ON THE HERNIA-LIKE PROTRUSIONS SUGGESTIVE OF REGENERATION OF THE HUMAN SEMINIFEROUS TUBULE

BY

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PREFACE

There have been, up to date, only two descriptions on the hernia-like protrusions of wall of the human seminiferous tubule. Spangaro described briefly on the protrusions seen exclusively in the old aged testicles, referring to it merely as diverticulum or hernia of the seminiferous tubular wall. Stieve reported that the similar protruding structures were found not only in the aging males, but also in the young adults of early third decade, and that they are spheroid in shape thin-walled, and contain moderate amount of atrophic germ cells. Little attention, however, was paid to morphological significance and histogenesis of the protrusions in their brief reports. In order to investigate this kind of little-appreciated changes, therefore, we performed a systemic and more detailed study of their morphology and tried to understand their histogenesis also from a statistical point of view.

MATERIALS AND METHOD

We observed human testes of 419 autopsy cases, 169 of which being hospital cases and the other Medical Examiner’s. Paraffin sections were stained by H. & E., Elaticum. Gieson, PAS, Azan and Pap’s methods. From every autopsied testis, a sagittal section through rete testis was obtained in order to observe geographical distribution of the changes. Particularly for the tridimensional view of the protrusions, serial sections were prepared in several representative cases. Tubule dissectioning method was also applied in several cases.

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FINDINGS

1. On distribution and shape of the protrusions of the seminiferous tubule

The protrusions tend to arise from the convex aspects of the wall of the seminiferous tubules which run very much wound and twisted. Corresponding sites along the strongest curvatures appear to be most pre-dilected. In the initial stage a minute elevation of a very localized part of the tubular wall develops into a hemi-spheroid or almost spheroid protruding (Figs. 3~4). When further developed, the protrusions become larger showing a somewhat complex appearance due to irregular foldings (Fig. 1~2) and infrequently secondary protrusions (Fig. 8), into the adjacent intertubular loose interstitium. The rather irregular configuration of the protrusions encountered might be attributable to the result of expansion of the wall of the structures against less resistant interstitium, their convexity corresponding to the freely expanding part, while their concavity to the presence of the vessels and seminiferous tubules. Such a constriction as seen in a sand-glass is commonly demonstrated at the opening of the protrusions to the original tubule. Not infrequently, a number of small and large protrusions are arranged in a row on the same aspect of a single tubule (Fig. 5). Very rarely, two different protrusions starting from two separate tubules are observed colliding with one another (Fig. 7). The greatest protrusion encountered in this series measured approximately 100 μ in long length, from its basis to the distal convexity.

Preference either of the hilar or peripheral region of a testis as a whole in distribution of the lesions has not been observed.

2. On structure of the protrusions

Histologically, hernia-like protrusions take place invariably in the slightly or moderately atrophic testes in which average calibres of the seminiferous tubules are diminished down to 100~150 μ from about 200 μ of the normal adult and there appears a broadening of the intertubular interstitial spaces in turn (Figs. 5~8).

Such atrophic tubule with the characteristic protrusions contain reduced number of germ cells indicative of moderate hypospermatogenesis, corresponding to the 2nd or 3rd grade testicular atrophy of Schinz u. Stolzolosky’s classification in which concomitantly decrease or disappearance of spermia and spermatid, and moderate thickening of the inner hyaline layer and hyperplasia of the outer elastic layer of the basement membrane are usually seen. The inner surface of the wall of a newly formed protrusion is covered with one or two layers of spermatogonia and Sertoli cells, but that of a well developed protrusion displays a differentiated germinal layer as in the original tubule, so that similarly constituted cellular lining
continuously extends into through the communicating slit. A protrusion appears never to have more active spermatogenesis than the original seminiferous tubules.

The walls of the protrusion are characterized by dehyalinosis of the inner hyaline layer and by attenuation of the outer elastic layer, both in continuity with that of the original tubular wall (Figs. 4~8). Dehyalinization is demonstrated by more intensive argentaffinity on Pap's silver impregnation and by poor stainability on conventional collagen stainings, so that the latter may give an impression of disappearance of the inner layer. Hence, the characteristic changes of the wall can be readily visualized by silver stain when included in the plane of the section. Hitherto masked silver fibers in the inner hyaline layer become apparent by intensive argentaffinity in the dehyalinization process. This phenomena have been called demasking or phanerosis of silver or reticulin fibers by K. Muto. Thus, demasked silver fibers featuring as thickened tape-like fibrous structures run through the inner layer of the protrusion in an irregular looisy network, merging with the hyaline layer of the original tubules around the opening of the outpocketing. The thin outer elastic layer is noticeable consisting of looisy fine silver fibers (Figs. 9~10). These changes in the features of the basement membrane are especially remarkable at the distal portion of the protrusions.

Such a dehyalinotic change of the wall of the protrusions is clearly distinguishable from those found in edema, inflammatory infiltration, cystic formation of the seminiferous tubular wall, where demasked network is composed of comparatively fine silver fibers. Dehyalinization under different conditions can be not the same. In case of dehyalinization concerned in the protrusions, it might be assumed that masked fibers of the inner hyaline layer become phanerotic, fuse in bundles and extend over on the basis of considerably rapid expansive development of the protrusion. After completion of dehyalinosis, the entire wall of the fairly well developed protrusions, except for the basic portion, changes into a primitive basement membrane, which indicates a membrane system composed of a silver meshwork with sol-like matrix of Muto (1987) (Fig. 11). It simulates the primitive membrane basement (Hatakeyama) of the early seminiferous tubule in the 2nd fetal month. However, there is great difference between the two as observed by Elastica-v. Gieson's stain: while the primitive basement membrane of the protrusions can be seen as a thin elastic membranous structure in which resorcin-fuchsins appears homogenously impregnated in fiber and matrix of the fine silver meshwork (Fig. 12), the corresponding fetal structure lacks all the features.

Shrinkage of the hernia-like protrusions is brought about with further
progress of atrophy of the original tubules. Almost all protrusions of rather markedly atrophic tubules become smaller in size displaying blunt contour with denser primitive membrane or elastic membrane of the wall. The wall of the protrusions remains thin all through the process in contrast with progressive thickening of that of the atrophic original tubules and become remodeled by hyalinisation of its inner surface. It appears ultimately very atrophic, only to be recognized as a tiny process of the tubular wall (Fig. 14). Such contracted protrusions and tubules, usually contain atrophic Sertoli cells. When tubular atrophy advances rather rapidly as in the case of focal atrophy, type 1 (Hatakeyama), the protrusion from such a hyalinized tubule may remain still as a thin-walled process containing a few flat Sertoli cells (Fig. 13).

3. Age incidence

As recorded in the Table, the protrusions never occur before puberty or below 15 years of age. Among the acute death cases, incidence rate of the lesions constitutes 2.5% (2 out of 79 cases) in the 3rd decade, 37% (13 out of 35 cases) in the 5th decade and 45% (14 out of 29 cases) in the 7th decade. Comparing data among the hospital cases are as follows; 35% (7 out of 21 cases) in the 3rd decade, 52% (21 out of 40 cases) in the 5th decade and 91% (30 out of 33 cases) in the 7th decade. No close relation with any endocrinological disorder was noted in occurrence of the lesions among the present autopsy series.

4. The hernia-like protrusions can be plainly differentiated from the blind ductules infrequently present in the seminiferous tubules. The blind ductules have the same appearance as normal contortous seminiferous

<table>
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<th>Age</th>
<th>Medical Examiner's cases</th>
<th>Hospital cases</th>
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<tr>
<td></td>
<td>Number of case</td>
<td>Number of protrusion</td>
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<tr>
<td>10-15</td>
<td>2</td>
<td>0</td>
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<tr>
<td>16-19</td>
<td>15</td>
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<td>20-29</td>
<td>79</td>
<td>2 (2.5%)</td>
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<td>30-39</td>
<td>36</td>
<td>7 (1.9%)</td>
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<td>40-49</td>
<td>35</td>
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<tr>
<td>60-69</td>
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<td>70-79</td>
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<tr>
<td>Total</td>
<td>250</td>
<td>59 (23%)</td>
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tubules in thickness and winding features. They range from about 0.5 mm to 2–3 cm in length. Their histological construction is the same as the normal tubules.

5. The Leydig cells present in the protrusion-positive testes show no significant alteration. There was neither hyperplasia nor regressive change of them.

**Comment**

A hernia-like protrusion arise from a seminiferous tubule in atrophy of moderate degree which displays moderate reduction in number of the germinal cells, and regression or disappearance of spermatid and spermia. This is in accordance with Stieve’s description. However, they are only encountered in the testis falling into atrophy through chronic course exhibiting moderate narrowing of the lumina of the seminiferous tubules with their wall sclerosing. It has not been observed in an acute atrophic testis without thickening of the wall of the tubules.

Incidence rate of the lesion amounts to 35% as early as in 3rd decade in our autopsy cases from the hospital in comparison with 2.5% among the cases of acute death obtained from the Medical Examiner’s Office. Its rate rises with aging of life up to 91% in the 7th decade.

All the evidences lead to the conclusion that chronic atrophy of the seminiferous tubule induced by aging factor and by various nosological causes throughout postpubertal ages bears a close connexion to the occurrence of the hernia-like protrusions therefrom.

The fully developed protrusions manifest complex outlines corresponding to the surrounding spaces of loopy connective tissue. The parenchymal cell layer of the original tubule is in continuity with that of the protrusions across the outpocket opening, lining over the dehyalinized inner basement membrane. Thus, morphology of the protrusions is consistent with herniation of the tubule with its contents, germinal cells, as Spangaro and Stieve have interpreted it.

After completion of dehyalinosis characteristic to this type of lesion, the inner layer of the protrusion wall undergoes certain changes and attain a form of primitive basement membrane with homogenous elastin-positive fibers and matrix. In lumina of such protrusions, there is spermatogenesis although it can be as hypoplastic as in the adjacent tubules.

The facts that the protrusions occur in a chronic atrophic testicle and are capable of maintaining germ cell production, might suggest that they could compensate reduction of the germ cell production in the rest of the tubule by increasing the spermatogenetic bed. If it is true, it might not
be a mere mechanical herniation but a progressive biological adaptation. This may lead to the interpretation that the protrusion of the seminiferous tubule is a type of abortive budding regeneration in the form of tubular herniation.

An evidence that the protrusions are almost always found in atrophic tubules might also offer a possibility that endocrinological environment provoking the lesion does not allow restoration to perfect spermatogenesis, once it starts. As to whether or not atrophic testis with the protrusions does mean irreversibility of hypo- or dysendocrinological status in spermatogenesis, the question remains open at present when general endocrinological situation and its relation to the protrusion formation are obscure. In this respects, biological implication of this kind of lesion appears important from the clinico-pathological point of view, especially concerning treatment of the male sterility.

**Summary**

1. Human testes of 419 autopsy cases, 169 of which being from hospital cases and the other 250 from Medical Examiner's ones, were observed for investigation of hernia-like protrusions of the seminiferous tubule.

2. The hernia-like protrusions occur in moderately atrophic tubules falling into through chronic course induced by aging of life and various nosological causes. They are seen in all ages of life except for prepubertal period, showing increasing tendency with aging.

3. The protrusions are usually almost spheroid with complex contour corresponding to the surrounding space of the loose connective tissue. Their wall are characterized by dehyalinization of the inner hyaline layer and attenuation of the outer elastic layer. This lesion may be attributable to relatively rapid expansion of the tubular wall during outpocketing process.

4. The wall of the fairly well developed protrusions becomes consisted of a primitive basement membrane with elastin-positive fibers and matrix, and parenchymal contents in the lumina display the same spermatogenesis as that in the original tubule.

5. Atrophy of the protrusions is noticeable concomittantly with progressive atrophy of the original tubule.

6. The hernia-like protrusions might be considered as budding regeneration in the form of tubular herniation.

7. Biological implication of this kind of lesion appears important from the clinico-pathological point of view, especially concerning treatment of the male sterility.
Acknowledgement

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Literatures

Plate 1

EXPLANATION OF FIGURES

Figures 1–3: Various appearance of the hernia-like protrusions of the dissected seminiferous tubules.

Figure 4: Two protrusions in fig. 3, are histologically demonstrated, one minute initial one on the left (arrow) and another spheroid on the right.

Figure 5: Three protrusions arrange in a row in a tubule. Elastica-v. Gieson stain.

Figure 6: A well developed protrusion occupies the surrounding interstitial space. Elastica-v. Gieson stain.

Figure 7: Two protrusions arising from independent tubules, collide with one another (arrow). Elastica-v. Gieson stain.

Figure 8: A secondary daughter protrusion is seen (arrow). Elastica-v. Gieson stain.
Plate 2

EXPLANATION OF FIGURES

Figures 9-10: Histological structure of the protrusion wall on Pap's silver impregnation. The inner hyaline layer are dehyalinized, including tape-like fibrous structures intensively silver-impregnated (arrows). The outer elastic layer are demonstrated consisting of loosy fine silver fiber network.

Figure 11: The wall of a well developed protrusion shows the primitive basement membrane constructed with the fine silver fiber meshwork with sol-like matrix (arrow). Pap’s silver impregnation.

Figure 12: A thin homogenous elastic membrane is seen consistent with the primitive basement membrane on silver impregnation (arrow). Elastica-v. Gieson stain.

Figure 13: A protrusion involved in focal atrophy, I type, of the tubule. The wall show slight proliferative outer elastic layer & edematous thickening of the inner hyaline layer. But, it remains lumina. Another protrusion is present on the left side. Elastica-v. Gieson.

Figure 14: Shrinkage of the lesion in the highly atrophic tubule (arrow). The inner layer of the protrusion are hyalinized. Elastica-v. Gieson stain.
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