesis / Implant is necessary. [11]

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