MELANOTIC WHITLOW (SUBUNGUAL MELANOMA)*

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Melanotic whitlow, § a relatively rare form of melanoma, is an entity seldom recognized for what it really is. We have found in the literature only 52 well-documented cases. In many of these cases the disease had been previously misdiagnosed and mistreated. It is the purpose of this study to define the clinical and pathologic entity of melanotic whitlow in the hope that its early diagnosis and treatment will be facilitated.

Although Hertzler (1) found earlier case reports, melanotic whitlow was named and classically described by Hutchinson (2, 3) in 1886. The name was inspired by its malignant course and by its resemblance, excepting pigmentation, to ordinary whitlow.

The sequence of pigmentation and ulceration has been discussed by several workers (4, 5) but is not well understood. The possibility that subungual melanoma may derive from nail-bed pigmentation is suggested in many case reports, but in only one instance (6) has a nevus in this location been observed and histologically proved.

Trauma in association with the onset of melanotic whitlow has been reported (7) in a high percentage of cases, but there is no real proof that this is a traumatic disease.

Melanotic whitlow has been estimated by several authors (7–11) to comprise between 2.9 and 15 per cent of all melanomas, and one study (12) indicates that about 9 per cent of all melanomas of the extremities are of the subungual variety.

The average age for patients with melanoma in all locations is between 47.1 and 47.9 years (8, 9), but a higher average prevails for the subungual type (13, 14). There is no agreement on which digit or extremity is most frequently involved. As is true of other types of melanoma, melanotic whitlow is rare in Negroes (15, 16), only four cases having been reported in that race.

Although two excellent papers have been published (14, 17) on the differential diagnosis of melanotic whitlow, a perusal of many case reports points up a striking low index of suspicion on the part of the attending physician. Diagnostic

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§ Melanoma, the official term in *Standard Nomenclature of Diseases and Operations* for malignant melanoma, will be used in the official sense in this paper. Melanotic whitlow is a synonym for subungual melanoma.

criteria have been delineated by many workers and are suggested in the numerous case reports. These criteria might be summarized as follows: (1) a history or the presence of any form of pigmentation in, under or about a single nail, especially if this pigmentation is increasing; (2) a history or the presence of chronic onychia, paronychia or granular excrescence that involves a single nail, that is essentially painless and that refuses to heal, or increases, despite all treatment; (3) a history or the presence of splitting, cracking or displacement of a single nail, not readily explained by some other concurrent disease; and (4) any of the above changes developing and persisting for an unusual length of time following trauma.

Simple surgical excision, or this combined with dissection of the regional nodes, is the treatment of choice for subungual melanoma (8, 12, 13, 18, 19). Most authors agree that melanoma is radioresistant, although this modality of treatment is reported (20, 21) efficacious in some cases. There is little agreement concerning the extent of surgical treatment indicated and the end results that may be attributed to it. Only a few reported cases have had adequate follow-up after operation. Furthermore, older patients are likely to die of other causes before the malignant lesion can recur or metastasize. These factors make it impossible to obtain significant prognostic figures. Therefore, information to be of any value must be interpolated from more extensive studies dealing with melanoma in general.

Some workers (13, 14, 19) have ascribed a relatively good prognosis to melanotic whitlow, while one (11) has said that it is no less malignant than melanoma in other locations and that all treatment is fruitless if metastasis has occurred. In one large general series (8), seven of 25 patients (28 per cent) with subungual melanoma survived 5 years or longer. This was compared with a 5-year survival rate of 19.7 per cent for all the melanoma patients of that series, but the difference was not considered statistically significant. Another study (22), in which 18 patients with subungual melanoma had been treated surgically and followed, revealed that seven patients (38.9 per cent) survived at least 5 years without recurrence. This was compared with a 5-year survival rate of 21.4 per cent for the authors' over-all group. Elective prophylactic dissection of the nodes, if done, should be performed a few weeks after removal of the primary lesion, thus allowing the nodes to entrap any migrating malignant cells (18, 23). That such dissection enhances survival remains to be proved.

Although doubt has been expressed (8) as to whether radical surgical procedures offer a greater chance for longer survival, some workers (22, 23) have advocated such treatment for malignant melanoma. When a hand or foot is involved, with regional metastasis, one group (22) would disarticulate the entire extremity with simultaneous removal of the nodes. The average survival time for these authors' general cases was longer after local excision than after radical procedures. A longer survival following simple excision has also been observed by others (12). This paradox is probably explained on the grounds that more radical procedures are elected for the more advanced cases of malignancy.

No special study of the histopathology of melanotic whitlow has been reported in the literature.

PRESENT STUDY

Material and method: The records of 40 patients with subungual melanoma, seen and diagnosed at the Mayo Clinic from May 15, 1914, through September 15, 1955, were reviewed. Two cases had not been histologically proved and were excluded. For the remaining 38 cases, data obtained from the case records, from extensive follow-up efforts and from recent examinations were summarized. For comparison, 52 well-documented cases were taken from the literature. These were abstracted and tabulated in detail elsewhere (see thesis, 24).

All available pathologic material, gross and microscopic, was reviewed. Slides from 33 of the 38 primary lesions, plus several preserved gross specimens, were available for study. Hematoxylin and eosin and silver nitrate stains were used. All characteristics that might prove helpful in grading malignancy or in making a prognosis were noted. Special effort was made to find some microscopic characteristics that might be peculiar to the cases in which the patients had enjoyed prolonged survival periods. In two suitable specimens the pigmented halo about the whitlow was studied in an attempt to ascertain its microscopic structure.

Illustrative cases: In order to present the total clinical picture of melanotic whitlow more effectively, abstracts of four cases are given.

Case 1: A 50-year-old housewife came to the clinic on October 3, 1944, complaining of bleeding from the left great toe. Small hemorrhages had been recurring for about 1 year, during which she had been treated for an ingrown nail. Part of the nail had spontaneously separated during this time. Examination disclosed a walnut-sized, pigmented, granulomatous tumor involving the distal part of the toe and displacing the nail from its bed (fig. 1*a*). No nodes were palpated, and the x-ray appearance of the thorax was normal. The toe was amputated on October 9, and the pathologic report was malignant melanoma (fig. 1*b*). At the next visit to the clinic 11 months later metastasis to the left inguinal region and to both lungs had occurred. The patient died in July, 1946, a year and 9 months after operation.

Except for pigmentation of the lesion, ingrowing nail might well have been diagnosed. This case points to the difficulty in assessing prognosis at the time of operation in a case in which there is no clinical evidence of metastasis to the nodes.

Case 2: A 46-year-old housewife was seen at the clinic on April 3, 1946, with the complaint of a bleeding, discharging lesion of the left thumb. Five years previously ridges had developed in the nail which split longitudinally. For many months an infection had persisted around the nail. An occasional aching sensation had extended up the arm. Treatment had been given for a fungous infection, and on at least one occasion the nail had been removed. Examination disclosed a nail fragment which was friable, piled-up, dystrophic, and bathed in pus. A band of pigment encircled the nail bed (fig. 2*a*). A node 1 cm. in diameter was palpated in the left axilla. X-ray examinations of the thorax and of the digit gave negative results. The thumb was amputated on April 12, and the pathologic diagnosis was malignant melanoma (fig. 2*b*). A "brain tumor" and other metastatic lesions developed and the patient died in April, 1952, six years after operation.

An earlier diagnosis might have been possible had the pigmented halo been appreciated. The axillary nodes were not dissected even though one was enlarged. Whether or not the patient would have lived longer than 6 years with more radical surgical treatment is problematical.

Case 3: A 54-year-old clerk and housewife came to the clinic on March 17, 1954, complaining of an indolent ulcer of the right index finger. Nine months previously a blue line

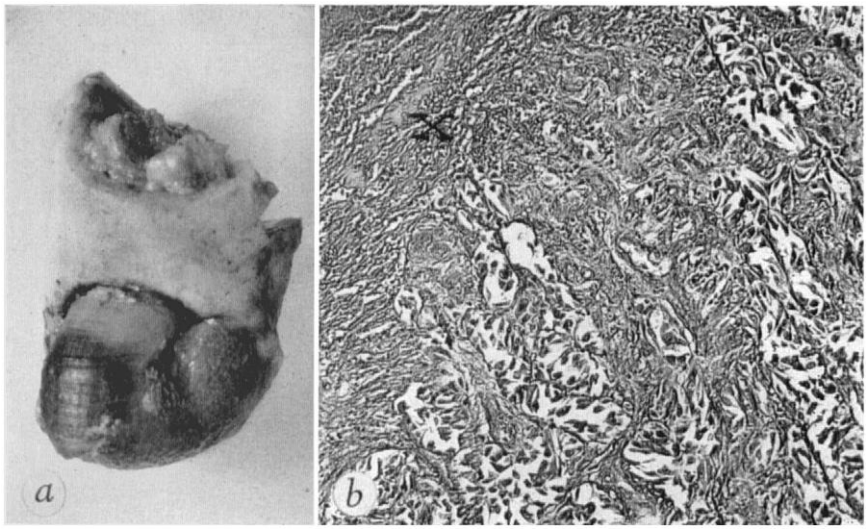

FIG. 1 (case 1). *a*. Amputated specimen. Note upward displacement of nail and absence of pigmentation in surrounding skin. *b*. Origin of melanoma from epithelium of nail bed is indicated by an X (hematoxylin and eosin; ×100).

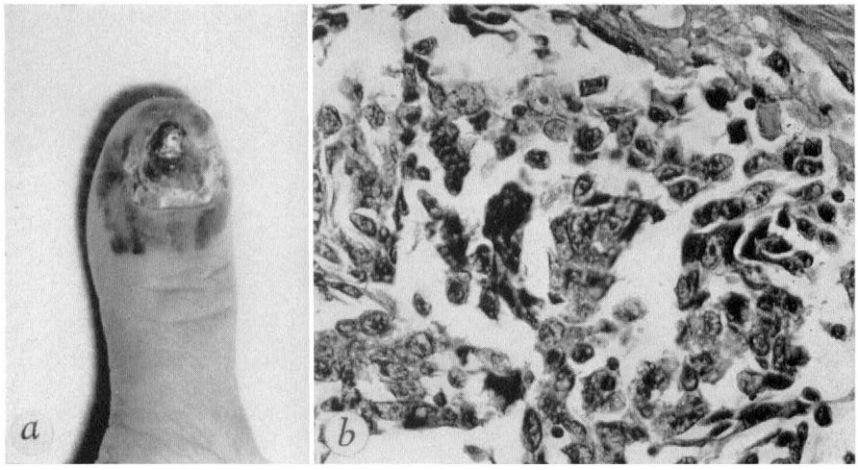

FIG. 2 (case 2). *a*. Digit before operation showing band of pigmentation surrounding entire nail bed. *b*. Section through nail bed showing downward invasion and numerous mitotic figures (hematoxylin and eosin; ×400).

—resembling a pencil mark—had appeared down the center of the nail of the finger. This widened in the next 3 months to involve the entire nail plate. Three months before admission the nail had disintegrated and "proud flesh" protruded from the nail bed. The end of the finger became tender and swollen and it bled easily. On examination the nail bed contained necrotic, hypertrophic, granular tissue. The major portion of the nail was missing, and the remnant, along with the entire distal phalanx, was darkly pigmented (fig. 3*a*). There were no palpable nodes, and x-ray examination of the thorax gave negative results. The finger was amputated on March 22, and pathologic examination of the specimen dis-

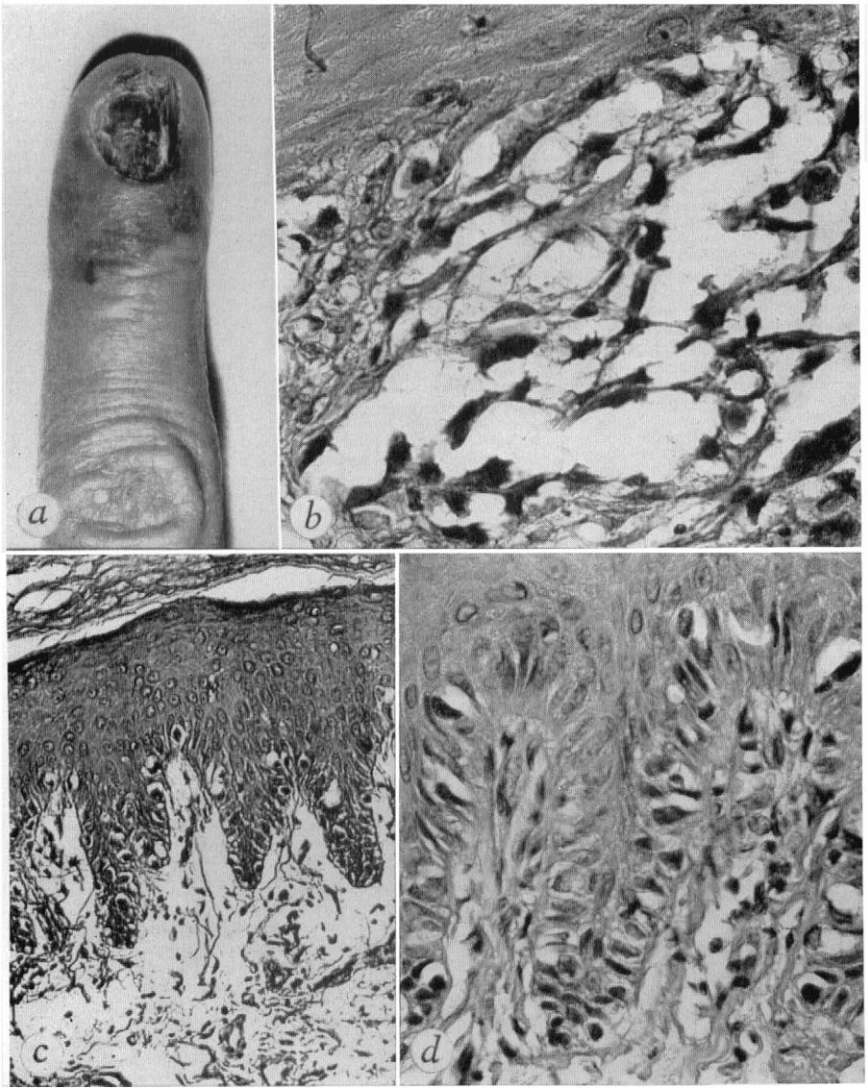

FIG. 3 (case 3). *a*. Digit before operation showing band of pigmentation extending proximally from nail bed. *b*. Section through nail bed showing junctional activity. Numerous mitotic figures are present (hematoxylin and eosin; ×400). *c*. Section through pigmented band of figure 3*a* showing lentigo structure (hematoxylin and eosin; ×175). *d*. Higher magnification of figure 3*c* showing increased number of clear cells and several mitotic figures (hematoxylin and eosin; ×400).

closed malignant melanoma (fig. 3*b*). Within 5 months metastasis to supraclavicular and axillary nodes had developed. The patient died of widespread melanoma in December, 1954, nine months after operation.

Apparently, the earliest sign in this case was either a lentigo or a junction nevus. The pigmented band made the lesion classic for diagnosis. This lesion

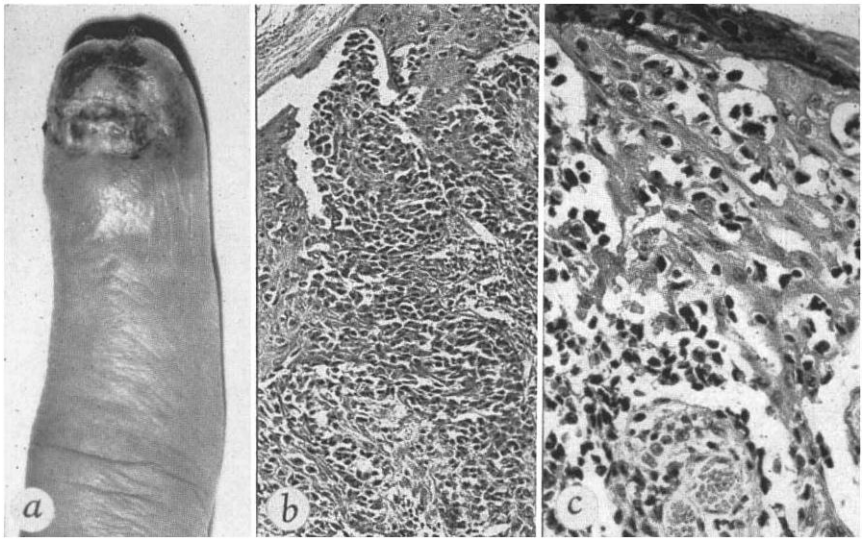

FIG. 4 (case 4). *a*. Digit before operation showing pigmentation extending from periphery of nail bed. *b*. Section through nail bed at lateral nail fold showing origin from epithelium of nail bed (hematoxylin and eosin; ×100). *c*. Section from pigmented band of figure 4*a* showing junctional activity and invasion (hematoxylin and eosin; ×200).

was relatively young, manipulations had not been done, and there was no indication of metastasis. Yet, a very malignant course is demonstrated for a case in which a better outcome might reasonably have been expected.

Case 4: A 65-year-old farm wife came to the clinic on July 15, 1954, complaining of soreness of the right index finger. About 10 years previously she had noted black stripes beneath the nail. These gradually widened to cover the entire plate. Six months previously part of the nail had been removed, and 2 months later the nail bed was purulent. Within the previous few months the skin beneath the distal part of the nail had turned black. Examination revealed a dark, brownish-gray nail remnant, the pigmentation extending over the distal tip of the finger (fig. 4*a*). A small, firm, movable node was palpated in the right axilla, but a roentgenogram of the thorax showed no evidence of metastasis. The finger was amputated on July 21, and nodes were removed from the axilla for diagnosis. Pathologic examination of the nail bed disclosed malignant melanoma (fig. 4*b*) but only an inflammatory reaction was found in the nodes. The patient was still living and in good health 2 years after operation.

In this case the earliest lesion was evidently a subungual nevus, and the increased pigmentation might have suggested activity or malignant change. Only inflammatory changes were found in the nodes of the axilla, although metastatic tumor had been fully expected.

Histopathology: Of the 33 primary lesions reviewed, it was possible to reaffirm the original diagnosis in every case. The attempt to grade malignancy or to predict outcome from the histopathologic picture was not successful.

Factors such as cell shape, density of mitotic figures, depth of invasion, or presence or absence of melanin all varied, sometimes widely, in different parts of the same lesion. In general, practically all lesions contained both polyhedral and

spindle-shaped cells, with the latter in a definite minority. Most lesions were deeply invasive, and the finding of four or more normal or abnormal mitotic figures per high-power field was not unusual. The inflammatory infiltrate referable to the melanoma could not be assessed since all lesions were to some degree ulcerated.

The lesions of nine patients who were clinically "cured" were not remarkably different from the other lesions in the group. Four of these lesions showed marked invasiveness, pleomorphism and mitotic activity. In three cases the slides were sufficient only to confirm the original diagnosis, and in two others no material was available for examination, the original diagnosis having been made from borrowed slides. No melanin was found in two cases.

Origin from the nail-bed epithelium was demonstrated in 25 of the 33 cases. Many sections were stained both with hematoxylin and eosin and silver nitrate. Pigment, presumably melanin, was demonstrated in at least one section from each of 27 cases. In none of the other six cases could pigment be found in the sections available.

Examination of sections through the pigmented, nonulcerated halo of two lesions revealed the structure of lentigo in one case (case 3, fig. 3*c* and *d*) and that of melanoma in the other (case 4, fig. 4*c*).

DIFFERENTIAL DIAGNOSIS

For arriving at the correct diagnosis of melanotic whitlow, proper evaluation of certain conditions in the differential diagnosis is very important. These include: (1) subungual nevus, (2) epithelioma, especially in association with radiation changes, (3) neuroma, a painful lesion frequently of traumatic origin, (4) neurofibroma, almost always associated with multiple lesions elsewhere, (5) warts, frequently found as multiple lesions and almost never completely subungual in location, (6) glomus tumor, typically subungual, painful and blue, (7) granuloma pyogenicum, a pedunculated or sessile tumor frequently found in the nail sulcus and sometimes associated with trauma, (8) subungual exostosis, a slowly growing tumor which displaces the nail but which may be easily diagnosed by x-ray, (9) pigmentation of the nails from drugs such as quinacrine (atabrine), phenolphthalein or heavy metals, (10) hematoma and splinter hemorrhages, secondary to trauma, subacute bacterial endocarditis, trichinosis, scurvy and certain blood disorders, (11) onychia and paronychia, due to infection with bacteria or fungi, secondary to trauma or foreign body, or associated with hangnails or concomitant dermatologic disease, (12) unguis incarnatus, a painful, disabling condition, especially of the great toe and (13) onycholysis, a separation of the nail from the nail bed and symptomatic of some types of arthritis and of syphilis, eczema and psoriasis.

Proper evaluation of the history and careful examination will ordinarily rule out these conditions, except nevus, provided pigmentation is present. In the absence of pigmentation, more subtle discernment is demanded with deeper evaluation of the diagnostic criteria as previously enumerated. Biopsy is helpful in some cases and is mandatory in the diagnosis of all chronic pigmented lesions.

DISCUSSION

From a review of the literature and of the 52 well-documented cases of melanotic whitlow, plus data from 38 additional cases encountered at the Mayo Clinic, considerable information was accumulated for this subgroup of melanoma. A summary of the data from each group and from the total of 90 cases sheds much light upon this entity and answers many questions related thereto.

Comparison of the data from the two groups showed agreement in most respects. More of the Mayo Clinic patients were in the seventh decade of life, but when the two groups were combined, approximately 80 per cent of the patients were about equally distributed among the fifth, sixth and seventh decades. The average age for the Mayo Clinic patients was 58.9 years; for those cited in the literature, 52.7 years; and for the two groups combined, 55.4 years. The ages ranged from 35 to 85 years for Mayo Clinic patients, and from 23 to 86 for those cited in the literature.

The sex distribution favored the male slightly in the Mayo Clinic cases (55.3 per cent), but there was no significant sex difference when the total of 90 cases was considered. In both groups the upper extremities were more frequently affected. The left thumb was involved in 26.7 per cent of the total cases, an incidence which was twice that for any other digit. Of the total patients, either a thumb or a great toe was involved in two thirds. The incidence of associated trauma, whatever its significance, was 39.5 per cent for the Mayo Clinic cases and 48.1 per cent for the cases from the literature. Although the exact role of trauma in the etiology of melanotic whitlow has never been fully assessed, this factor may well be coincidental to the malignancy, common as trauma is about the digits.

A low incidence of painful lesions in both groups was noteworthy; in only 12.2 per cent of the total cases was pain a complaint.

A pigmented initial lesion was less frequently reported in the cases from the literature (30.8 per cent) than in the Mayo Clinic cases (42.1 per cent), but gross pigmentation of the lesion at the time of examination was more often observed in the former group. For the entire series of cases, the initial lesion was most often inflammatory (37 per cent) or pigmented (32 per cent) in type. An abnormality in the nail or a tumor contiguous to the plate comprised the remainder of the early lesions.

Two thirds of the Mayo Clinic patients had been subjected, elsewhere, to various surgical procedures before the correct diagnosis was made; this was true for only one half the patients referred to in the literature. In only one half of the total cases was the diagnosis made within the first 2 years of onset of the initial lesion.

About one third of the patients in both groups had apparent metastatic lesions by the time the correct diagnosis was made. This figure correlates with the factors of delay and manipulation operative in most of the cases.

All 38 of the Mayo Clinic patients came to the clinic because of the chronic, indolent nature of their lesions. Seventeen of the patients were aware of the

possible malignant character of their condition at the time of admission, this awareness having been gained only a few days or weeks previously.

The surgical approach in the Mayo Clinic cases was not radical. Although subsequent surgical treatment was required in some cases, the initial treatment consisted of amputation of all or part of a digit with dissection of regional lymph nodes in three patients, simple amputation of all or part of the digit in 30 patients, amputation of a leg in two patients, ionizing radiation alone in two patients, and no treatment for one patient who refused operation. The initial operation was supplemented by ionizing radiation in 12 patients, but neither radium nor roentgen rays have been employed for melanotic whitlow since 1949. In the majority of patients with obvious metastasis conservative amputation was done because it was felt that more radical procedures would not change the prognosis.

Follow-up information was obtained for 37 of the 38 Mayo Clinic cases. Twenty-five of the patients have died, 19 from melanoma and six from other causes. Of those succumbing to melanoma, three died more than 5 years postoperatively, and the longest survival among these was 11½ years. One patient has been lost to follow-up and 12 patients are still living. Six of these 12 living patients are postoperative for a period of less than 5 years, and three of these are known to have metastasis.

Twelve of 13 patients with metastasis at the time of diagnosis and initial treatment were dead within 2½ years of operation. The exceptional case probably represented an instance of multiple primary lesions rather than true metastasis from a single primary lesion. Absence of discernible metastasis at the time of treatment did not necessarily herald a better prognosis. Metastasis developed subsequently in several of this group, and three of these patients succumbed to melanoma within 2 years of operation.

With a standard period of 5 years without recurrence of the melanoma being adopted as an arbitrary criterion of "cure," nine cases qualified for this category and were scrutinized. With the exception of absence of metastasis to the regional nodes, and consequent lack of nodal dissection, these cases were found to differ in no significant way from the entire clinic group in regard to age, sex, clinical history and course. Had these patients undergone nodal dissection, then that procedure, no doubt, would have been given credit for the better outcome.

Valid conclusions may not be drawn from this study in regard to preferred treatment, survival rates and prognosis. This will be possible only when numerous other cases, complete with follow-up, are added to the literature.

SUMMARY AND CONCLUSIONS

A review of 52 cases of melanotic whitlow reported in the literature and an analysis of 38 cases encountered at the Mayo Clinic disclosed the following information.

Melanotic whitlow probably represents some 3 or 4 per cent of all melanomas. Approximately 80 per cent of the patients with this lesion are about equally distributed among the fifth, sixth and seventh decades of life. Patients with this

form of melanoma are older than patients with all forms of melanoma. There is no significant difference in incidence between the sexes. The lesion most frequently involves the upper extremity, especially the left thumb; two thirds of the lesions involve either a thumb or a great toe. Although of questionable significance, trauma is related by patients as an associated factor in more than 40 per cent of the cases and is found as frequently in one sex as in the other. The initial lesion is most likely to be either inflammatory or pigmented in type. Only one eighth of the lesions are painful. Gross pigment may be found in more than half of the cases. In two thirds of the cases some form of minor surgical procedure has been carried out before the diagnosis is suspected. In only half of the cases is the diagnosis made within the first 2 years of onset of the initial lesion. In at least one third of the cases obvious metastasis has occurred by the time the diagnosis is made. The chief complaint of all 38 Mayo Clinic patients was related to the chronic and inflammatory nature of their lesions. Seventeen patients were aware of the malignant nature of the whitlow at the time of admission. Absence of discernible metastasis at the time of operation does not necessarily imply a better prognosis. Presence of involved regional nodes at the time of diagnosis heralds a short survival. Except for absence of involved regional nodes at the time of diagnosis and treatment, nine "cured" patients did not differ in any significant manner, clinically or histologically, from those of the entire clinic group.

Study of tissue from 33 of the 38 Mayo Clinic cases disclosed no practical criteria for grading malignancy or predicting outcome in individual cases. Practically all the lesions were invasive and mitotically active. On the basis of failure to demonstrate pigment in sections stained with hematoxylin and eosin and with silver nitrate six cases were classified as amelanotic melanoma. Origin of the tumor from the nail bed was demonstrated in 25 of the 33 lesions. The structure of a lentigo was found in the pigmented border of one lesion and that of frank melanoma in the border of another.

Of the 38 Mayo Clinic patients, 19 died of melanoma, three of these having survived longer than 5 years after operation, six died of other causes, one has been lost to observation and 12 patients are still living. Six of the 12 living patients are not yet postoperative for a 5-year period, and three of these are known to have metastasis. No conclusions regarding preferred treatment, survival rates or prognosis are drawn from this study.

REFERENCES

1. Hertzler, A. E.: Melanoblastoma of the nail-bed (melanotic whitlow). Arch. Dermat. & Syph., **6**: 701–708, 1922.
2. Hutchinson, Jonathan: Melanosis often not black: Melanotic whitlow. Brit. M. J., **1**: 491, 1886.
3. Hutchinson, Jonathan: Notes toward the formation of clinical groups of tumors. Am. J. M. Sc., **91**: 470–478, 1886.
4. Galloway, James: On a form of pathological pigmentation preceding malignant growth of the skin. Brit. M. J., **2**: 873–876, 1897.
5. Johnson, J. C.: Melanoma. J. Cut. Dis., **23**: 49–71, 1905.

6. Noble, J. F., Ferrin, A. L. and Merandino, K. A.: Pigmented nevus of the fingernail matrix: Report of a case. Arch. Dermat. & Syph., **65:** 49–52, 1952.
7. Womack, N. A.: Subungual melanoma: Hutchinson's melanotic whitlow. Arch. Surg,. **15:** 667–676, 1927.
8. Allen, A. C. and Spitz, Sophie: Malignant melanoma: A clinicopathological analysis of the criteria for diagnosis and prognosis. Cancer, **6:** 1–45, 1953.
9. Pack, G. T., Gerber, D. M. and Scharnagel, Isabel M.: End Results in Treatment of Malignant Melanoma: A Report of 1190 Cases. In Gordon, Myron (ed.): Pigment Cell Growth. Proceedings of the Third Conference on the Biology of Normal and Atypical Pigment Cell Growth, pp. 177–188. New York, New York, Academic Press, Inc., 1953.
10. Scannell, R. C.: Subungual melanoma: Report of a case. Am. J. Surg., **53:** 163–167, 1941.
11. Wright, C. J. E.: Prognosis in cutaneous and ocular malignant melanoma: A study of 222 cases. J. Path. & Bact., **61:** 507–525, 1949.
12. Bickel, W. H., Meyerding, H. W. and Broders, A. C.: Melanoepithelioma (melanosarcoma, melanocarcinoma, malignant melanoma) of the extremities. Surg., Gynec. & Obst., **76:** 570–576, 1943.
13. Newell, C. E.: Malignant melanomas with particular reference to the subungual type. South. M. J., **31:** 541–547, 1938.
14. Pack, G. T. and Adair, F. E.: Subungual melanoma: differential diagnosis of tumors of nail bed. Surgery, **5:** 47–72, 1939.
15. Bauer, J. T.: Malignant melanotic tumors in the Negro. Arch. Path. & Lab. Med., **3:** 151, 1927.
16. Dickson, J. A. and Jarman, T. F.: Subungual melanoma in Negroes. Ann. Surg., **95:** 470–473, 1932.
17. Pardo-Costello, V.: Diseases of the nails. South. M. J., **27:** 377–385, 1934.
18. Cintract, J. M.: Tumeur mélanique sous-unguéale. Presse méd., **56:** 247–248, 1948.
19. Farrell, H. J.: Cutaneous melanomas with special reference to prognosis. Arch. Dermat. & Syph., **26:** 110–124, 1932.
20. Miescher: Über Klinik und Therapie der Melanome. Arch. f. Dermat. u. Syph., **200:** 215–238, 1955.
21. Miescher, G.: Die neuere Entwicklung der dermatologischen Röntgentherapie. Dermatologica, **107:** 225–238, 1953.
22. Pack, G. T., Scharnagel, Isabel and Gerber, D. M.: The Treatment of Malignant Melanoma of the Skin. S. Clin. North America, pp. 517–523. April, 1953.
23. Raven, R. W.: Problems Concerning Melanoma in Man. In Gordon, Myron (ed.): Pigment Cell Growth. Proceedings of the Third Conference on the Biology of Normal and Atypical Pigment Cell Growth, pp. 121–137. New York, New York, Academic Press, Inc., 1953.
24. Gibson, S. H.: Melanotic Whitlow. Thesis, Graduate School, University of Minnesota, 1956.