GONADAL INVOLVMENT IN LEPROSY — STUDY OF GYNAECOMASTIA, TESTICULAR AND EPIDIDYMAL INVOLVEMENT AND THERAPEUTIC EFFICACY OF INDIGENOUS DRUGS

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ABSTRACT — Sixty male patients of leprosy (mean age = 27.2+5.04 years) selected at random, were studied for gonadal involvement and therapeutic efficacy of two indigenous drugs. Of these 34 were married, with the mean duration of illness 4.17+3.27 years. Only those with lepromatous and dimorphous leprosy developed testicular and epididymal changes. Testicular pain and/or swelling (lepromatous =62.5%, dimorphous 30%) was the commonest presenting feature. Altered sexual function was observed in 34 (56.6%) cases, while 11 patients revealed altered sexual hair pattern and nine gynaeco-mastia. Reduced testicular size associated with soft feel was present in 25% of cases with no testicular sensation in 8 (13.3%) and impaired testicular sensation in 9 (15%) patients. Spermogram revealed azoospermia in 19 (35%) and oligospermia in 16 (26.6%) patients. Histopathological findings of testicle biopsy revealed evidence of leprous pathology irrespective of testicular size, semen picture and clinical manifestations. Histopatho-logical changes had shown marked variation and so did not enable categorising them into vascular, interstitial and obliterative phases. These changes were believed to be due to the altered gonadal state in leprosy. The therapeutic efficacy of the indigenous preparations, Speman and Tentex forte (Himalaya) was evaluated subjectively as well as objectively in 34 patients. 823% of cases showed subjective improvement while objective improvement in spermogram was noted in 87.5% cases with oligospermia. The drugs have no side effect and were well tolerated.

Key words: Gonads. Gynaecomastia. Testicle, Epididymes. Hanseniasis. Leprosy. Indigenous drugs.

1. INTRODUCTION

It is well known that leprosy affects the skin, peripheral nerves and internal organs1.17 which has also been confirmed by biopsy and autopsy studies. The effect of leprosy on the testes was first studied by Grabstald and Swain in 1952[9], who reported definite microscopic evidence of severe involvement in 20 patients with lepromatous leprosy in 3 biopsy and 17 autopsy specimens. Mitsuda16 in the same year was able to demonstrate lepra bacilli in the form of globi in the seminiferous tubules. Gynaecomastia has been observed in varying number of lepromatous

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patients in endemic countries[1,9]. This study is an attempt to assess the involvement of the testis, sexual behaviour and prevalence of gynaecomastia in male leprosy patients.

2. MATERIALS AND METHODS

Sixty male leprosy patients selected random-ly were studied and classified into various types according to the New Indian Classification of Leprosy 1982[3,4,7]. There were 32 patients of lepromatous, 10 of dimorphous and 18 of tuberculoid leprosy. Their age ranged from 14 to 50 years and the duration of illness varied from 3 months to 18 years (Table l).

A detailed clinical and family history was taken and each of them was subjected to full clinical and bacteriologic examination for lepra bacilli in the nasal smear and also after skin slit and scrapings, and histopathological study of the skin lesions. The seminal fluid was obtained by masturbation after an interval of not less than 3 days of abstinence and analysed imediate-ly. Counts of 80 million/ml or above were considered normal, those below 40 million/ml were taken as oligospermic and total absence of sperms as azoospermia. Testicular biopsies were examined after fixation in paraffin and stained with haematoxylin and losin, PAS and for A.F.B. Liver biopsies were done in patients having gynaecomastia using the Vim-Silverman biopsy needle.

Details of testicular involvement, gynaeco-mastia, hair growth pattern and history of sterility, impotence, loss of libido, ejaculation etc., were recorded. Testicular size was measur-ed with callipers.

Prior to treatment the semen was examined for its amount, total number of sperms, percent-age of motile sperms and grading of motility of sperms. The semen examination was repeated after every month for 3 months and then after 6 months of therapy. Thirty four patients who had sexual symptoms and/or changes in semen etc., were given the indigenous drugs Speman, 2 tablets three times a day and Tentex forte, 2 tablets at night for 6 months or more, the period of the clinical trial. The results were compared with cases who did not receive these drugs. The response to the treatment was graded as belowl9:

l. Marked improvement: — The sperm count rose to more than 40 million/ml, with motility of sperms more than 60% at the end of one hour after semen collection.
2. Moderate improvement: — The sperm count varied between 20-40 million/ml with 50% sperm motility.
3. No improvement: — There was either no Improvement or the sperm count and motility improved only marginally.

3. RESULTS

Of these sixty patients 34 were married. Forty one (68.3%) of them gave a history of testicular pain and swelling of one or both testes in the past or at time of examination. Thirty four (56.6%) patients had sexual symp-toms in the form of impotence, loss of or diminished libido and sterility (9 patients). The semen analysis revealed azoospermia in 9 (15%) and oligospermia in 17 (28.3%) patients whereas 24 of them had normal sperm count (Table 2). Oligospermia and azoospermia were mostly seen in lepromatous cases (38% and 50% of cases respectively), whereas in dimor-phous leprotics it was seen in patients with predominant features of lepromatous leprosy. Two cases of lepromatous leprosy of 3 months duration had oligospermia. Oligospermia and azoospermia were seen in two patients of tuberculoid leprosy but these patients had suffered from mumps in their childhood and were having small atrophied testes.

The testes were smaller and soft in 14 cases (23.3%) (Table 3). All the 9 patients with gynaecomastia (figure l) had small and soft testes. Testicular sensation was preserved in all patients of tuberculoid leprosy, 7 of dimorphous and 18 of lepromatous leprosy.

Twenty five biopsy specimens of the testicle were available out of 27 attempted. Six biopsy specimens were essentially normal. Primary testicular atrophy, characterised by germ cell hypoplasia (hypospemiatogenesis), was seen in 4 cases of lepromatous leprosy (Table 4). Fifteen biopsy specimens showed definite histological changes which varied markedly and hence it was not possible to categorise them into vascular, interstitial and obliterative phases[9,13] because all specimens showed features of more than one phase as shown in

figures 2 and 3. These changes were grouped under three categories[14] i.e., minimal, intermediate and maximal changes (4, 6 and 5 cases respectively). Presence of A.F.B. in the specimens (9 cases) had no correlation with the severity of histopathological changes.

All the patients with gynaecomastia (9 cases) showed severe involvement of testes, and liver biopsy in 6 of them showed lepromata and fatty changes in liver cells as well. (fig. 4)

Out of 34 patients who received the indigenous drugs Speman and Tentex forte, 9 had azoospermia. Results were evaluated objectively (semen analysis) and subjectively (sexual history of the individual patients regarding libido, premature ejaculation, frequency of coitus per week, post-coital mental status etc.). Subjectively 17 patients improved markedly, while 11 of them have shown moderate improvement. These 28 patients (82.3%) were satisfied with their sexual performance after the completion of therapy.

Objective assessment of 16 patients (oligospermic with sperm count less than 40 million/ml) revealed marked improvement in 10 (62.5%) and moderate improvement in 4 (25%) cases. In all these patients post-treatment analysis showed a fertile semen profile. Sperm motility was also increased and more than 60% of sperms were motile in 19 cases out of 25 (76%), while 50-60% motility of sperms was seen in 4 cases (16%). Azoospermic patients showed no change in their semen analysis while patients with normal semen revealed increased sperm count and more motile sperms. No side effects were observed in any of the treated cases. A further analysis of results revealed that the improvement in a majority of these cases started two months after the commencement of therapy and was established after three months of treatment. However, 2 patients showed improvement as late as five months after therapy.

4. DISCUSSION

The study revealed that testicular affection with leprosy occurs mainly in the lepromatous type of the disease, whereas all the patients with the tuberculoid type showed normal spermograms and normal testicular histological findings, except in two patients who had suffered from mumps in the past resulting in damage to the testes. Dimorphous leprosy patients who revealed changes in spermograms and testicular histology were having predominant features of the lepromatous type. The testes are the most frequently involved internal organs in leprosy (lepromatous)[6] and in advanced cases the testes are reported to be small, firm and atrophic. As it is presumed that leprosy bacilli reach the testes via the blood stream, one should suspect bilateral involvement of the testes in every patient[8].

Nodular thickening and preserved testicular sensation were found in early cases, while atrophy and impaired testicular sensation were found late in the disease. Evidence of testicular involvement has been recorded in almost all cases of lepromatous leprosy and histological changes have been divided into [3] phases[9]:

a) ***Vascular:*** Vessels of all sizes are infiltrated by lymphocytes. The vessel walls are tickened resulting in narrowing of the lumen. The lepromas may occasionally project as nodules into the lumen. Macrophages are visualised in intraluminal lepromas and in the vessel walls. Perivascularly there are numerous lymphocytes, large pale cells with vacuoles. A.F.B. was demonstrated in large number. During this phase seminiferous tubules, Sertoli's cells and interstitial cells of Leydig are apparently unaffected.

b) ***Interstitial:*** No evidence of active inflammation is noticed but masses of Leydig cells and interstitial fibrosis is seen. Seminiferous tubules are relatively small and their lumen is filled with Sertolian syncitium.

c) ***Obliterative:*** Fibrosis is marked resulting in obliteration of seminiferous tubules. The involvement is both inter — and intratubular and usually bilaterals. Seminiferous tubules are involved early leading to hyalinisation. The epithelial cells may contain bacilli in groups mainly around the nucleus. The basement membrane and tunics propria show marked thickening and hyaline degeneration in such tubules. Spermatogenesis ceases and atrophy of the epithelium ensues.

Due to haematogenous spread of infection the changes in the interstitial tissue occur earlier and all stages of infiltration, from small round cell to overt leproma, may be encountered. As the disease progresses diffuse fibrosis will be followed by islets of hyaline degeneration resulting in sclerosis with complete fibrous replacement of all tubules[4]. In the late stages occasional bacilli may be seen in the cells. With progressive fibrosis the blood supply may be jeopardised causing damage to the Leydig cells[2]. El-Shiemy et a1[8]. reported non-inflammatory cellular oedema, in addition to Leydig cell hyperplasia, in lepromatous cases and postulated a spermatic stasis. Grabstald and Swan[9] found it difficult to correlate any degree of atrophy with the age of the patients or severity of the disease. Kumar *et al*[14] were also unable to establish any correlation in the histological picture, testicular size, sperm count and other clinical parameters. The same is true in the present series of cases.

Quite a good number of cases (34 out of 60) complained of diminished or absent sexual function. Not all of them showed histopathologic evidence of destruction of Leydig cells. This is in agreement with the fact that even castrated adult males do not always lose their potency[11]. We believe that this disturbance in sexual potency in these patients is due at least partially to an associated psychological state produced in the patients by such a disfiguring disease. This has also been mentioned by Grabstald and Swan[9] and El-shiemy *et al* [8] who. found no relationship between impotence and testicular involvement in leprosy.

Azoospermia or oligospermia is related to the degree of testicular involvement as the lumen of the epididymis was patent although its wall was infiltrated by lepromatous reaction. So azoospermia is mainly attributed primarily to the testicular involvement and not to obstruction of the epididymis as occurs in cases of tuberculous epididymitis.

Gynaecomastia has been reported in 18%36% cases of lepromatous leprosy[8],[9],[14]. In the present series of lepromatous leprosy patients, gynaecomastia was present in 25% of cases. In all these cases there was severe involvement of the testes. The emphasis has been laid on the decrease in Leydig cells with relatively greater decrease of androgens than estrogens. All these patients in the present series showed involvement of the liver. The importance of the liver cannot be ignored in the genesis of gynaecomastia. The liver plays an active role in the inactivation of estrogens, whereas Cameron[2] is of opinion that there is an altered balance between the estrogenic and androgenic concentrations at the site of action.

Sex is a dominating force in life which is a single motivating factor in human behaviour and reactions. Sexual disorders in human beings are more common than they are thought to be. In human beings various factors play a part, which makes an individual sexually neurasthenic and functionally impotent. This may lead to a train of psychological complexes leading to sexual inferiority and its allied syndromes.

The treatment of certain sexual disorders with gonadal and/or pituitary hormones have not yielded favourable results[10]. Recently several indigenous compounds have been reported to be effective in improving sexual disorders, sperm count and motility.

In the present study, two indigenous preparations, Speman and Tentex forte (Himalaya) have been used with good results. Subjective improvement was noted in 92% of oligospermic patients, while azoospemrics confessed improvement in the sexual act, libido etc., in 55% of cases. There was no improvement objectively i.e., in sperm count and motility in azoospemtic patients, while 87% of oligospermic patients revealed improvement in the sperm count and its motility. In the ancient medical science, Ayurveda — a group of medicinal substances has been described as Wageekaran' which are believed to be sex tonics. In modem medicine the substances which arouse sexual disire are known as aphrodisiac agents and Yohimbine, Strychnine etc., have been advocated as aphrodisiac agents.

Experimental studies have revealed the beneficial effects of the components of Speman and Tentex forte on seminiferous tubules and the prostate. The prostate gland showed more fluid-filled alveoli, while the cells of the seminal vesicles were hypertrophied)[11]. In many clinical trials it has been proved that therapy with these herbal preparations lead to an increase in sperm concentration and sperm motility along with

TABLE 1

General features of leprosy patients (60 cases)

	Types of Leprosy		
	Lepromatous (32 cases)	**Dimorphous (10 cases)**	**Tuberculoid (18 cases)**
1. Age in years = range	14 — 48	20 — 50	16 — 46
= mean± SD	24.2±5.2	27.4±4.8	30.2 ± 5.2
2. Duration of illness (years)			
= range	0.25-18	0.25-16	0.4-9
= mean ± SD	5.4 ± 2.4	3.9 ± 4.2	3.2 ± 3.2
3. Marital status = married	23	4	7
4. Sexual symptoms	19(59.4%)	6(60%)	9(50%)
5. Gynaecomastia (Fig. 1)	8(25%)	1(10%)	—
6. Alteration in sexual hair	9(28%)	2(20%)	—
7. Testicular pain and/or swelling	20(62.5%)	3(30%)	—

TABLE 2

Laboratory findings

	Types of Leprosy		
	Lepromatous (32 cases)	**Dimorphous (10 cases)**	**Tuberculoid (18 cases)**
A.F.B. Demonstration:			
Positive nasal scraping	25 (78%)	5 (50%)	5 (29%)
Positive slit scraping	32 (100%)	5 (50%)	—
Semen analysis:			
Normal sperm count	4 (12%)	5 (50%)	16 (88%)
Oligospermia	12 (38%)	3 (30%)	1 (6%)
Azoospermia	16 (50%)	2 (20%)	1 (6%)

TABLE 3

Testicular findings

	Types of Leprosy		
	Lepromatous (32 cases)	Dimorphous (10 cases)	Tuberculoid (18 cases)
1. Pathological changes — nodular thickening	9 (28%)	1 (10%)	–
2. Size of testes — Normal	20 (62%)	8 (80%)	17 (94%)
— Smaller (atrophied)	12 (38%)	2 (20%)	1(6%)
3. Testicular sensation — Preserved	18 (56%)	7 (70%)	18 (100%)
Impaired	7 (22%)	2 (20%)	–
Absent	7 (22%)	1 (10%)	–

TABLE 4

Histopathological findings of testes and epididymis.

	Types of Leprosy (25 cases)		
	Lepromatous (18 cases)	Dimorphous (6 cases)	Tuberculoid (1 case)
1. Essentially normal	3	2	1
2. Acid Fast Bacilli	8	1	
3. Primary testicular atrophy	4		
4. Minimal changes:— variable degree of involvement, some normal size tubule with hypospermatogenesis, few small size tubules lined with Sertoli cells only and fewer with total sclerosed tubules. Interstitium showed endarteritis obliterans, mild focal fibrosis, mild diffuse infiltration of mononuclear cells and Leydig cell hyperplasia.	2	2	
5. Intermediate changes:— Half of the tubules sclerosed, the other half small with thick basement membrane and lined by Sertoli cells and/or occasional germ cells. Interstitium showed marked endarteritis obliterans with diffuse fibrosis, a few Leydig cells and moderate infiltration of mononuclear cells (Fig. 2).	4	2	
6. Maximal changes:— Most of the tubules hyalinised and very few Sertoli cells. Interstitium showed diffuse fibrosis, a few thin walled vessels and occasional Leydig cells (Fig. 3).	5		

marked improvement in the sexual act, satisfaction, libido etc.[15, 19, 20] Jayalatika et al.[12] studied the effect of Speman on spermatogenic and androgenic functions of the human testes and observed improvement in the sperm count and motility. It increases the prostatic function and glycogen metabolism of the seminal fluid. It has been shown that Speman has an 'unexplained' beneficial effect in oligospermia,[15, 19] as we too observed in 23 out of 25 cases of the present series of oligospermic leprotics.

The results of this study show that Tentex forte and Speman definitely enable individuals to overcome their various sexual problems and male sterility. Extensive trials with these preparations would be of value in lepromatous patients with impotence, diminished libido and male sterility.

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TABLE 5

Therapeutic response to indigenous drug therapy

	Before treatment	After treatment (months) 1	2	3	6
A. *Effect on sperm count:*					
l. Azoospermia	9	9	9	9	9
2. Oligospermia	9	9	6	4	2
less than 20 million/ml					
20 - 40 million/ml	7	6	5	4	4
40 - 60 million/ml	4	5	6	8	10
3. Normal sperm count more than 60 million/ml	5	5	8	9	9
B. *effect on sperm motility:*					
l. no motile sperm	9	9	9	9	9
2. less than 50% motile sperms	11	10	8	4	2
3. 50% - 60% motile sperms	8	7	6	4	4
4. more than 60% motile sperms	6	8	11	17	19

TABLE 6

Overall therapeutic response

Grades of improvement	Evaluation		
	Objective	Subjective	
		Oligospermic	Azzospermic
	(16 cases)	(25 cases)	(9 cases)
1. Marked improvement	10 (62%)	16 (64%)	1 (11%)
2. Moderate improvement	4 (25%)	7 (28%)	4 (44%)
3. No improvement	2(13%)	2(18%)	4 (44%)

Figure 1 — Young patient with gynaecomastia.

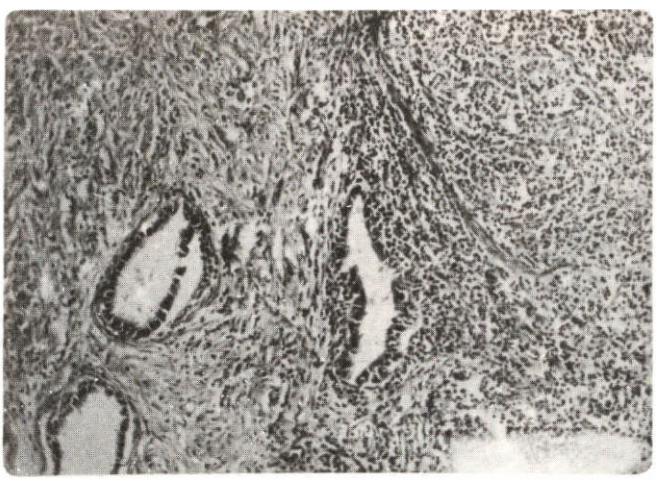

Figure 2 — Microphotograph showing testicular tissue with an attempt to form granuloma having mononuclear and epithelioid cells Left half of microphotograph shows marked fibrosis with three non-functioning seminiferous tubules. (H &E x 70)

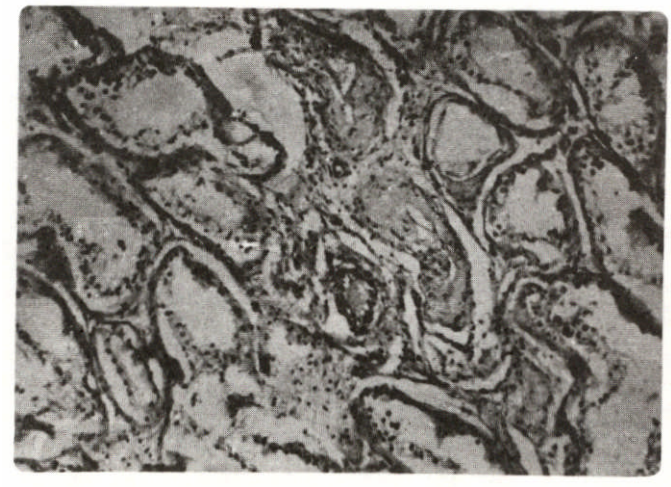

Figure 3 — Microphotograph of testicular tissue showing complete arrest of spermatogenesis (H & E 280).

Figure 4 — Liver biopsy showing microgranuloma and some periportal fibrosis. The granuloma is represented by a collection of foamy cells (H &E 70).

RESUMO

Sessenta pacientes masculinos de hanseníase (idade média = 27,2 ± 5,04 anos), selecionados aleatoriamente, foram estudados quanto ao envolvimento gonadal e à eficácia terapêutica de duas drogas nativas. Destes pacientes 34 eram casados, com duração média da doença de 4,17± 3,27 anos. Somente os pacientes com hanseníase virchowiana e dimorfa desenvolveram alterações testiculares e de epidídimos. Dor e/ou sensibilidade testicular (virchowianos = 62,5%, dimorfos = 30,0%) foi a sintomatologia mais comum. Função sexual alterada foi observada em 34 (56,6%) casos, enquanto 11 pacientes apresentaram padrão sexual de distribuição pilosa alterado e ginecomastia. O espermograma revelou azoospermia em 19 (35%) dos casos e oligospermia em 16 (26,6%) pacientes. Os achados histopatológicos da biópsia testicular revelaram evidência de lesões específicas não relacionadas ao tamanho do testículo, aos achados do sémen e às manifestações clínicas. As alterações histopatológicas mostraram grande variabilidade, não tendo sido possível classificá-las em vasculares, intersticiais ou obstrutivas: acredita-se que as alterações encontradas sejam devidas ao estado alterado das gônadas na hanseníase. A eficácia das preparações terapêuticas nativas Speman e Tentex forte (Himalaya) foi avaliada de um ponto de vista objetivo e subjetivo em 34 pacientes. Melhora subjetiva foi observada em 82,3% dos casos, enquanto objetivamente o espermograma melhorou em 87,5% dos casos com oligospermia. As drogas não apresentaram efeitos colaterais e foram bem toleradas.

Palavras chave: Gônadas. Ginecomastia. Testículo. Epidídimos. Hanseníase. Preparação nativa.

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