Secondary Carcinoma of the Spleen*

Its Incidence in 544 Cases and a Review of the Literature

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METASTATIC carcinoma in the spleen is relatively infrequent, if not rare. In the literature, it is stated to range from 2 to 6 per cent.[1-6] Abrams, et al[7] and Shaw Dunn[8] however, have reported higher frequencies—9 and 16 per cent, respectively. Harman & Dacorso[9] have recorded 50 per cent splenic involvement when there was generalized matastasis of carcinoma.

Over a period of years, theories for the infrequent matastasis to the spleen have been proposed, but none have fully or adequately explained this finding. The purpose of this paper is to present a clinical study on the frequency of carcinomatous metastasis to the spleen. A review of the literature and its several aspects will follow.

MATERIALS AND METHODS

Necropsy reports from the pathology files of Freedmen's Hospital were examined for cases in which patients had carcinoma of various organs or organ systems. The neoplasms were not necessarily the cause or even a contributing factor in the patients' deaths. Over a period of 11 years, 1955 to 1965 inclusively, 544 cases of carcinoma were found.

The reports of these cases were examined for metastatic lesions in the splenic pulp. The incidence of direct dissemination of carcinoma to the splenic capsule and/or pelvis was recorded, but not used in the percentage calculations. All cases with metastatic growth in the splenic pulp were reexamined microscopically. It is reasonable that the percentages reported in this article may be somewhat below actual frequencies because of undetected microscopic neoplastic foci. However, care was taken to avoid this source of error. It also follows that the percentages could not be higher than those given.

TABLE I.—SITES AND PERCENTAGES OF SECONDARY CARCINOMAS OF THE SPLEEN

Organ Primary	*Total Number of Cases*	*Number of Splenic Metastases*	*Percentage*
Breast	41	4	9.7
Colon	45	4	8.8
Pancreas	37	2	5.4
Rectum	25	1	4.0
Lung	75	2	2.7
Cecum	10	2	20.0
Vulva	2	1	50.0
Other organs	309	0	0
Total	544	16	100.0

RESULTS

Of 544 reported cases of carcinoma, 16 metastasized to the pulp of the spleen. Thus 2.9 per cent of the carcinomas studied presented splenic pulp metastasis. Table 1 shows the sites of primary caricinomatous growth in patients with splenic metastases. The breast, as a primary, had the highest per cent of splenic metastasis. The cecum and vulva were excluded because of poor sampling.

Fifteen of the 16 patients having metastasis in the spleen showed, microscopically, one or more focal growths and the remaining case showed a diffuse pattern of splenic dissemination (Figs. 1, 2 and 3).

While nine of the primary sites were from abdominal viscera and one perineal, only three showed metastases in the splenic capsule as well as in the pulp. In these cases, extension from the capsule to the pulp was not evident.

The 544 cases were further studied to obtain the frequency of metastatic carcinoma in other organs (Table 2).

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TABLE 2.—FREQUENCY OF METASTASES IN PATIENTS WITH CARCINOMA

(F.H. Series of 544 Patients)

Organ	*Percentage*
Lymph node	45.0
Liver	39.0
Lung	31.0
Bone marrow	11.7
Kidney	9.7
Brain	3.2
Heart	2.9
Spleen	2.9

DISCUSSION

Metastasis of carcinoma to the spleen is as rare as that to any organ receiving a significant vascular flow. As an adult lymphatic organ, it fails to approach the lymph nodes in frequency of metastatic carcinoma.

It is stated that carcinoma metastasizes more frequently by way of lymphatics than by the blood vascular system. The lymph nodes were the sites of metastasis in 45 per cent of the cases studied. Bailey's Textbook of Histology,[10] Dial,[11] and Milton[5] deny the existence afferent lymphatics in the spleen whereas they exist in lymph nodes. Some authors believe that no lymphatics enter the parenchyma of the spleen, but are limited to the capsule and capsular trabeculae.[2,3,4,8,9,12-13]

Snook,[14] however, claims to have demonstrated deep lymphatics in the white pulp of experimental animal spleens. More recently, Goldberg[6] reported that lymphatics run into the white pulp with blood vessels, and further, that by these lymphatics, metastatic cancer may occur in the spleen. Goldberg[15] also reported the visualization of deep parenchymatous lymphatics by noting a mucous-producing carcinoma within the vessels. Rusznyak, et al.[16] cited several works in favor of deep lymphatics in the spleen.

It is not certain that afferent lymphatics and/or deep lymphatics exist in the spleen. If they do not exist, a factor, in the infrequency of metastatic carcinoma to the spleen, could be established. The observation of endothelial cells in the deep parenchymal vessels which are visible in relation to metastatic tumor emboli suggests that lymphatics are present. Figure 4 presumably demonstrates this finding.

It has been shown that more than one pattern of metastatic seeding to the spleen exists. Mary-

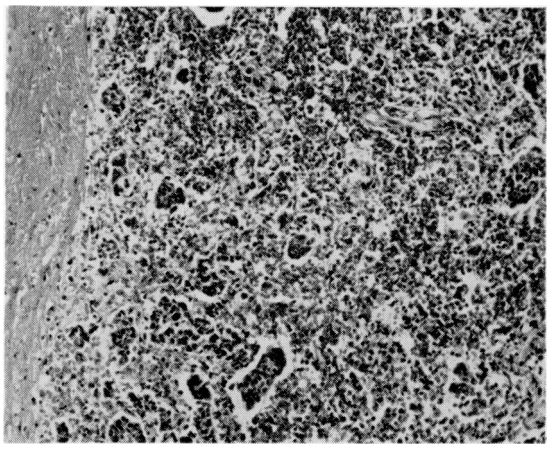

Fig. 1. Spleen showing a diffuse pattern of metastatic tumor. Primary site breast. H. & E. 125X.

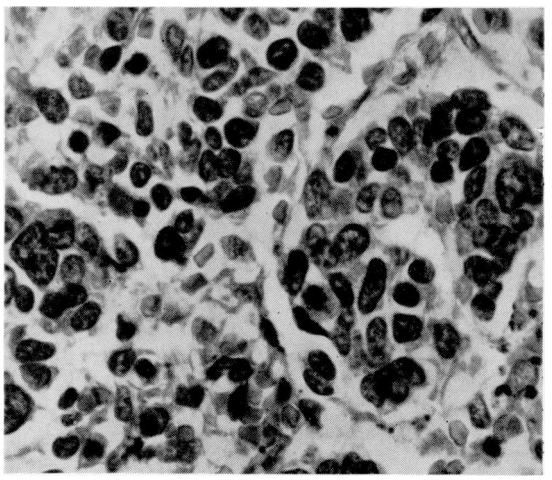

Fig. 2. Spleen showing a higher magnification of Figure 1. H. & E. 430X.

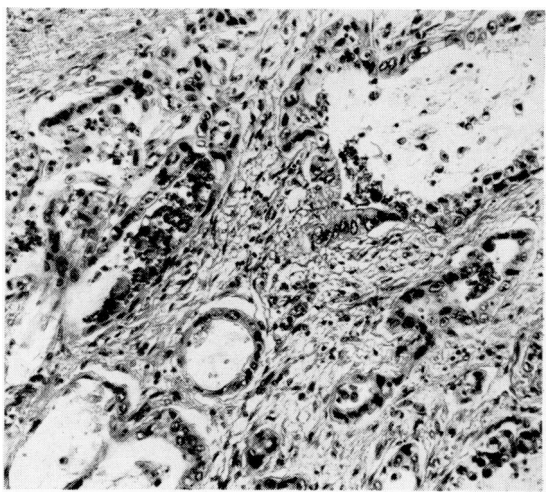

Fig. 3. Spleen showing metastatic adenocarcinoma. Primary site, pancreas. H. & E. 250X.

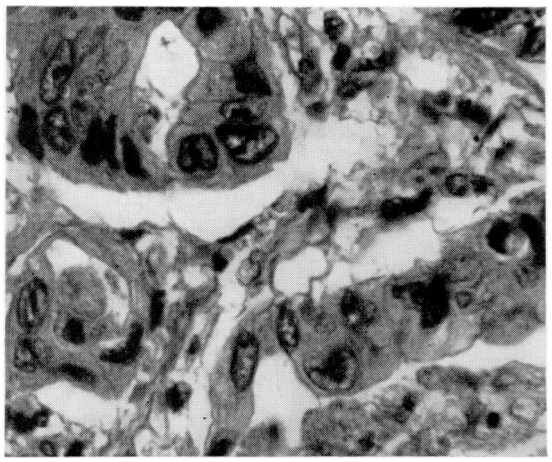

Fig. 4. Spleen showing a tumor embolus in a vascular-like space lined by flattened endothelial cells (upper left hand corner). H. & E. 450X

mount and Gross[17] and Orlandi,[18] observed that vascular as well as lymphatic invasion may occur.

Warren and Witham,[19] stated that breast metastasis is usually by emboli in lymphatic channels and is rarely blood born. The results of our study show that breast primaries exceed others in metastatic spread to the spleen. Other studies also report that the breast is the major primary for metastatic carcinoma in the spleen.[7,9,19,20]

Nonetheless, many authors have generally accepted that metastasis to the spleen is by the vascular system. The lymphatics are considered to be questionable. The contractile action of the spleen has been postulated as having a relationship to infrequent splenic metastasis.[2,21,22] It was proposed that the splenic contractions prevent the lodging and subsequent growth of tumor emboli. Dial[11] recognized this possibility, but further stated that the lungs were more active and demonstrated more neoplastic seeding.

When considering this theory, it should be understood that whether the human spleen contracts significantly or not at all, is debatable. Shaw Dunn[8] feels that regardless of the extent of the intrinsic movement of the spleen, the movement of the surrounding tissue may still lend favor to this theory.

Table 2 shows that the spleen and myocardium are in the low order of metastatic seeding. It is plausable that the contractile action of the heart is responsible for the low incidence of metastases. The spleen certainly does not contract to the extent of the heart and yet the incidence of seeding, in our series, is similar. The entire answer does not appear to be that movements of the spleen decrease the lodging of tumor emboli.

It has been theorized that the angle of the splenic artery from the celiac trunk is too acute to allow significant passage of emboli.[22] However, the frequency of splenic infarcts due to arterial emboli appear to rule out this theory.[11] Paget[23] states that arterial emboli to the spleen can not be avoided because the splenic artery is larger than the hepatic.

The lymphatics of the spleen, splenic contractions, and the angle of the splenic artery are believed to be contributing factors in the infrequency of splenic metastasis. These have been termed as the "mechanistic" view by Herbut and Gabriel.[3] In opposition to this is the "antipathic" view in which there is an inherent antipathy of the spleen toward metastatic tumor growth.

Woglom,[24] in a comprehensive review of the literature, stated that resistance to transplantable tumors was unrelated to immunity. He further stated that most investigators observed the acceptance of splenic tumor implants by the spleen in experimental animals. Only a few investigators reported an adverse reaction to tumor transplants in the spleens of experimental animals. Among the latter group, Lazarus-Barlow and Parry[25] concluded that there is a greater local resistance to the growth of tumor in the spleen and a greater resistance to neoplastic growth following intrasplenic immunization in animals.

In 1934, Warren and Davis[2] regarded the antineoplastic action of the spleen as debatable. Dial[11] in 1930 reported controversial results in treating cancer with splenic extracts. The experimental results show either no change or a decrease in tumor growth with splenic extract. The positive seems more important than the neutral in cancer research. Therefore, the work of Lewisohn[26] and Pollard and Bussell,[27] who demonstrated tumor regression in experimental animals with splenic extracts, should be cited. Watson, et al.[28] concur with Lewisohn and present clinical experiments in which splenic extracts were used in treating cancer. Some of the results appear promising.

The spleen is credited with greater immunologic properties than the lymph nodes. The spleen is the primary site of plasma cell production and plasma cells are more effective in antibody production than lymphocytes.[29] Ellis and Smith[30]

claim that the spleen is the primary R-E organ. Also the spleen combines immunologically competent tissue and effective sinusoidal circulation through a macrophage system. Further, the lymph nodes are similar in both respects, but handle lymph and not blood.

Miller and Milton[31] counted mitotic figures in a metastatic bronchogenic carcinoma in the liver and spleen. They noted that mitoses in the primary and the liver were similar, but that the spleen showed fewer mitotic figures. These authors subsequently suggested the possibility of "antineoplastic" humors. Prior to this, Hirst and Bullock[4] reported no evidence of decreased mitotic counts. When Willis[32] counted mitotic figures in a metastatic carcinoma, he noted a greater count in the liver than in the primary. This was attributed to high carbohydrate content and low arterial vascularity. Thus it may be suggested that the spleen may not be anti-neoplastic, but that certain organs are favored over others.

In considering splenic "antipathy," it is most informative to examine some of the extrinsic factors that have been incriminated in increased metastasis which also includes increased splenic metastasis. Of significance is the finding that steroids, notably cortisone, facilitate tumor growth and/or metastasis in experimental animals.[33-36] Goldie, et al.[36] feel that there is an inhibition of the local cellular reaction to tumor. Pomeroy[35] and Green and Whiteley[33] believe that a blockage of the host antibody production is related. It has also been claimed that cortisone decreases the activity of the reticulo-endothelial system—specifically the phagocytic capacity of the R-E cells.[37,38]

In 1951 a subcommittee of the A.M.A. on steroids and cancer reported a transient beneficial effect from the use of cortisone and ACTH in clinical cancer cases.[39] And further, it was stated that this beneficial effect was followed by increased metastases—often involving the spleen. These same findings were reported in a clinical study by Arraztoa, et. al.[40] Similar results were noted by Iversen and Hjort.[41]

CONCLUSIONS AND SUMMARY

1. Of 544 cases of carcinoma, 16 showed splenic metastasis, or 2.9 per cent which is in keeping with reports dating back 40 years or more.

2. Evidence is accumulating that questions the absence of afferent and parenchymatous lymphatics.

3. The mechanical and anatomic considerations of arterial metastasis to the spleen are discussed.

4. Evidence indicates that steroids increase metastasis—including metastasis to the spleen. Reasons for this lend favor to the concept of immunologic antipathy of tissues, notably the spleen, to metastatic cancer. However, in the authors' series, the percentage of splenic metastases has not increased in 40 years, in spite of increased steroid therapy.

5. Further study on the subject of the "antineoplastic" capacity of the spleen is warranted.

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EFFICIENCY EXPERT'S REPORT ON A SYMPHONY CONCERT

For considerable periods the four oboe players had nothing to do. The number should be reduced and the work spread more evenly over the whole concert, thus eliminating peaks and valleys of activity.

All the twelve violins were playing identical notes; this seems unnecessary duplication. The staff of this section should be drastically cut. If a larger volume of sound is required, it could be obtained by means of electronic apparatus.

Much effort was absorbed in the playing of demi-semi-quavers; this seems to be an unnecessary refinement. It is recommended that all notes be rounded up to the nearest semi-quaver. If this were done, it would be possible to use trainees and lower-grade operatives more extensively.

There seems to be too much repetition of some musical passages. Scores should be drastically pruned. No useful purpose is served by repeating on the horns something which has already been handled by the strings. It is estimated that if all redundant passages were eliminated the whole concert time of 2 hours could be reduced to 20 minutes and there would be no need for an intermission.

In many cases the operators were using one hand for holding the instrument, whereas the introduction of a fixture would have rendered the idle hand available for other work. Also, it was noted that excessive effort was being used occasionally by the players of wind instruments, whereas one compressor could supply adequate air for all instruments under more accurately controlled conditions.

Finally, obsolescence of equipment is another matter into which it is suggested further investigation could be made, as it was reported in the program that the leading violinist's instrument was already several hundred years old. If normal depreciation schedules had been applied, the value of this instrument would have been reduced to zero and purchase of more modern equipment could then have been considered.

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