

were organs of touch. Having combined in it the elements of the organs of touch of both reptiles (structure and pigmentation) and mammals (hair), the pigmented hairy mole may be regarded as a transition from the pigmented tactile spot of the reptile to the hairy sensory organ of the mammal. The periodic eruption of pigmented moles parallels the periodic appearance of new hair follicles. The cutaneous melanomas appear at birth, next at puberty, and then, in diminishing numbers, are scattered through later years. This corresponds to the development of new hair follicles. Presumably, hormones controlling the formation of new hair follicles have a similar action on the aberrant "reptilian" cells, that is, the cells giving rise to cutaneous melanomas.

In addition to the evidence furnished by comparative anatomy, the neurogenic origin of the melanomas is confirmed by a curious biologic test. One of the varieties of the German minnow changes color during the mating season. Ferguson and his coworkers, while investigating the influence of the posterior lobe of the pituitary gland on the secretion of urine, accidentally discovered that, by injecting posterior pituitary extract into a German minnow, this striking change of color could be induced within a few minutes. This reaction proved not to be specific of the posterior lobe of the pituitary, but could be brought about by the use of extracts of nervous tissue or its other derivatives. It is very significant, therefore, that although extracts of non-neurogenic tissues, whether normal or neoplastic, are inactive, extracts of melanomas are highly effective in changing the color of the minnows.

The term "melanoma" is preferable to that of "nevus" which may designate a capillary hemangioma, or to "mole" which would limit the lesion to the skin. The terms "melanosarcoma" and "melanocarcinoma" should be supplanted by the proper name—malignant melanoma.

Although the malignant tumor most frequently arises from a cutaneous melanoma (especially if the latter has been irritated), it may develop from the choroid of the eye, the meninges, the anal canal, or the adrenal medulla—all structures of ectodermal origin. Primary melanomas in other organs are exceedingly rare.

Unfortunately, the name "melanoma" implies a dark color. Pigment, however, is not essential, and nonpigmented melanomas are common.

490 Post Street.

LEONID S. CHERNEY,
San Francisco.

Tuberculin testing of mental patients at the Peoria Hospital in Illinois disclosed the fact that 52 per cent of the patients who were not in tuberculosis wards were positive to tuberculin and 23 per cent showed definite evidence of pulmonary tuberculosis with an additional 11 per cent who were classed as questionable. Among the schizophrenics, 23 per cent had tuberculosis. In view of this incidence it would seem that tuberculin testing should become a routine procedure in admitting patients to mental disease hospitals and that positive reactors be x-rayed at regular intervals with particular attention to the dementia praecox group.—M. Pollak and I. L. Turow, Conf. U. S. Vet. Adm. Phys., 1938.

ORIGINAL ARTICLES

CARCINOMA TO THE SPLEEN : METASTASES *

By PAUL H. GUTTMAN, M.D.
Sacramento

THE infrequent occurrence of carcinomatous metastases to the spleen has always impressed pathologists. Mallory¹ stated that in twenty-five years prior to 1922, he found but ten instances of cancer metastasis in 4,265 examinations. Ludwig Aschoff² added that, whereas metastatic sarcoma to the spleen is quite frequent, only rarely one finds metastatic carcinoma. Similarly, Ewing³ observed that the spleen seems to escape metastasis with peculiar frequency.

REPORTS IN THE LITERATURE

In an analysis of the available statistical data, one finds considerable variation in the findings of various observers. Di Biasi⁴ found splenic involvement 182 times in a series of 9,761 cases of carcinoma. Gusenbauer⁵ observed carcinomatous metastasis in thirteen cases, or 0.9 per cent, in a series of 1,445 cases. Marscheff⁶ found tumor metastasis in only eight instances in a series of 1,078 cases of carcinoma, or 0.7 per cent; Kauffmann⁷ reported 0.7 per cent in a series of 1,078 cases; Kettle,¹² eight instances in a series of forty cases; and Handley,⁸ in an examination of 422 carcinomas of the breast, found metastasis to the spleen in only one case, or 0.3 per cent.

Warren and Davis,⁹ in a recent and comprehensive review of the subject, found that, in 1,140 cases of carcinoma of all types, forty-two cases, or 3.7 per cent, showed indisputable metastasis to the spleen. However, only in twenty-two of these was the metastasis visible to the naked eye, while the others were microscopic in character. In twenty-six instances, or 56.5 per cent of the total number of metastatic tumors, the metastasis occurred independent of capsular involvement.

More thorough study of the spleen by serial section shows that microscopic metastasis occurs more frequently than the studies of Warren and Davis indicate. Yokohata,¹⁰ in a careful study of twenty-nine spleens obtained from patients who had died of carcinoma, found, by serial section of this organ, ten instances of microscopic metastasis, or an incidence of 34 per cent. Deelman¹¹ found microscopic metastasis in seven of seventy-five instances of generalized carcinomatosis. These results are certainly out of proportion to the incidence of gross metastasis. The question, therefore, is raised as to whether or not these can be considered true metastasis.

DEFINITION OF METASTATIC TUMOR

Although by definition a metastatic tumor is considered an unconnected secondary nodule, one must

* From the laboratory of the Sutter Hospital, Sacramento.
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necessarily differentiate between tumors which grow at the site of metastasis and emboli of tumor cells which have lodged in an organ, but show no evidence of growth. It is quite evident from the above findings that tumor emboli are extremely common, whereas very few of these develop into visible nodules. Both conditions must be regarded as true metastasis, since it is difficult to state whether or not a cluster of cells lodged in a capillary or sinus is capable of growth if left undisturbed. However, one must admit that in the spleen, microscopic growths only rarely take on sufficient growth to assume macroscopic proportions. This brings up the question of the so-called resistance of the spleen to invasion by tumor cells.

Experimental evidence is available which supports the belief that splenic tissue has a definite inhibitory effect on the growth of experimental tumors. Woglom,¹⁶ in a comprehensive review of this subject, states that "observations on the inhibitory effect of the spleen on tumor growth is one of the most significant in the whole bibliography of cancer research, for these cannot but suggest that the spleen of a resistant animal possesses some factor able to delay or sometimes even to destroy a sarcoma when retained in contact with its cells for a sufficient length of time." Woglom, however, admits that this substance is too feeble in action to affect tumor cells when introduced at a distance.

These observations carry a plausible explanation for the discrepancy between the frequency of microscopic metastasis and visible metastasis. However, before accepting this experimental evidence as fact, more experimental and pathological data are necessary, particularly to determine whether or not a similar relation exists in the incidence of microscopic and visible metastasis in organs other than the spleen.

ON THE INFREQUENCY OF SPLENIC METASTASIS

Numerous anatomical explanations have been offered to explain the infrequency of splenic metastasis, namely, (1) the motility of the spleen; (2) the lymphatic system; and (3) the peculiarity of the vascular system.

Support has been given to the theory that the rhythmic contraction of the spleen is an important factor in the prevention of metastasis. Kettle¹² states that it is easily conceivable that the microscopic nests may fail to become implanted in the walls of the sinuses or capillaries, because of the movement of the spleen. However, it is hardly probable that clusters of tumor cells could be forced to pass through the fine passages of the sinuses by the aid of the feeble contractions of the spleen.

A more plausible explanation is found in the peculiar arrangement of the lymphatic supply of the spleen. This organ does not possess afferent lymph vessels in the parenchyma; these vessels are limited to the capsule and trabeculae. Since carcinoma tends to follow the lymph vessels in its spread, metastasis through these channels can occur in the pulp only by means of retrograde extension along the efferent vessels. This can occur only after involvement of the capsule with blockage of the

efferent lymph vessels. That this phenomenon occurs but rarely is well illustrated in many cases in which the capsule is extensively involved, with little or no involvement of the parenchyma. Therefore, the pathway for metastasis of carcinoma to the spleen in most instances is limited to the blood vessels, which is not the usual method of carcinomatous spread.

The peculiarity of the vascular supply of the spleen has been suggested by Sappington¹⁸ as an important factor in preventing metastasis to the spleen. The splenic artery, in leaving the iliac axis, makes a sharp turn. Sappington believes that this turn prevents emboli from entering this vessel. However, as pointed out by Warren and Davis,⁹ this factor is negligible, because of the large size of the lumen of this vessel. Also, it is difficult to account for the frequency of emboli of other types to the spleen, particularly thrombi, if this anatomical peculiarity were a barrier.

TYPES OF TUMOR METASTASIS

Two types of tumor metastasis are described: (1) The large nodular type, and (2) the diffuse, finely nodular type. The former is by far the most frequent. The diffuse type is rarely seen. The large nodular type shows presence of one or more nodules which are usually spherical in shape and located, as a rule, near the periphery of the organs, although nodules are frequently seen in the center of the spleen. These are sharply defined against the dark background of the splenic parenchyma. Microscopic examination usually shows a sharp delimitation of the tumor from the parenchyma. Di Biasi⁴ describes a dense reaction of plasma cells and lymphocytes immediately about the tumor nodule. Connective tissue reaction is minimal, but depends to a large extent upon the type of carcinoma.

The diffuse, nodular type, shows presence of innumerable, minute, poorly defined nodules which are scattered throughout the spleen. Dial¹⁴ has collected twenty cases of this type from the literature and reports one of his own. Warren and Davis⁹ found one case which they illustrate by photograph.

Most frequently the origin of metastatic carcinoma is from carcinoma of the breast. Warren and Davis⁹ found the breast the primary site of the tumor in over one-half of their cases of splenic metastasis. Aschoff² also states that the primary source of the metastasis is usually the breast. The microscopic structure of the primary, as well as the metastatic growth, is usually carcinoma simplex, although four cases of adenocarcinoma were found. Other sites of origin are the cervix, lung, ovary, and rectum. Welch¹⁵ describes a primary source in the prostate gland. Di Biasi found that carcinomatous metastasis in the spleen is twice as common in the female than in the male.

The following case is reported as an illustration of an unusually massive metastasis of carcinoma of the breast to the spleen.

REPORT OF CASE

Mrs. R. F., housewife, age 55, entered Sutter Hospital on February 21, 1938, complaining of a lump in the left

breast. Noticed lump three days prior to admission. History of trauma to breast one year ago, followed by swelling. No pain or discharge. *Past history* irrelevant; menopause at 45. Half-brother died of carcinoma of stomach. *Physical examination* shows a large, pendulous breast, nipple erect. Tumor nodule noted in upper inner quadrant of breast, 3 to 4 inches in diameter. No attachment to skin or underlying muscles. Illumination is dark. No axillary nodes.

Breast amputated radically, using Greenough's method.

Surgical-pathological report: A tumor was present in the inner and upper quadrant of the breast which had a diameter of six centimeters. Structure was firm; color, light gray; consistency, cartilaginous. Sharp processes were present which extended into the surrounding tissues. Microscopic examination showed a newgrowth, consisting of small alveolar nests of cells which are separated by a stroma consisting of dense hyaline connective tissue. The nuclei were deeply stained. The cytoplasm was scant and basophilic. Mitotic figures were few in number. No differentiation into glandular structure was seen. No evidence of metastasis to the axillary lymph nodes.

Diagnosis: Carcinoma of the breast—scirrhous type.

Postoperative course: The patient was readmitted on October 26, 1938, with fluid in chest. X-ray showed metastatic growth in right lung. Course steadily downhill despite extensive radiation therapy. The patient died on November 22, 1939.

Autopsy findings: The body was that of a female of about 55 years of age. The left breast had been completely removed. The subcutaneous tissues beneath the scar were markedly indurated. The thickening and induration were especially marked in the axilla. The left pleura was markedly thickened. Many firm nodules were attached to the parietal pleura and to the rib margins. Both lungs were riddled with tumor nodules, which varied in size from two millimeters to about one centimeter. The nodules were well defined, moderately firm and light gray in color. A large tumor mass was present in the posterior mediastinum.

The heart showed no essential pathologic changes.

The liver contained scattered tumor nodules, which had the same appearance as those in the lung.

The spleen was 220 grams in weight. Located in the upper and medial aspect was a large, circumscribed, roughly spherical growth which had a diameter of eight centimeters. The tumor was located in the splenic parenchyma and lying adjacent to the capsule, but did not involve it. The color was light gray; consistency, moderately firm.

A small nodule of similar appearance was seen in the central portion of the spleen. The diameter of this nodule was eight millimeters.

The gall-bladder was enlarged. Its walls were thickened. Several pigmented stones were seen in the lumen. There was no obstruction of the common duct.

No changes were seen in the structure of the adrenals, pancreas, or gastro-intestinal tract.

Both kidneys contained small metastatic nodules, which were most numerous in the cortical portion. No changes were seen in the pelvic organs.

Microscopic examination of the spleen: Sections obtained from the small nodule showed a newgrowth, consisting of alveolar clusters and broad strands of epithelial cells which were compactly arranged. These were separated by a stroma, consisting of highly vascular, loose connective tissue, which, in places, was infiltrated with lymphocytes. The tumor cells contained hyperchromatic nuclei which vary markedly in size. Mitotic figures were quite numerous. The cytoplasm was basophilic and moderate in amount. In the center of the growth, marked degenerative changes were seen in the tumor cells. Here, extensive leukocytic infiltration was noted. A moderate lymphocytic and plasma cell infiltration was noted at the periphery of the metastatic nodule. Fibroblastic proliferation was not conspicuous. Near the edge of the tumor mass was seen an occasional thickened arteriole.

The structure of the larger nodule was similar to that described above. However, necrosis of the tumor elements was more extensive.

No structural changes were seen in the structure of the pulp of the spleen. The arterioles were moderately thickened. Isolated clusters of tumor cells were not found.

Diagnosis: Metastasis of medullary carcinoma (medullary) of breast to lungs, pleura, liver, mediastinum, kidneys, and spleen; cholecystitis; cholelithiasis.

COMMENT

This case illustrates the gross nodular type of metastasis to the spleen. The metastasis is considered hematogenous in origin, since there is no evidence of involvement of the capsule and extension along the efferent lymphatics. The tumor is a rapidly growing, medullary type of carcinoma of the breast.

IN CONCLUSION

1. Metastasis to the spleen is extremely rare.
2. The rarity of metastasis is due to several factors: first, and most important, is the absence of afferent lymphatics to the spleen; second, the motility of the organ; and, third, the presence of a specific tumor-resisting substance in the spleen, which is supported by experimental evidence.
3. Two types of metastasis are described; the nodular type and the diffuse type; the latter is extremely rare.
4. An example of the gross nodular type of metastasis to the spleen is described.

Sutter Hospital, Sacramento.

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HARD OF HEARING PROBLEMS*

FIFTH ANNUAL REPORT OF THE SPECIAL COMMITTEE ON "PROBLEMS OF THE HARD OF HEARING"

By FRANCIS L. ROGERS, M.D.

Long Beach

THIS annual report of your "Committee on Problems of the Hard of Hearing" may well be opened with an excerpt taken from a clinical lecture by Dr. Walton Burge of Philadelphia on "The Pennsylvania Plan for Tuberculosis."† He

* Read before the Section on Eye, Ear, Nose and Throat of the California Medical Association at the sixty-eighth annual session, Del Monte, May 1-4, 1939.

† *Journal of the American Medical Association*, November 12, 1938.