Malignant Melanoma

Ten-Year Results following Excision and Regional Gland Resection*

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MELANOMAS ARE UNCOMMON but highly malignant tumors. Because of the uncertainty of their origin, their susceptibility to trauma and their tendency to recur or metastasize after extremely variable periods of time, they have fascinated the medical profession for centuries. Among the surgeons who have contributed to our knowledge of them were such men as Dupuytren,[6] who first recognized melanosis as an entity in the early part of the nineteenth century, and Laenec,[11] who called the attention of the medical profession to it in a paper read before the Faculty of Medicine in Paris in 1806. Few improvements have been suggested in the treatment of these lesions during the past 50 years. As long ago as 1858, Pemberton[15] recommended removal of the tumor by wide excision including the deep fascia under it, and was the first to describe a groin dissection to irradicate metastases. In 1865 Paget[14] reported 18 cases treated surgically with five four-year survivals. Probably the most significant contributions to therapy were made by Handley[9] and Pringle[16] in 1907 and 1908, respectively. Handley demonstrated the spread of melanotic cells along lymphatics and fascial planes. He dissected the path of tumor cells from a lesion of the foot through the lymphatics to glands in the groin. Based upon this work, Pringle recommended removal *en bloc* of the original lesion and a strip of skin, lymphatics and deep fascia from it to the regional glands, with resection of the glands themselves. This remains the operation of choice today.

Most melanomas occur at the site of a previously existing pigmented lesion, usually a nevus of the skin. Driver and MacVicar[5] reported that 80 per cent of their patients gave this history. The origin of the nevus cells, however, is not clearly understood. Rawles[17] has carried out an experimental study which was noted by Clark and White[2] in a paper read before the Southern Surgical Association in 1951. By grafting portions of a pigmented strain of mouse embryo to an embryonic chick coelom, she demonstrated that pigment formation is dependent upon a highly specialized type of branched pigment-forming cell which originates in the neural crest. Such cells or melanoblasts occur in pigmented areas in human tissue such as the epidermis adrenal medulla, iris, choroid and leptomeninges. In the skin they appear as the clear cells of Masson in the layer of the epidermis. Since they are dopa positive they contain melanin. Nevus cells seem to be formed by proliferation of melanoblasts. They differ from epidermal cells in that they are round or oval in the deeper areas but are more fusiform near the epidermis. They may or may not contain melanin.

Malignant melanomas (Fig. 1) originate at the dermal epidermal junction, usually in so-called junction nevi (Fig. 2A). The cells are oval or fusiform with irregularity in shape. The nuclei are enlarged and irregular and are poorly differentiated (Fig. 2B). They invade the dermal layer of the skin and, as pointed out by Gage and Daw-

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TABLE I. *Malignant Melanoma.*

10 Year Study of 26 Therapeutic Gland Resections (Palpably Enlarged Regional Glands)

	No Cases	Lost Track of	Survival 2 years only	Survival 5 years only	Survival 8 years only	Survival 10 years—no recurrence	Per Cent
Advanced Cases Biopsy only	4		0	0	0	0	0
Excision and Gland Resection							
Metastases	20	1	3	1	0	0	0
No Metastases	2		1	0	0	0	0

TABLE II. *Malignant Melanoma.*

10 Year Study of 14 Prophylactic Gland Resections (Regional Glands not Palpably Enlarged)

	No Cases	Lost Track of	Survival 2 years only	Survival 5 years only	Survival 8 years only	Survival 10 years—no recurrence	Per Cent
Proven Metastases	7		3		1	2	43% 8 years 29% 10 years
No Metastases	7	1				5	71%

son,[8] vary greatly in appearance even in the same tumor. A confusing difference in terminology has arisen from the uncertain origin of the cells and their differing appearances. Now, however, melanosarcoma and melanotic carcinoma are both commonly included in the term *malignant melanoma.*

DIAGNOSIS AND TREATMENT

The diagnosis of a malignant melanoma usually is not difficult. Brown flat moles occur commonly, most individuals having from 20 to 30 scattered over the skin of their bodies. These lesions usually are not malignant, especially if they contain hairs. Raised black lesions which make their first appearance after the age of puberty are more apt to be malignant, especially if they are of the junction type. Any type of pigmented mole which begins to increase in size and vascularity, or begins to change in color or in degree of pigmentation, must be considered malignant until proven benign by microscopic study.

The peculiar characteristic of apparently benign moles to become malignant following trauma is well known. Whether cells previously benign are stimulated by injury to become malignant, as believed by Cohnheim,[3] or whether these cells are malignant from the start, as indicated by Ewing,[7] the frequent history of trauma preceding the appearance of malignant changes cannot be denied. Tod[18] reported that in an alarmingly high percentage of cases the injury consists in inadequate or improper treatment of benign lesions by physicians (Fig. 3A and B). Practically, therefore, any pigmented lesion which may be subjected to irritation by clothing, or otherwise, should be removed with a safe margin of skin about it. This is particularly true on the soles of the feet and lower extremities where the appearance of malignant changes has been frequent, as noted by Pack *et al.*[13] Excision should be performed under general anesthesia, or at least under regional block anesthesia, to prevent injury of the nevus by needle injection. Moles of the face which do not show changes suggesting malignancy should not be disturbed. If removal is necessary for cosmetic reasons, it must be performed by as wide an excision as in other parts of the body. Cauterization or electrodesiccation must never be used on any pigmented lesion, and since a considerable number of malignant melanomas originate in nonpigmented lesions having the appearance of warts or moles, the use of

electrodesiccation for skin lesions of any kind is dangerous.

Once a melanotic lesion becomes malignant, invasion occurs locally into the skin, the deeper layers of the subcutaneous tissue and the deep fascia. Extension then occurs along the deep fascia through the lymphatics or through the blood stream. As in all types of malignancy, the extent of invasion or metastasis cannot be determined by

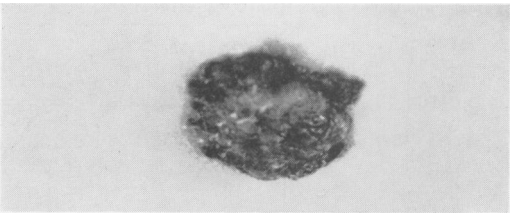

FIG. 1. Melanoma of lower leg. Sudden enlargement and increased vascularity in a previously existing mole.

the appearance of the primary lesion itself. Therefore, although undoubtedly it is true that a number of melanomas have been treated successfully by local excision alone, this method of treatment provides no greater guarantee of cure than does simple mastectomy in carcinoma of the breast. In fact, as the limited number of cases which we have followed indicates, there is a striking similarity in the results of treatment of malignant melanoma and those of carcinoma of the breast.

Metastases by way of the lymphatic channels are present at the time of removal of a primary melanoma in a surprisingly high percentage of cases. In this series, patients who demonstrated glandular enlargement at the time of removal of the primary lesion were found to have microscopic metastases in the glands of 91 per cent of cases. In prophylactic gland resections of this series without glandular enlargement microscopic metastases were present in 50 per cent of cases. The importance of performing prophylactic gland dissections, therefore, as recommended by Pringle nearly 50 years ago, is obvious.

In order to assure removal of any implants of tumor cells along regional lymphatic channels a strip of skin, subcutaneous tissue and deep fascia should be removed *en bloc* between and including the widely excised primary lesion and the regional lymph nodes. Midline lesions on the chest or back may, of course, metastasize to either or both axillary groups of glands. Consequently, bilateral axillary dissection should be performed in such cases. An example of the advisability of this procedure is demonstrated in Figure 4. The patient is a 30-year-old married woman who developed a large melanoma in the midline of her back. A wide excision of the local lesion, the strip of skin leading to each maxilla and bilateral axillary dissection, was performed. Positive nodes were found in both axillae but she has remained well for a period of five years without evidence of recurrence. Lesions of the face should be treated by cervical gland dissection. Melanomas of the rectum carry a particularly poor prognosis. They should be treated by abdominal perineal resection and, if they lie in the anus itself, by bilateral groin dissection as well. The only patient of this type whom we have seen in recent years died two years after operation with multiple metastases in the liver, lungs and bone.

When lesions are far advanced there is little palliative treatment which is of value. Radiation therapy is of no avail. Nitrogen mustard occasionally causes temporary regression of primary lesions but is of no permanent benefit. Orchidectomy in male patients has also been reported by Herbst[10] to give palliation for a time in some cases.

CLINICAL MATERIAL

For the past ten years we have been following a group of 40 patients treated during World War II for malignant melanoma. A preliminary report of some of these was made in 1949.[12] In many instances, the patients were first seen after removal of the primary lesion when microscopic study had

FIG. 2 A.

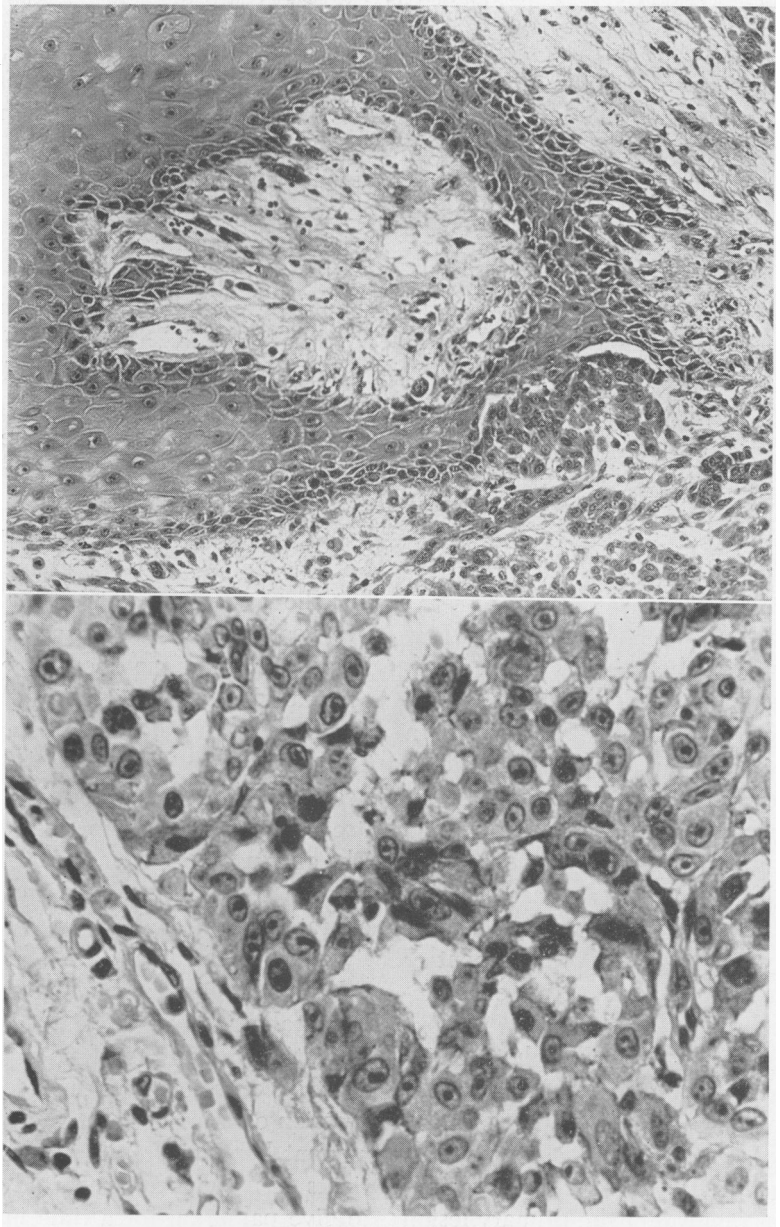

FIG. 2 B.

FIG. 2. (A) Photomicrograph of a dermal-epidermal junction nevus (lower right corner). Note rounded cells, and situation at dermal-epidermal line. (B) Photomicrograph of malignant melanoma. Note irregular cell margins, variation in size and shape, prominent nucleoli.

revealed its character. The sections were always reviewed, and following this in all but four advanced cases re-excision of the scar and block dissection of the regional lymph nodes was carried out. In most instances, the skin, subcutaneous tissue and deep fascia were included between the tumor and the regional nodes. In lesions of

FIG. 3 A and B.

FIG. 3. (A) Melanoma of the temple, and (B) large melanoma of the face. Both lesions were recurrent following electrodesiccation elsewhere.

the face and neck, a unilateral neck dissection was performed on the side of the tumor. Midline lesions on the anterior or posterior chest wall were excised locally, together with the glands in both axillae and intervening lymphatic areas. Groin dissections were performed for lesions of the lower extremity. All except two of the 36 patients treated in this manner have been followed for a period of ten years. The results are shown in Tables I and II. Two of the patients were lost track of after a period of about two years when both were known to be living.

Since regional lymph glands were removed in all cases, regardless of whether or not they were palpably enlarged, the cases may be divided into two groups: (1) therapeutic gland resections where regional lymph glands were palpably enlarged, and (2) prophylactic gland resections where lymph glands were not palpably enlarged. A review of these groups after ten years shows a striking difference in favor of prophylactic gland resections (Tables I and II). In the therapeutic group 18 of the 20 patients revealed tumor metastases in the glands removed. One patient lived five years only, three patients two years only, but none is known to have lived for longer than five years. Excluding one patient who could not be traced, 16 (76 per cent) died in less than two years. In group two, on the other hand, of the 14 patients undergoing prophylactic gland resections only two died in less than two years and seven (50 per cent) are known to have survived without evidence of recurrence for ten years. Of the seven prophylactic patients showing evidence of tumor cells in the regional glands,

FIG. 4. Result following excision of melanoma of back, and bilateral axillary dissection in continuity with skin graft.

three (43 per cent) lived for eight years, and two (29 per cent) are living after ten years, without evidence of recurrence. Of the seven prophylactic gland resections, without evidence of microscopic metastases, five (71 per cent) are known to be living after ten years.

The findings in the prophylactic resection group are strikingly similar to those of radical mastectomy in breast cancer. In carcinoma of the breast, without glandular metastases, radical mastectomy was followed by 82.7 per cent five year survivals in a large group of cases reported by Bryant, Lampe and Coller,[1] whereas, in patients with positive lymph nodes, five year survivals were reduced to 38.7 per cent. Glandular enlargement seems a more unfavorable sign in melanoma than in breast cancer, due in part to the insusceptibility of the former to radiation therapy. This failure of irradiation or of any treatment except surgery to benefit these patients emphasizes the findings in this group of cases, namely, that routine prophylactic gland resection is indicated in all except far advanced cases of malignant melanoma.

SUMMARY

A review of the diagnosis and treatment of malignant melanoma has been presented. A group of 36 patients undergoing block regional gland resection has been followed for a period of ten years. Twenty-two of these had glandular enlargement at the time of their operation. Only five of these survived for two years, and only one for five years. Of 14 patients with no glandular enlargement seven, or 50 per cent, are known to have survived for ten years without evidence of recurrence. The importance of prophylactic gland resection in all cases of malignant melanoma is stressed.

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DISCUSSION.—DR. ALTON OCHSNER, New Orleans, La.: I think we should be very grateful to Dr. McCune for calling attention to this condition, about which there has been so much confusion. Physicians have either considered melanoma of no consequence whatsoever, and done nothing about them, or have burned them, or have thrown up their hands in utter despair. Dr. McCune has shown that none of these concepts is correct. He has shown so beautifully what can be accomplished if lymph node dissections are done. I believe it is obligatory for every physician who treats a patient with melanoma to perform regional lymph node resection unless there is evidence of widespread dissemination. The evidence is here, and Dr. McCune has shown us definitely what can be accomplished by prophylactic dissection in individuals with melanoma when there are no nodes which are palpable. There is no cure for melanoma except surgical extirpation. We have used everything that has been suggested. Our best results in the hopelessly inoperable cases have been with one of the chemotherapeutic agents, TEPA. It is not a cure, but we have obtained some palliation, better than with any other chemotherapeutic agent, and I would suggest that one try TEPA in those instances in which the lesion is widespread.

DR. GILBERT HORRAX, Boston, Mass.: It occurred to me that I should say something about two patients. One was a man who had a melanoma of the chest region, the breast, operated upon at another hospital. He subsequently had lymph nodes in the axilla which were removed, also at another hospital, and we have pathologic slides of those dissections. He came to me some months later with symptoms of brain tumor, and thinking it might possibly be something else, we operated on him because he had localizing signs. We did a ventriculogram, which showed the situation, and it turned out to be a melanoma of the brain. I had never seen one that went on for more than a few months, and I gave the family and the local physician a pretty bad prognosis. However, he got over it and has gone now for seven years without symptoms except that during this time he has had two or three convulsions, but he is alive and well, and is doing all his work.

The other case is a patient who was sent to Dr. Cushing many years ago with a brain tumor. There was no evidence of melanoma of the skin. At operation a melanoma was found. When the patient came to autopsy, they went over the body from A to Z to see if there was any melanoma of the skin anywhere, and could find none. Finally, in