

Malignant Tumors of the Skin Among Leprosy Patients^{1 2}Jorge Michalany³

The concept that leprosy is rarely associated with cancer prevailed until 1937 to such an extent that it was believed that persons with leprosy were immune to malignant tumors. This point of view was due principally to the conclusions of Soegaard (⁴⁷), who, in 1910, analyzed the deaths caused by cancer in leprosaria.

Impressed by the fact that in the United States Levin (²³) had not found a single case of cancer among leprosy patients, Soegaard (⁴⁷), suggesting the possibility of immunity to cancer in persons with this disease, decided to investigate the facts in Norwegian leprosaria. Among 2,269 deaths, he found only 19 cases of cancer, i.e., 0.84 per cent. In view of these results and in the light of the opinion that cancer was rare among persons with leprosy, stressed by directors of various sanatoria outside Norway, including Bjarnhjedinson (³) of Reykjavik, Soegaard held no further doubts about his views as to the relative immunity of leprosy to malignant tumors (^{48, 49}). His reports had wide repercussion and in 1911 an editorial was published in the *Presse Médicale* (¹⁰) in which the limited susceptibility of patients with leprosy to cancer was pointed out, and reference was made to the opinions of Hansen and Neelsen, who stated that they had never seen a case of cancer among leprosy patients. Even in the Far East, Toyama (⁶¹) appeared to confirm the rarity of leprosy-cancer association.

However by 1912 Lie (²⁴) held doubts regarding Soegaard's conclusions, and in 1914 Biehler (²), from Riga, submitted sta-

tistics showing 10 cases of cancer from 160 autopsies on persons with leprosy (6.3%). He concluded that the mortality rate due to cancer in the leprosarium was equal to that in the nonleprosy Riga Municipal Hospital (5.2%), and that his findings did not permit him to accept an immunity or even a lesser degree of predisposition to cancer among persons with leprosy.

Despite such objections, statistics were later published in which the incidence of cancer among leprosy patients continued to be very low (Pineda (³⁶)), or null (Businco (⁵)). The latter author, however, held doubts regarding the alleged resistance of leprosy patients to malignant tumors and recalled that an apparent incompatibility between malignant tumors and tuberculosis had also been claimed. Contrary to Businco, two Japanese authors, Sugai and Monobe (⁵¹), in view of the fact that few lepra cells had been found in the organs of a tuberous leprosy patient, who died of carcinoma of the pylorus, suggested that the Hansen bacilli might have been affected or destroyed by substances produced by cancer cells. Hopkins (¹⁴), in the United States, was likewise of the opinion that the condition of leprosy improved as cancer progressed.

In published papers Kobayashi (¹⁹), Terra (⁵⁸) and Portugal (³⁷) still insisted upon the rarity of the cancer-leprosy association, but in 1930 two Argentine authors, Puente and Quiroga (³⁸), again expressed doubt about this rarity, despite the low percentage (0.56%) found in their own material. In a four-year period, among 700 leprosy patients, only four were found with carcinoma, two of the skin, one of the breast and one of the gallbladder. In the U.S.S.R., Stein and Karpichina (⁵⁰) continued to insist on the low incidence of cancer in persons with leprosy: among 133

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autopsies there was only one case of cancer.

In contrast to the view of an antagonism between cancer and leprosy, there arose, in the 1930's, a belief that leprosy could favor the development of malignant tumors. Although Tisseuil (⁶⁰) affirmed that leprosy might prepare a favorable soil for cancer, he gave no reasons for such a statement. Natali (³⁴)⁴, after analyzing 22 cases he collected from the literature, which led to conclusions contrary to the supposed immunity of the leprosy patient to cancer, suggested that leprosy lesions of the skin and perhaps of the viscera might constitute a starting point for carcinoma.

Finally, in 1937, two Brazilian authors, Martins de Castro and Martins de Castro Jr. (²⁹) submitted the highest series of cases to date on the leprosy-cancer association. Forty-four cases were reported, of which 25 were of the skin, 10 of mucous membranes and 9 of other organs, all proved by biopsy or autopsy, and all noted within the short period of three years in the Department of Prophylaxis of Leprosy of the State of São Paulo (Brazil). They concluded not only that cancer was not rare in leprosy patients, but also that there was no reason to believe in an incompatibility of the two diseases or in a slender susceptibility of a leprosy patient to cancer.

Despite such an influential publication, in 1941, Serra (⁴⁶) in Italy, continued to refer to a rarity of neoplasms in leprosy, declaring that he had never found any cases among his leprosy patients. Hayashi and Fukuda (¹¹) suggested that cancer in leprosy was rare because the average age at death among leprosy patients, especially those of the lepromatous type, is earlier than the cancer age among persons free from leprosy. However, in 1958, the findings of Caldas (⁶) and of Kosolopkeena and Saveenich (²⁰) confirmed those of the two Brazilian authors. Caldas (⁶) from the Department of Prophylaxis of Leprosy of the State of São Paulo, reported, in a three-year period, 160 cases of leprosy patients

with malignant tumors, 110 (68.8%) of whom were living and 50 (31.2%) dead. Kosolopkeena and Saveenich (²⁰), reporting from Astrakan in Soviet Russia, after analyzing 499 autopsies of leprosy patients, found 38 cases of malignant tumor (7.6%). They attributed this high incidence to modern therapeutics, resulting in greater longevity among leprosy patients. More recently, in 1964, Sakurai *et al.* (⁴⁴) found 14.2 per cent with cancer in 115 autopsies in cases of leprosy.

ANALYSIS OF LITERATURE ON THE ASSOCIATION OF LEPROSY AND MALIGNANT TUMORS OF THE SKIN

The first case that we were able to find in the literature in which an association of leprosy and skin cancer was noted, was demonstrated by Blaschko (⁴) in 1897, during a conference on leprosy in Berlin. The case was a canceroid tumor of the lower lip, associated with leprosy infiltration and presence of leprosy bacilli.

Not until 1910 were additional cases of skin cancer in leprosy patients noted in the literature, and then, by coincidence, in the very works of Soegaard, the author who had insistently proclaimed the immunity of patients with leprosy to cancer. In the statistics furnished by the leprosaria, reference was made of five cases, three of them among males and two among females (^{47, 48}). In 1912 Savatard (⁴⁵) of Manchester reported the case of a male leprosy patient with a fibrosarcoma in a scar resulting from x-ray treatment for lupus, and in 1913 Toyama (⁶¹) referred to a case of carcinoma of the penis.

Possibly because of the views sustained by Soegaard on the supposed resistance of the leprosy patient to cancer, the third reference in western literature appeared only 13 years later, in 1926, when Terra (⁵⁸) reported a case of prickle cell carcinoma of the lower lip in a patient suffering from neural leprosy. Thereafter appeared the observations of Kobayashi (¹⁹) and Portugal (³⁷) and, in 1930, that of Puente and Quiroga (³⁸). In the chapter by Klingmüller on leprosy in Jadassohn's handbook (¹⁸), besides an illustration (Fig. 121) contributed by M. Hirschberg of Riga,

⁴"On the contrary, it would not be strange if in the near future more nearly complete statistics, especially those on pathologic anatomy, would reveal more cancer among leprosy patients than is believed to be the case today. . ."

which shows a leprosy patient with a cancer affecting the lips, nose and adjoining parts of the face, there is a reference to a case described by Hoffman (12) of Cuba of a man with a prickle cell carcinoma associated with leprosy infiltration without bacilli. Jeanselme (16) pointed out, however, that cancroids grafted on a leprosy background were exceptionally rare. Immediately afterward the reports of Natali (34) and Roldan (42) appeared in literature.

In 1937, in the course of extensive research, Martins de Castro and Martins de Castro Jr. (29) described 32 cases of cancer of the skin and external mucous membranes (25 of the skin, five of the lips, one of the penis, and one of the anus), and in 1939, Rodrigues de Souza (41) referred to a case of Bowen's disease associated with leprosy.

After these publications various other cases were observed in Brazil (27, 31, 33), Cuba (22, 26), French Guiana (26), Spain (28, 43, 53, 54, 55, 56, 57, 63, 64), Italy (59), Norway (Waalers (65)), U.S.S.R. (35), Japan (11, 52), India (17) and former Netherland East Indies (21).

It is interesting to point out that among these cases there were seven in which cancer was related to chronic ulceration of the feet, in four of which it had metastasized to the regional lymph nodes (11, 17, 21). In another case, quoted by Terencio de las Aguas (57), cancer was reported as provoked by constant self-biting of the hand.

Vilanova (63) and Rubió (43), admitted that rarity of cancer of the skin among leprosy patients could be due to atrophy of the skin, in contrast to lupus vulgaris, in which the phenomenon of hyperplasia is nearly always present. Rarity could likewise be due to the nonuse, in leprosy, of local irritative treatments (radiotherapy, cauterization, pyrogallol acid, etc.), which are responsible for epithelial destruction and regeneration (pseudoeplitheliomatous hyperplasia), which may be forerunners of

⁵Waalers misunderstood the information about Portugal's case in the paper of Puente and Quiroga (38). Instead of new case ("nuevo") he translated *nine cases*. Hence the reason for his total of 42 cases instead of 34 of skin cancer in the literature.

cancer. Contreras (7) affirms that skin cancer among leprosy patients is rare, but believes that electrocoagulation and cauterization of resistant lesions and of the edges of leprosy ulcers, as well as the sunny climate of the Mediterranean region, are factors that could increase the frequency of tumors.

According to the data published up to now, 94 cases of malignant tumors of the skin and external mucosae have been described. Analysis of these cases demonstrates various interesting facts, as follows.

Source. Of the 94 published cases, 52 occurred in South America and six in Cuba. In Brazil alone, 48 cases have been observed. In Europe there were 23 cases, of which 11 were in Spain. The remaining 13 cases were verified in Asia.

Sex. There were 86 cases in which the sex was recorded, and 8 in which it was not. The group in which it was recorded consisted of 63 males and 23 females.

Age. In ten cases age was not recorded. The 84 recorded cases occurred in the following age brackets: 20-29 years, four cases; 30 to 39, 11 cases; 40 to 49, 23 cases; 50 to 59, 23 cases; 60 to 69, 17 cases; 70 to 79, 6 cases.

Color. In the European cases, and one case from Asia, totalling 24 cases, even though skin color was not always recorded, it is surmised that they were all white. The six cases in Japan were surmised to be orientals. The other Asiatic cases and one European were represented by four Hindus, one Eurasian and one Papuan. Despite the skin color variation in America, cancer occurred almost exclusively in whites, i.e., in 54 patients. Two patients were mulattoes and in only two cases the color was not recorded.

Occupation. Occupation was recorded in only 44 cases (50 cases nonrecorded), of which 21 were among urban workers, 21 among farmers and 2 among sailors.

Types of leprosy. In only eight of the 94 cases the type of leprosy was not recorded. On comparison of the actual classification of leprosy into three types (lepromatous, tuberculoid and indeterminate) with the types described in the original publications, it can be said that among the remaining

86 cases, 71 were of lepromatous, ten of tuberculoid, and five of indeterminate type.

Anatomic site. In only three of the 94 cases was the anatomic site of the cancer not recorded. Among the remaining 91 cases the malignant disease was located as follows: head, 52 cases; lips, 12; neck, 1; trunk, 2; limbs, 21; genitalia, 2; anus, 1. It should be borne in mind that cancer present in more than one site was not noted in these figures.

Histologic type. In the 94 cases, tumors occurred 96 times. The histologic type was not recorded in 11 cases. Among the 85 cases in which the histology was recorded, there were 40 squamous cell or similar carcinomas, 37 basal cell or similar carcinomas, four cases of Bowen's disease, two sarcomas and two melanomas.

Association of leprosy and cancer in the same histologic examination. Among the 96 cases of tumors, leprosy lesions together with tumor were noted in 26 cases. Leprosy lesions were absent in 25 cases. In 45 cases the association was not recorded.

Interval of time between the duration of leprosy and beginning of cancer. Reference was made to this factor in 73 cases. In 21 it was not recorded. Other periods were as follows: 5 to 9 years, 17 cases; 10 to 14 years, 15 cases; 15 to 19 years, 5 cases; 20 to 24 years, 5 cases; 25 to 29 years, 2 cases; and finally 30 to 34 years, 6 cases.

From this analysis, it is interesting to point out that 61.7 per cent of the cases were described in Latin America. The majority of patients were males (67.0%) and the age of greatest frequency was found to be in the 40 to 49 and 50 to 59 year groups (24.5% in each). Cases occurred almost exclusively among whites (83.0%), who were farmers in 24.5 per cent of the cases. In the majority of cases the leprosy was of the lepromatous type (75.5%), and in 55.3 per cent of the cases the tumors were located in the head. Squamous cell carcinoma was the most frequent type (42.6%), and cancer-leprosy association was verified in 27.7 per cent of the histopathologic examinations. Finally, the greatest frequency of cancer occurred exactly in those cases where cancer appeared no more than four years after the onset of leprosy (24.5%).

MATERIAL AND METHODS

The material examined by the author consisted of 539 cases of malignant tumors of the skin and external mucosae found in a series of 60,000 histopathologic examinations, the greater part of which were from skin biopsies made for diagnosis of type of leprosy and follow-up in the *Secção de Anatomia Patológica do Departamento de Profilaxia da Lepra do Estado de São Paulo*, during a period of 31 years (1934-1965). This material does not include the 32 cases to which reference was made in the publication by Martins de Castro and Martins de Castro Jr. (²⁹), which was based on observations in the same department.

The cases were classified according to sex, age, type of leprosy, association or not with the malignant tumor, site and histologic type of tumor. The leprosy lesion was considered positive when leprosy cells, with or without bacilli, were present, or when there were bacilli only. In several cases, and for reasons beyond our control, some of these data could not be submitted.

Besides the hematoxylin-eosin stain and Faraco's method for acid-fast bacilli, Mason's trichrome and elastic fiber staining was carried out in each case in order to verify the degenerative state of the dermis at biopsy. This research was possible in skin fragments which, apart from the neoplastic tissue, presented portions of adjacent skin free from tumor.

RESULTS

The results of examination are presented in Tables 1, 2, 3, 4, 5 and 6. Analysis of the data in the tables shows that malignant tumors of the skin among leprosy patients occurred more frequently in males (59.7%), and in the 50 to 59 year age group (25.4%). The cases with recorded type of leprosy (somewhat less than half of the total, i.e., 37.5%) were all lepromatous, and in 35.6 per cent of the cases leprosy and cancer were found in the same histologic examination. In 64.8 per cent of the cases the tumors were located in the head, basal cell carcinoma being the most frequent histologic type (50.5%).

TABLE 1. Sex distribution of malignant tumors of the skin among persons with leprosy.

Sex	Frequency	Per cent
Males	322	59.7
Females	217	40.3
Total	539	100.00

TABLE 2. Age distribution of malignant tumors of the skin among persons with leprosy.

Age	Frequency	Per cent
00-09	0	0.0
10-19	0	0.0
20-29	12	2.1
30-39	51	9.5
40-49	86	16.0
50-59	137	25.4
60-69	89	16.6
70-79	35	6.5
80-89	7	1.2
Unknown	122	22.7
Total	539	100.00

TABLE 3. Type distribution of leprosy in cases of malignant tumors of the skin among persons with leprosy.

Type of leprosy	Frequency	Per cent
Lepromatous	202	37.5
Unknown	337	62.5
Total	539	100.00

TABLE 4. Distribution of leprosy and cancer in the same lesion in cases of malignant tumors of the skin among persons with leprosy.

Lesion	Frequency	Per cent
Leprosy + cancer	192	35.6
Cancer only	347	64.4
Total	539	100.00

DISCUSSION

The finding of 539 cases of malignant tumors of the skin among patients with leprosy makes this the largest collection of cases presented to date, and demonstrates, contrary to previous belief of some authors,

that the person with leprosy is as subject to the development of cancer as any person without this disease. On addition of the 94 cases previously recorded in literature, the total reaches 633.

The concept of a relative immunity to cancer in the person with leprosy does not appear to be reasonable, and one cannot understand why recent authors, such as Contreras (7) and Terencio de las Aguas (55, 56) on the one hand, should emphasize a relatively low incidence, or why others, such as Kosolopkeena and Saveenich (20), should attribute a high incidence only to the longevity of leprosy patients achieved as a result of modern therapeutic methods.

In view of our finding of 539 cases, it is remarkable that only 94 cases of skin cancer have been found to be recorded in pre-

TABLE 5. Anatomic site distribution of malignant tumors of the skin among persons with leprosy.

Anatomic site	Frequency	Per cent
Head	349	64.8
Lips	42	7.8
Neck	14	2.6
Trunk	24	4.4
Limbs	41	7.6
Genitalia	4	0.7
Anus	1	0.2
Unknown	64	11.9
Total	539	100.00

TABLE 6. Histologic type distribution of malignant tumors of the skin among persons with leprosy.

Histologic type	Frequency	Per cent
Basal cell carcinoma	272	50.5
Squamous cell carcinoma	194	36.0
Senile keratosis and Bowen's disease	28	5.2
Sarcomas	25	4.6
Melanoma	14	2.6
Adnexal carcinoma	6	1.1
Total	539	100.00

vious literature, an insignificant number for so long a period, nearly 70 years (1897-1964), particularly if one takes into account that nearly one-third (thirty-two) of the cases were found by Martins de Castro and Martins de Castro Jr. (²⁹) during a short period of three years. The frequently proclaimed rarity of cancer, principally of the skin, among leprosy patients, can be attributed only to faulty diagnosis. As stressed by the two Brazilian authors (²⁹), many cases escape clinical diagnosis because of difficulty in distinguishing a tumor in leprosy skin, particularly a carcinoma among lepromas. Even the contrary can happen. Curren and Furniss (⁹) published a case of leproma presenting as a carcinoma of the penis.

Comparing our findings with those of the analyzed literature regarding skin cancer among leprosy patients, we find that practically all facts coincide: major frequency in males, high frequency of cancer in the lepromatous type of leprosy, the head as the anatomic site of predilection, and the existence of a great number of cases where histologically there was a leprosy-cancer association in the same lesion. The most frequent type of malignant tumor in our series was the basal cell carcinoma, whereas in reports in previous literature squamous cell carcinoma predominated. The most frequent age group in our series was the 50 to 59 year period; in the literature the highest incidence was found equally in the 40 to 49 and 50 to 59 year groups.

Considering that the number of known leprosy patients in the state of São Paulo between the years 1934 and 1964 (30 years) was 53,235 (¹), of whom one-half were lepromatous in type, and that the number of cases verified by us amounted to 539, we have come to the conclusion that there was one cancer for every 100 patients. It is therefore surprising that Büngeler (¹⁵), who worked at the same Department of Leprosy of São Paulo, stated that association of leprosy with cancer of the skin was very rare. The incidence may be even greater than 1/100. Apart from the already mentioned diagnostic difficulties, Caldas (⁶) referred to cases of skin cancer that had not been submitted to histopathologic ex-

amination, and which, consequently, were not included in our research.

For reasons that are obvious, our results are far from being statistically controlled. However, the differences between the frequency of skin cancer in persons with and without leprosy are so great that they must be considered significant. For example, in the city of Santos (state of São Paulo) the frequency of skin cancer is 0.26 for every 100 inhabitants (³⁰), almost one-fourth of that among leprosy patients. Should there be leprosy patients in the state of Texas (USA) where the ethnic groups are similar to those of the state of São Paulo (²⁵), the frequency of cancer in these patients would be 20 times greater than in persons without leprosy.

In our opinion, these apparent differences could be attributed to the skin atrophy found in patients with leprosy, particularly of the lepromatous type, after regression of the lesions. The skin of these patients is prematurely aged and could provide a state favorable for the onset of cancer. To this may be added the fact that a large proportion of the leprosy patients in the state of São Paulo are white, who have been subjected to the heat of intense sun rays, not only because they come from rural localities but also because, once interned in the leprosaria, they continue to work in the agricultural colonies of a region such as the state of São Paulo, where the climate is almost wholly tropical.

The atrophy of the skin leads us to suppose that, contrary to what has been suggested, a person with leprosy, particularly of the lepromatous type, should be more subject to the development of malignant tumors of the skin than the person without leprosy. According to Cowdry (⁸), the epidermis and its derivatives show a loss of stability as age increases. In some areas of an aged skin, hypoplasia (atrophy) vies with hyperplasia, depigmentation with hyperpigmentation, demineralization with hypermineralization. These are factors that should influence the percutaneous absorption of cancerogenic agents. Adding the lepromatous infiltrations, their regressions, exacerbations, the scars, and acute inflammatory reactions of the suppurative type,

i.e., lepra reaction, to the foregoing, we can conclude that the skin of lepromatous patients presents a high degree of degeneration, histologically characterized by atrophy of the epidermis and elastic degeneration of the dermis, and therefore offers a favorable field for action of cancerogenic agents (Figs. 1, 2, 3).

We do not agree with Vilanova's (63)

concept that in leprosy an epithelioma loses its local malignancy as well as its capacity to disseminate when faced with a supposed occlusion of lymphatic vessels due to leprosy scar sclerosis. Also, no differences in the evolution of cancer among leprosy patients have been verified by Martins de Castro and Martins de Castro Jr. (29) or by the present author, and cases with metas-

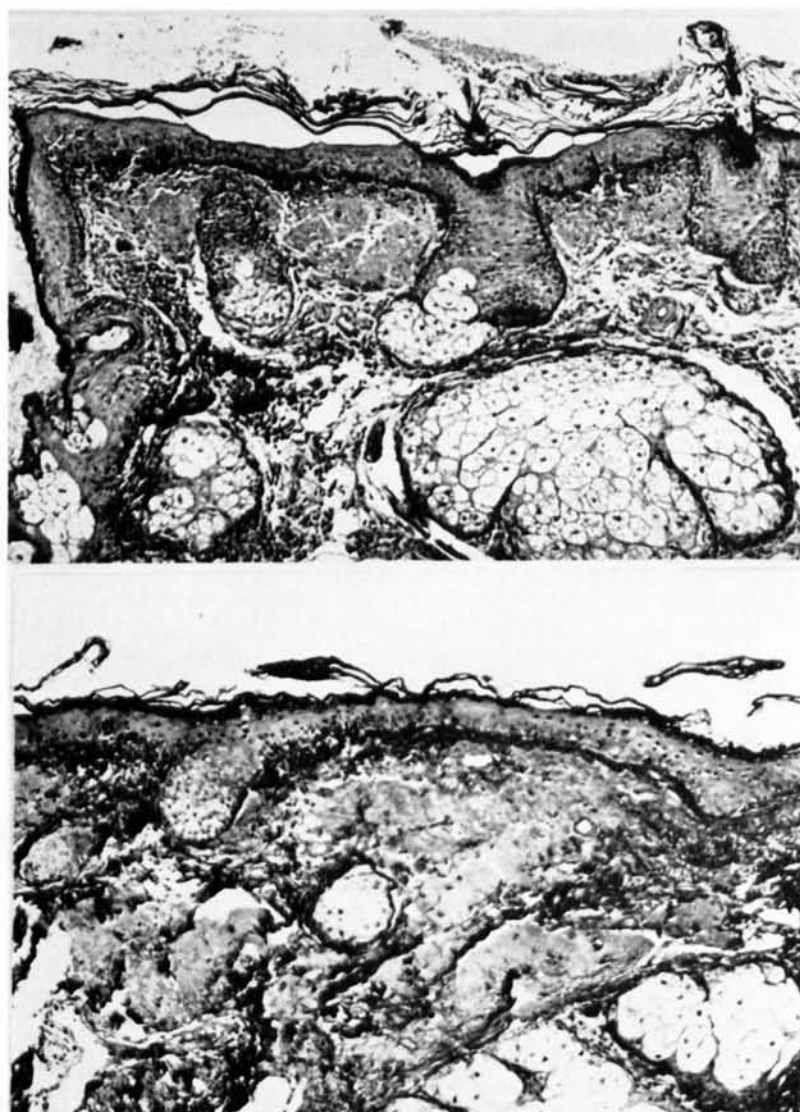


FIG. 1. Advanced atrophy of the epidermis and elastic degeneration of the papillary dermis. Case of senile keratosis of the face in a 58 year old female patient with lepromatous leprosy. (Masson's trichrome stain.)

FIG. 2. Advanced atrophy of the epidermis and elastic degeneration of the papillary dermis. Case of a 63 year old male patient with lepromatous leprosy and a basal cell carcinoma of the face. (Masson's trichrome stain.)

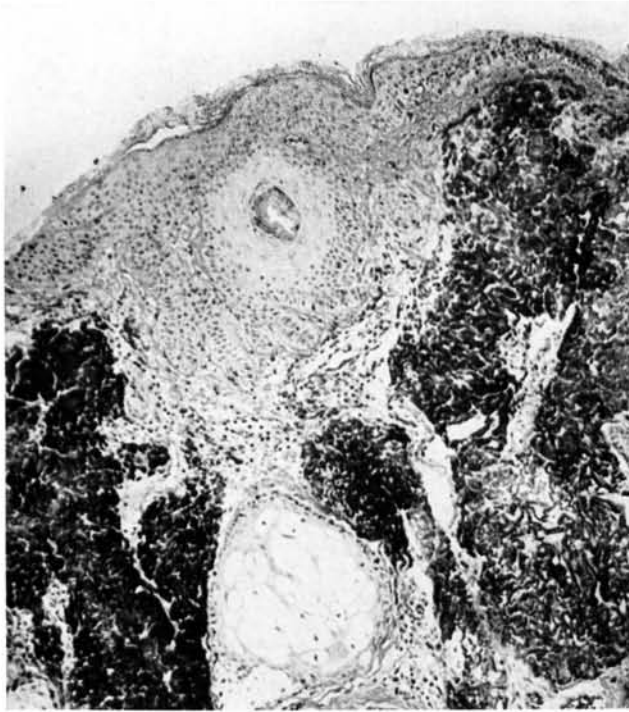


FIG. 3. Advanced elastic fiber degeneration of the dermis. Case of basal cell carcinoma of the face in a 65 year old male patient with lepromatous leprosy. (Weigert stain for elastic fibers).

tases have already been quoted in the literature (^{11, 71}).

It is interesting to point out that the high incidence of lip cancer in our material (42 cases) could be related to the insensitivity brought about by lepromas and the habit of smoking. The low incidence of adnexal carcinomas prevalent, likewise, among persons free from leprosy, might be explained by atrophy of cutaneous appendages, so frequent in persons with leprosy. As is known, the leprosy patient, particularly the patient of the advanced lepromatous type, has dry skin, alopecia, feminoid appearance in males, straight hair, and diminished sudoresis.

Although a parasite of the normal reticuloendothelial system cells, the leprosy bacillus can be found in the skin not only within the nerves and arrector pili muscles, but also within the normal epithelial structures (hair follicles, epidermis), melanoblasts, nevus cells, and likewise in cancer cells, as pointed out by Martins de Castro and Martins de Castro Jr. (²⁹). It is to be supposed that in tumors of the reticuloendothelial system leprosy bacilli would also find a favorable field for multiplication. Actually Mota and Portugal (³²) described

the transformation of a histiocytoma into a leproma. The discovery of bacilli within neoplastic cells in a case of mycosis fungoides led Rath de Souza *et al.* (⁴⁰) to attempt the *in vitro* tissue cell cultivation of the *Mycobacterium leprae*.

In our material, few of the cases had leprosy bacilli within cancer cells. In the majority of cases these were found within lepra cells in the periphery of the tumor. The absence of bacilli was more accentuated in cases where suppuration, due to necrosis or secondary infection, of the tumor had ensued, a fact similar to that which occurs in lepra reaction (¹³). This may explain the "improvement" of leprosy lesions referred to by Sugai and Monobe (⁵¹) and by Hopkins (¹⁴). Nor was the leprosy lesion found frequently in the stroma proper of the tumor (Figs. 4, 5). In many cases, the leprosy granuloma was supplanted and even replaced by the common chronic inflammatory infiltrate of the stroma reaction of the tumor. This explains the finding of the leprosy granuloma only in the periphery of tumors, as verified in the majority of cases. In many of the cases in which no leprosy was found associated with cancer, the absence of lepra cells and/

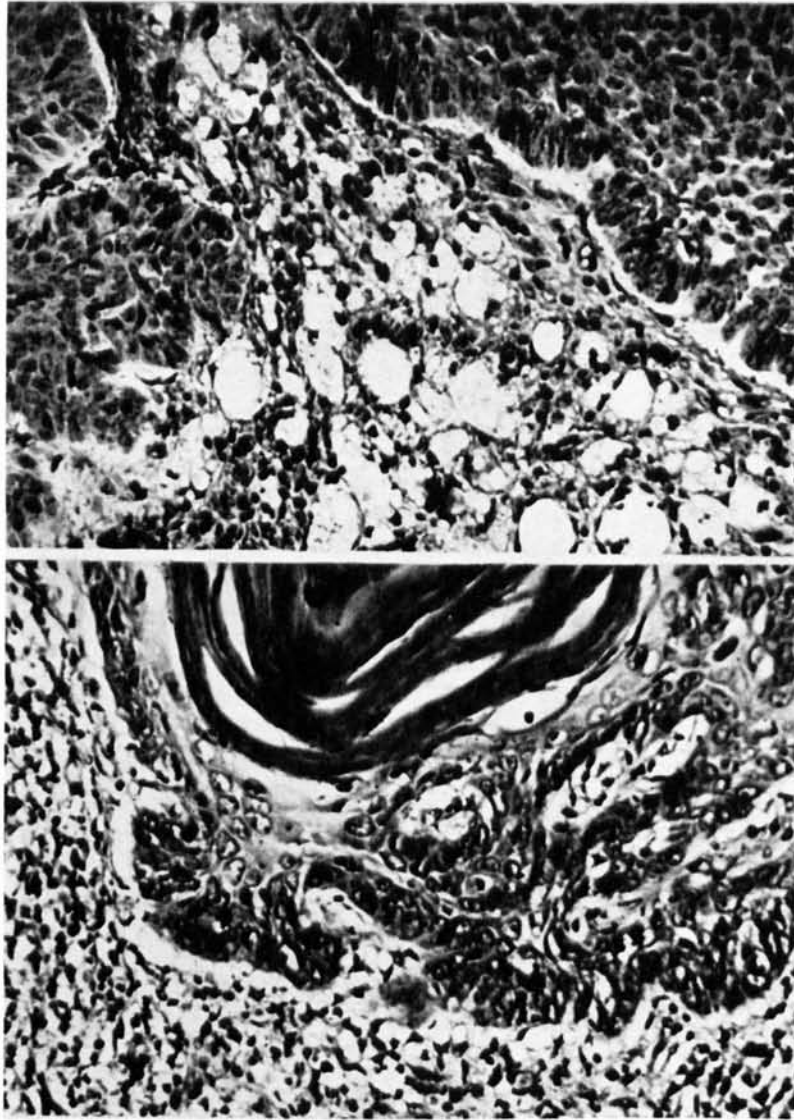


FIG. 4. Lepromatous infiltration in the stroma of a basal cell carcinoma. (H & E stain.)

FIG. 5. Lepromatous infiltration in the stroma of a squamous cell carcinoma. (H & E stain.)

or of bacilli could be explained by the causes cited above. It is interesting to point out that since leprosy is a disease principally of the skin and the nerves, leprous lesions and/or the leprosy bacillus would rarely be found associated with the tumors of internal organs.

The bacilli found within cancer cells have shapes similar to those found in lepra cells, i.e., typical (either isolated or forming globi) with granular aspect and bacil-

lary dust. In these two last-mentioned cases, cancer cells presented vacuoles similar to Virchow cells (lepra cells with fatty degeneration and nuclear pyknosis). Consequently, we can conceive that the lepra cell-bacillus complex upon which the lepra cell depends (³⁹), does not occur exclusively with histiocytes.

The majority of carcinomas in whose cells bacilli were found were of the basal cell type. This fact could be attributed to

the lesser invasive capacity and more chronic evolution of the basal cell carcinoma, as compared with these phenomena in the squamous cell carcinoma.

SUMMARY

A review of literature on the association of cancer and leprosy, and an analysis of 539 cases of malignant tumors of the skin found in a series of 60,000 histopathologic examinations in the Department of Leprosy of São Paulo (Brazil) between the years 1934 and 1965, are presented. This finding of 539 cases constitutes the highest casuistic in literature to date. Adding the 94 cases previously recorded in literature, the total reaches 633.

Analysis of these 539 cases showed that malignant tumors of the skin among leprosy patients are more frequent among males (59.7%) and in the 50 to 59 year age group (25.4%). The cases in which the type of leprosy present was recorded (37.5%; i.e., somewhat less than half of the total) were all lepromatous, and in 35.6 per cent of the cases the leprosy/cancer association was evident in the same histologic examination. The tumors were located chiefly in the head (64.8%) and their most frequent histologic type was the basal cell carcinoma (50.5%).

In view of the finding of 539 malignant tumors of the skin and the number of leprosy patients in the state of São Paulo from 1934 to 1964 (53,235), of whom one-half were lepromatous, it can be said that there is one skin cancer for every 100 patients. Such a high incidence would imply that, contrary to the belief of some authors, persons with leprosy, particularly of the lepromatous type, seem more vulnerable to skin cancer than the nonlepromatous population. In the author's opinion, such an apparent difference could be attributed to the atrophy and consequently, to the premature aging of the skin of the lepromatous patient, which facilitates the action of cancerogenic agents.

In view of the high frequency of malignant tumors of the skin among persons with leprosy and the fact that cancer lesions are in some respects clinically similar to lepromas or to lepromatous infiltrations, it is

possible that in many cases the diagnosis of cancer may be overlooked. In order to make an early diagnosis of skin cancer among leprosy patients, the leprologist should proceed to more careful clinical examination.

Leprosy bacilli are rarely found in cancer cells. When apparent they have the typical shapes (isolated or forming globi), with a granular aspect and bacillary dust. Suppuration due to necrosis or to secondary infection leads to disappearance of the bacilli. The lepromatous lesion is rarely found in the stroma of the tumor; rather, in the majority of cases, it is present in the periphery of the neoplastic growth.

RESUMEN

Se hace una revisión de la literatura sobre la asociación de cáncer y lepra, y un análisis de 539 casos de tumores malignos de la piel encontrados en una serie de 60,000 exámenes histopatológicos, en el Departamento de Lepra de San Pablo (Brasil) entre los años 1934 y 1965. El encuentro de 539 casos constituye la casuística mas alta en la literatura hoy en día. Sumando los 94 casos anteriormente registrados en la literatura, el total alcanza a 633.

El análisis de estos 539 casos demostró que los tumores malignos de la piel, en los enfermos de lepra, son mas frecuentes en los hombres (59.7%) y en el grupo de edad de 50-59 años (25.4%). Los casos en los cuales se dejó constancia del tipo de lepra (37.5%; v.g., algo menos que la mitad del total) fueron todos lepromatosos y en 35.6% de los casos la asociación cáncer y lepra fué evidente en el examen histológico. Los tumores se localizaron principalmente en la cabeza (64.8%) y el tipo histológico mas frecuente correspondió al carcinoma de células basales (50.5%).

En vista del hallazgo de 539 tumores malignos de la piel y el número de enfermos de lepra en el Estado de San Pablo entre 1934-1964 (53,235) de los cuales la mitad fueron lepromatosos, se puede decir que hay cáncer de la piel en un enfermo de cada cien. Una incidencia tan alta significaría que, al contrario de lo que piensan algunos autores, personas con lepra, particularmente con la forma lepromatosa, parecen mas susceptibles al cáncer de la piel que la población no enferma de lepra. En opinión del autor tal diferencia podría atribuirse a la atrofia y, por consecuencia, al envejecimiento prematuro de la piel de los

enfermos lepromatosos, lo que facilitaría la acción de los agentes carcinogénicos.

Teniendo en consideración la alta frecuencia de tumores malignos en la piel de los enfermos de lepra, y el hecho que las lesiones cancerosas son, en algunos aspectos, clínicamente parecidas a los lepromas, o a los infiltrados lepromatosos, es posible que en muchos casos el diagnóstico del cancer se omita. Para hacer un diagnóstico temprano de cancer de la piel, en los enfermos de lepra, el leprologo debería hacer un examen clínico mas cuidadoso.

El bacilo de Hansen se encuentra escasamente en las células cancerosas. Cuando se presenta, ellos tienen las formas típicas (aislados o formando globi) con un aspecto granular y polvo bacilar. La supuración producida por la necrosis, o como consecuencia de la infección secundaria, lleva a la desaparición del bacilo. La lesión leprosa se encuentra escasamente en el estroma del tumor; mas bien, en la mayoría de los casos, se presenta en la periferia del crecimiento neoplásico.

RÉSUMÉ

La littérature traitant de l'association entre cancer et lèpre est passée en revue. On a procédé à l'analyse de 539 cas de tumeurs malignes de la peau observées dans une série de 60,000 examens histopathologiques effectués au Département de la Lèpre de São Paulo (Brésil) de 1934 à 1965. L'observation de 539 cas représente le chiffre le plus élevé sur lequel ait porté ce genre d'études jusqu'à présent. Si l'on y ajoute les 94 cas déjà rapportés dans la littérature, le total atteint 633.

L'analyse de ces 539 cas a montré que les tumeurs malignes de la peau chez les malades de la lèpre sont plus fréquentes chez les hommes (59.7%) et dans le groupe d'âges allant de 50 à 59 ans (25.4%). Lorsqu'on examine les cas pour lesquels le type de lèpre a été noté (37.5%, soit moins de la moitié), on s'aperçoit que tous étaient lépromateux. De plus, dans 35.6% des cas, l'association de la lèpre avec le cancer apparaissait dans la même coupe histologique. Les tumeurs étaient situées principalement à la tête (64.8%) et le type histologique le plus fréquent était le carcinome à cellules basales (50.5%).

Vu l'observation de 539 tumeurs malignes de la peau et le nombre de malades de la lèpre dans l'état de São Paulo entre 1934 et 1964 (53,235), dont la moitié environ étaient lépromateux, on peut dire qu'il y a un cancer de la peau pour 100 malades. Une incidence telle implique que, contrairement à ce que

croient certains auteurs, les individus atteints de lèpre, et particulièrement ceux du type lépromateux, semblent plus vulnérables au cancer de la peau que ne l'est le reste de la population qui ne souffre pas de lèpre. C'est l'opinion de l'auteur que la cause d'une telle différence apparente pourrait être l'atrophie de la peau, c'est à dire son vieillissement prématuré, chez les malades lépromateux, ce qui pourrait faciliter l'action d'agents carcinogéniques.

Du fait de la fréquence élevée des tumeurs malignes de la peau chez des personnes atteintes de lèpre, et vu que les lésions cancéreuses sont à certains égards cliniquement semblables aux lépromes ou aux infiltrations lépromateuses, il est possible que dans de nombreux cas le diagnostic de cancer n'est pas posé. Le leprologiste devrait procéder à un examen clinique soigneux afin de faire précocement le diagnostic de cancer de la peau chez les malades de la lèpre.

On trouve rarement des bacilles de Hansen dans les cellules cancéreuses. Lorsqu'ils sont mis en évidence, ils revêtent les formes typiques (isolés ou en globi), avec aspect granuleux et poussière bacillaire. La suppuration suite à la nécrose ou infection secondaire entraîne la disparition des bacilles. La lésion lepreuse est rarement observée dans le stroma de la tumeur; au contraire, dans la plupart des cas, elle est située à périphérie de la croissance néoplasique.

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