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Study of Spermatic-Lymphatic Circulation in Leprous Patients with Gynecomastia

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Before studying gynecomastia in leprosy and describing seven cases, we would like to recall the different theories about gynecomastia-pathogenesis in general. The mammary gland develops normally under the influence of a mammogenic and a mammotropic compound.

The mammogenic compound. This compound is made up of estrogens inducing the development of the galactophorous tubules and of progesterones which develop the secreting acini. Other hormones like desoxycorticosterone, testosterone and insulin have a part in the induction of mammogenesis.

The mammotropic compound. This is secreted by the hypophysis. It enables the action of the forenamed hormones: it is the mammotropic hormone. Corticotrophin and the thyroid-stimulating hormone (TSH) are components of this mammotropic compound. According to the usually admitted diencephal-hypophyseal theory, when a pathologic state occurs, gynecomastia is related to an abnormality of these different factors. This theory explains most cases of gynecomastia, including gynecomastia designated as physiologic, as at birth, at puberty and at the andropause.

This theory takes into consideration the following different contributing factors: (1) absolute hyperestrogenism, (2) relative hyperestrogenism provoked by a disturbance of the estrogenic-androgenic ratio, (3) hyperandrogenism, and (4) encephalic troubles.

Other factors playing a part with these hormonal factors are heredity, local tissue factors and peripheral and neurovegetative nervous systems.

Gynecomastia, in a considerable proportion of leprosy cases, usually lepromatous, is related to a testicular lesion. In fact, the direct action of *Mycobacterium leprae* on the seminiferous tubules is well known; lesions of the seminiferous tubules are observed in 90 per cent of lepromatous cases. But how do we explain the fact that only six to 19 per cent of lepromatous cases present gynecomastia, whereas in 90 per cent of cases *M. leprae* provokes testicular lesions? Still another problem has to be solved. How can the Leydig cells be modified toward hyperplasia when *M. leprae* has no action on them?

We have found the solution of these problems by discovering a spermatic-lymphatic stasis and by the use of testiculo-funicular lymphographies. In fact the testiculo-funicular lymphographies show two types of lesion: (1) blocking of the inferior branches of the spermatic collector delta with downward reflux of the lymph, and (2) blocking of the spermatic collector at the usual level of the Horowitz-Zeisl node.

From the histologic point of view we must indicate two frequent testicular lesions: (1) noninflammatory acellular edema of static type, and (2) Leydig cell hyperplasia (Fig. 1).

The occurrence of gynecomastia in leprosy requires the conjunction of two factors: (1) seminiferous tubule lesions caused by *M. leprae* and (2) mechanical lymphatic stasis due to blocking provoked by a lesion of a deep node.

This theory is illustrated by observations on seven leprous patients presenting gynecomastia, who have been treated at a general hospital in 1967 and 1968. We shall see, by studying two cases of gynecomastia in nonleprous patients, that blocking of spermatic lymphatic circulation can be found in other diseases than leprosy.

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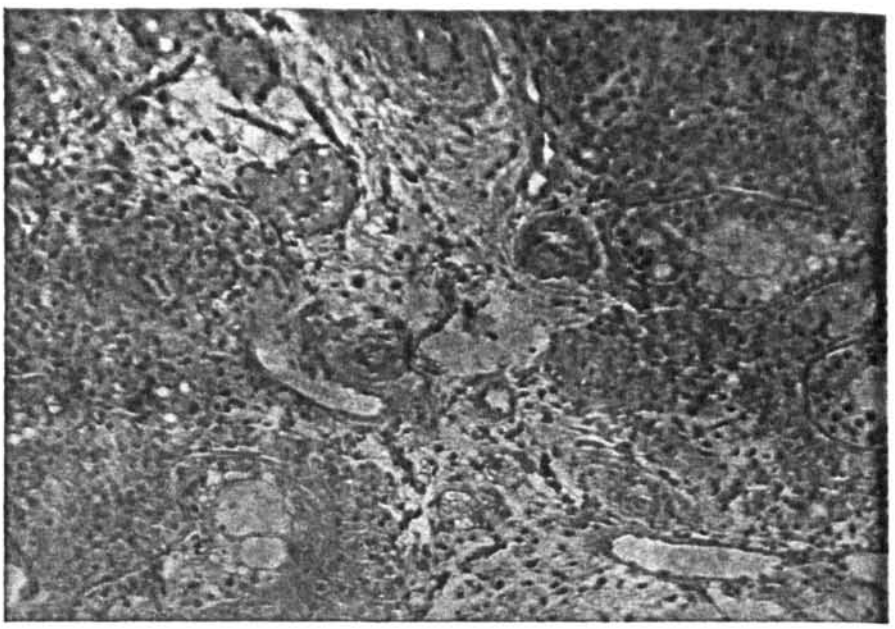

FIG. 1. Hyperplasia of Leydig's cells and interstitial acellular edema.

OBSERVATIONS

Observation No. 1. Ba . . . Bi . . . 16 years of age. *Lepromatous leprosy.* Bilateral gynecomastia. 17-ketosteroids: 3.1 mgm; 17-hydroxysteroids: 5.8 mgm; 50 SU< FSH<100 SU. *Testicular biopsy*: Some seminiferous tubules are immature, but spermatogenesis is normal. Islets of Leydig cells are normal. Slight acellular edema in the interstitial tissue between the tubules. Normal vessels. *Testiculo-funicular lymphography*: Subdiaphragmatic high blocking with stasis and very important reflux.

Observation No. 2. D . . . Iss . . . 39 years of age. *Lepromatous leprosy.* Bilateral gynecomastia. FSH≧100 SU. *Lymphography*: low tubular blocking of the spermatic collectors. On the lymphogram the blocking was situated at L-5 and S-1. Hypertrophy of the Horowitz node.

Observation No. 3. D . . . G . . . 30 years of age. *Lepromatous leprosy.* Bilateral gynecomastia. Elephantiasis of the lower limbs. FSH: limit-level at 5 SU. 17-ketosteroids: 0.45 mgm; 17-hydroxysteroids: 2.8 mgm. *Testicular biopsy*: Very important interstitial edema separating the seminiferous tubules. There are very few cells, but most of them are lympho-plasmocyte infiltrates. The seminiferous tubules are sclerosed or the Sertoli cells are regressing. Mature spermatozoids are very scarce. Leydig cell islets: adenomatous, big clusters of secreting cells without pigmentary degenerative accumulation. *Bush-Hayegh lymphography*: Latero-vertebral blocking at the L-3 level.

Observation No. 4. F . . . Gn . . . 25 years of age. *Lepromatous leprosy.* Bilateral gynecomastia. FSH limit-level at 5 SU. 17-ketosteroids: 4.9 mgm; 17-hydroxysteroids: 2.5 mgm. *Testicular biopsy*: Normal seminiferous tubules. Spermatogenesis leads to spermatozoid stage. Interstitial tissue: some edematous regions. Elsewhere the interstitial tissue is abundant and dense, with numerous collagen fasciae and few fibrocytes. The Leydig cell islets are neither atrophic nor hyperplastic. *Lymphography*: The lympho-spermatic collector is very distended and varicose on each side. There is a reflux. Latero-vertebral and prevertebral lymphatic varices are due to a subdiaphragmatic blocking.

Observation No. 5. S . . . Ma . . . 45 years of age. *Lepromatous leprosy.* Bilateral

gynecomastia. FSH 25 SU/liter. 17-ketosteroids: 2.5 mgm/24 hours; 17-hydroxysteroids: 2.1 mgm./24 hours. *Testicular biopsy*: Interstitial tissue largely distended by loose edema, with few cells, almost none of which are inflammatory. In places there is a collagen deposition. All the few seminiferous tubules observed are degenerated in a sclerous or sclero-lepromatous way. The Leydig cell islets present a voluminous edema including secreting cells. *Lymphography*: Latero-vertebral blocking at the L-2 level.

Observation No. 6. T... Ma... 58 years of age. *Lepromatous leprosy.* Bilateral gynecomastia. FSH: 5 to 25 SU. 17-ketosteroids: 5.8 mgm.; 17-hydroxysteroids: 4.8 mgm. *Testicular lymphography*: Obstruction of both cords.

Observation No. 7. P... Do... 50 years of age. *Lepromatous leprosy.* Bilateral gynecomastia predominant on the left side. Perforating ulcer of foot. Bilateral testicular atrophy. 17-ketosteroids: 4.2 mgm.; 17 hydroxysteroids: 3.1 mgm.; FSH 25 SU. Anatomico-pathologic examination shows an acellular edema and hyperplasia of Leydig cells. The *funiculo-testicular lymphography* shows: (1) on the right side, distinct complete blocking at the L-3 level, with dilatation and moniliform aspect upstream; (2) on the left side, incomplete blocking at the L-2 level, with very important upper stasis; (3) reflux in the lumbo-aortic lymphatic system, and (4) a lumbar node presenting a lacuna open at the inferior edge (Figs. 2 and 3).

Synthetic study of these seven cases indicates: (1) all patients were lepromatous; (2) gynecomastia was bilateral in all seven; (3) the FSH level was increased in four patients among the six for whom it was determined; (4) the 17-ketosteroid rate was lessened in all patients; (5) testicular

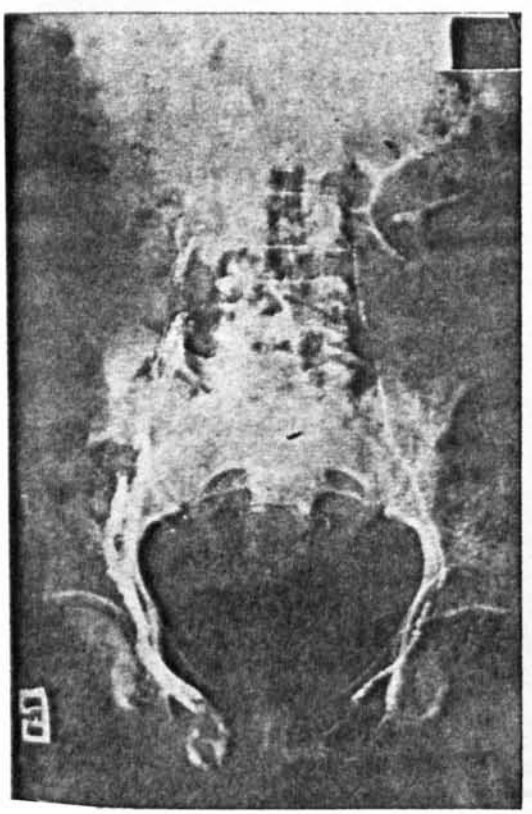

FIG. 2. Block of lympho-spermatic collectors at L_3L_4 level.

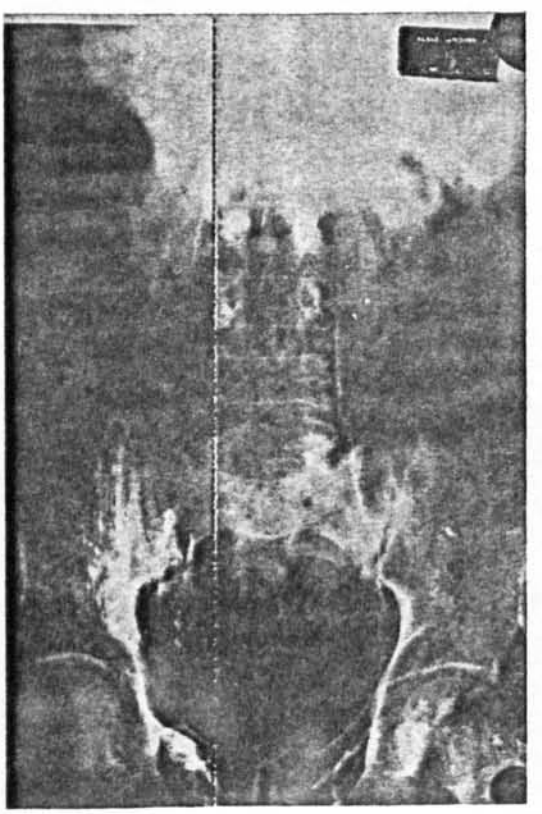

FIG. 3. Persistent block. Extravasation of lipiodol.

TABLE 1. *Summary of data on seven cases of gynecomastia in leprosy.*

Identification of patients	Type of leprosy	Gynecomastia	F.S.H.	17-keto-steroids	17-hydroxy-steroids	Testicular biopsy	Testicular lymphography (Bush-Sayegh)
Ba. Bi	Lepromatous	Bilateral	> 50 S.U. <100 S.U.	3.1	5.8	Acellular edema. Normal Leydig cells.	Subdiaphragmatic high blocking.
Di. Iss	Lepromatous	Bilateral	>100 S.U.			Not made.	Low blocking of the spermatic collectors at L.5 and S-1 levels.
D. Gab	Lepromatous	Bilateral. Elephantiasis of the lower limbs.	5 S.U.	0.45	2.8	Very important interstitial edema. Adenomatous islets of Leydig cells.	Latero-vertebral blocking at L.3 level.
F. Gni	Lepromatous	Bilateral	5 S.U.	4.9	2.7	Edema, in places in the interstitial tissue. Normal Leydig cells.	Subdiaphragmatic blocking. Very distended collectors with latero-vertebral and prevertebral lymphatic varices.
S. Matt	Lepromatous	Bilateral	> 25 S.U.	2.5	2.1	Important edema with few cells. Voluminous Leydig cells.	Latero-vertebral blocking at L-2 level.
T. May	Lepromatous	Bilateral	5 to 25 S.U.	5.8	4.8	Not made.	Very low blocking at the level of the two cords.
P. Dou	Lepromatous	Bilateral. Preponderant on the left side and perforating ulcer of foot.	25 S.U.	4.2	3.1	Acellular edema. Many Leydig cells.	Latero-vertebral blocking, complete on the right side, incomplete on the left, with very important upward stasis and reflux toward latero-vertebral nodes.

biopsy, when carried out, clearly showed an acellular edema; (6) finally, testicular lymphography showed lymphatic blocking in all seven cases, with (a) high blocking (two cases with reflux in the latero-vertebral chains), (b) latero-vertebral blocking at the terminal of the collector in the vertebral chains (four cases) and (c) low blocking (funicular one case) (Table 1).

Moreover, our seventh observation enabled us to notice the appearance of a lacunar node of still unknown etiology. First, as we knew the frequency of lymph-node tuberculosis in leprosy, we assumed a tuberculous etiology. Desikan and Job did actually find six cases of deep tuberculous adenopathies in necropsy of 27 leprous patients.

Eighth and ninth comparative observations of gynecomastia were made on nonleprous patients: S... Ab... 32 years of age. No etiology was discovered after clinical examination and biologic investigation of this patient (FSH 5 to 50 SU; 17-ketosteroids, 5.3 mgm. 17-hydroxysteroids: 3.2 mgm.

In one case testicular lymphography revealed a subdiaphragmatic blocking with stasis and important downward reflux. In the ninth patient contra-lateral passing was observed with impediment provoked by a sclerous node in a gynecomastia of intermediary origin.

These observations show a prevailing role of spermatic-lymphatic blocking in gynecomastia pathogenesis, but indicate that leprosy is not the sole cause of this blocking. Although no etiology was found in the latter case, a nondiscovered infectious or parasitic cause could induce the lymphatic blocking demonstrated by testicular lymphography (e.g., filariasis or streptococcic infection).

CONCLUSIONS

Thus, we see that the study of these seven new observations of gynecomastia in leprous patients enables us to corroborate the lymphatic blocking theory, based in part on hypertrophy of the Leydig cells. These Leydig cells have an important part in the occurrence of gynecomastia. The knowledge of this fact was made possible thanks to funiculo-testicular lymphographies, which were systematically performed on leprous patients presenting gynecomastia.

SUMMARY

Study of seven cases of lepromatous patients affected by gynecomastia, including in each case a testiculo-funicular lymphography, strengthens the arguments supporting the theory, already presented, of spermatic lymphatic blocking leading to an up-stream stasis with acellular edema and hypertrophy of the Leydig cells. This mechanical factor, associated with specific testicular lesions caused by *M. leprae* is an essential element in the search for a pathogenic explanation of the gynecomastia of leprosy.

Study of two cases of gynecomastia in non-hansenians affected by blocking of spermatic lymphatics brings up the problem of etiologic variation in this localization of lymphatic blocking in tropical pathology.