

Leiomyosarcoma of the Skin and Subcutaneous Tissue

JAMES P. FIELDS, MD,* AND ELSON B. HELWIG, MD

In a study of 65 primary cutaneous leiomyosarcomas and 15 primary superficial subcutaneous leiomyosarcomas, tumors occurred at any age but were more common in middle age and most common on the extremities. They developed as solitary painful or tender intracutaneous or subcutaneous nodules. Microscopically, the cutaneous leiomyosarcomas consist of a poorly delineated proliferation of spindle-shaped atypical myomatous cells arranged in interlacing fascicles which merge into collagenous stroma. Subcutaneous leiomyosarcomas are more sharply circumscribed and typically include a vascular pattern. About 40% of the cutaneous leiomyosarcomas recurred, but none metastasized despite a high mitotic frequency and marked cytologic atypia. Among the 12 patients with subcutaneous leiomyosarcomas, one-half of the tumors recurred and one-third eventually died in metastasis or tumor-related death. Cutaneous leiomyosarcomas have a relatively benign biologic course and may be excised conservatively, but are less likely to recur if the local excision is wide enough to require a skin graft for closure of the surgical defect. For primary subcutaneous leiomyosarcoma, early wide local excision with adequate clear histologic borders constitutes rational treatment.

Cancer 47:156-169, 1981.

THE CLINICOPATHOLOGIC FEATURES and biologic behavior of cutaneous and subcutaneous leiomyomas are well documented,^{9,15,16,27} but similar information about the malignant counterparts has not been established. The purpose of this paper is to describe and correlate the clinical and pathologic features of a series of 80 primary malignant smooth muscle tumors, 65 located in the skin and 15 in the superficial subcutaneous region.

Stout,²⁷ in his detailed account of solitary cutaneous and subcutaneous leiomyomas, was aware of only seven cases of "malignant leiomyomas" involving the skin and subcutaneous tissue. All the cases had been reported between 1901 and 1936, none in the English language, and only one documented by published photomicrographs that could be fully accepted.¹ We are aware of 18 additional case reports of leiomyosarcoma arising in either the skin or subcutis (Table 1). This total excludes the second reported by Levack

and Dick,¹⁹ which has been considered by other reviewers^{5,21} to represent a rhabdomyosarcoma, and the second case reported by Haim and Gellei,¹⁰ which was not convincing to us nor documented by photomicrographs as smooth muscle in type. Although six of the 19 lesions were described as multinodular, all apparently developed at a single site. Careful analysis of these reports reveals that six of the 19 leiomyosarcomas were cutaneous lesions; one was a congenital scalp lesion apparently of subcutaneous origin; two were recurrent superficial lesions presumably of subcutaneous origin; and the remaining ten were leiomyosarcomas involving both subcutaneous tissue and overlying skin. Treatment usually consisted of local excision; however, two were treated by amputation at the shoulder joint. In nine cases where follow-up information was available, regional lymph node metastases occurred in three patients, widespread metastases in two, and local invasion in one. It is noteworthy that the primary lesion in each of these instances involved the subcutis as well as the skin (cutis). No metastases occurred in the four cases for which follow-up information was given of leiomyosarcoma clearly arising from smooth muscle structures within the skin.^{14,17,21,26}

In 1958, Stout and Hill²⁸ published a study of 36 cases of leiomyosarcoma of the superficial soft tissue and reported a 61% incidence of local recurrence and a 56% incidence of metastases. Of the 19 patients with metastases, all had metastases to the lung and four

From the Department of Skin and Gastrointestinal Pathology, Armed Forces Institute of Pathology, Washington, DC.

* Present address: Departments of Medicine and Pathology, Vanderbilt University Medical Center, Nashville, Tennessee.

Address for reprints: Elson B. Helwig, M.D., Department of Skin and GI Pathology, Armed Forces Institute of Pathology, Washington, DC 20306.

The opinions or assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the Department of the Army or the Department of Defense.

Accepted for publication January 20, 1980.

TABLE 1. Case Reports of Leiomyosarcoma of the Skin or Subcutis

| Case | Author(s) | Year | Sex | Age (yr) | Size (cm) | Anatomic site | Histologic localization | Treatment | Behavior |
|------|-------------------------------------------|------|-----|------------------------------|-----------------|-------------------------------|-------------------------|----------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------|
| 1 | Bartkowak ¹ | 1936 | F | 59 | "Dove egg" | Foot | Skin/subcutis | Excised | Widespread metastasis |
| 2 | Kilgour ¹⁸ | 1955 | F | 29 | 6.5 | Scapula | Skin/subcutis | Excised Forequarter amputation | Local invasion No other follow-up |
| 3 | Levack, Dick ¹⁹ | 1955 | F | 56 | 1.5 | Forearm | Skin/subcutis | Excised × 3 Interscapulothoracic amputation and axillary cleanout | Multiple recurrences, local invasion, regional lymph node metastasis Living and well 4½ years |
| 4 | Montgomery, Winkleman ²¹ | 1959 | F | 32 | 1.0 | Thigh | Skin | Fulgurated Radium plaque Excised | Recurrence Persisted Living and well 21 years |
| 5 | Heitanen, Saskai ¹⁴ | 1960 | M | 56 | 1.5 | Nose | Skin | Excised | Dead in 8 months of unrelated cause |
| 6 | Tappeiner, Wodniansky ³⁰ | 1961 | M | 70 | 8.0 | Chest | Skin/subcutis | Excised | Reurred from pre- existing leiomyoma |
| 7 | Daoud, Mescaro ⁶ | 1962 | M | 50 | 10.0 | Shoulder | Skin | Widely excised, grafted | Not stated |
| 8 | Charlton ² | 1964 | M | 69 | 2.5 | External auditory canal | Skin | Excised, grafted | Not stated |
| 9 | Rising, Booth ²⁵ | 1966 | M | 32 | 0.7 | Neck | Skin/subcutis | Excised radical node dissection | Local recurrence and lymph node metastasis |
| 10 | Panabokke, Attygalle ²² | 1967 | F | 40 | 2.0 | Buttock | Skin/subcutis | Excised Re-excised | Recurred Not stated |
| 11 | Stout, Lattes ²⁹ | 1967 | M | 82 | 5.0 | Submental | Skin/subcutis | Excised | Recurrence, metastasis, death |
| 12 | Jain ¹⁷ | 1969 | F | 30 | 3.0 | Knee | Skin | Excised | Living and well 2½ years |
| 13 | Pendse, Saxena ²³ | 1969 | F | 62 | 4.0 | Upper arm | Subcutis | Excised, grafted | Not stated |
| 14 | Haim, Gellei ¹⁰ | 1970 | F | 41 | "pea- sized" | Shoulder | Skin/subcutis | Excised; radical neck dissection | Regional lymph node metastasis; patient not followed |
| 15 | Heieck, Organ ¹² | 1970 | M | 8 weeks (con- genital) | 6.0 | Scalp | Skin/subcutis | Excised | Living and well 4 years |
| 16 | Smith ²⁶ | 1971 | M | 58 | 3.0 | Back | Skin | Excised | Living and well 11 years |
| 17 | Chaves <i>et al.</i> ³ | 1972 | F | 61 | 12.0 | Anterior abdominal wall | Subcutis | Excised | Patient not followed |
| 18 | Duperrat <i>et al.</i> ⁷ | 1973 | F | 70 | — | Cheek | Skin/subcutis | Excised Re-excised, grafted | Recurrence |
| 19 | Headington <i>et al.</i> ¹³ | 1977 | F | 49 | 4.0 | Buttock | Skin/subcutis | Widely excised and grafted | 4 prior local recurrences over 30 years |

to the regional lymph nodes. All of the primary lesions were apparently of subcutaneous or peripheral soft tissue origin. Phelan *et al.*²⁴ in 1962 reported results of ten patients with soft tissue leiomyosarcoma, two of which arose in the superficial soft tissue and eight of which occurred somewhat deeper. Nine tumors in their series recurred locally, one metastasized to the

lungs and regional lymph nodes, and three eventuated in generalized metastases and death. In 1974, Dahl and Angervall⁵ reported the results of a retrospective study of 47 patients with leiomyosarcoma of superficial (skin and subcutaneous) soft tissue. They placed their patients into two categories: (1) a group of 40 patients with solitary leiomyosarcoma including 19 tumors

TABLE 2. Age Distribution at Time of Biopsy or Excision of 78 Patients with Primary Cutaneous and Subcutaneous Leiomyosarcoma

| Age (years) | Cutaneous tumors | | Subcutaneous tumors | |
|-----------------------------|------------------|----|---------------------|----|
| | No. | % | No. | % |
| 1-9 | | | 1 | 7 |
| 10-19 | 1 | 2 | | |
| 20-29 | 8 | 13 | 3 | 20 |
| 30-39 | 11 | 17 | 1 | 7 |
| 40-49 | 10 | 16 | 3* | 20 |
| 50-59 | 11 | 17 | 3 | 20 |
| 60-69 | 17 | 27 | 2 | 13 |
| 70-79 | 3 | 5 | 2 | 13 |
| 80 and over | 2 | 3 | | |
| Total patients of known age | 63 | | 15 | |
| Age range | 19-81 years | | 7 months-74 years | |
| Median age (years) | 50 | | 47 | |

* One patient had a primary lesion of the dermis ten years previously which was diagnosed at age 31.

situated predominantly in the corium, and 21 tumors located in the soft tissue and muscle, including the retroperitoneal region and peripheral nervous system; and (2) a group of seven patients in whom multiple subcutaneous leiomyosarcomas developed during the

clinical course. The overall incidence of recurrence was 40%, and in the entire series 27% of the patients died with known metastatic tumors with the lung as the most frequent site. Lymph node metastases were suspected in three patients, but were not histologically verified.

Information derived from the more than 90 cases of peripheral soft tissue leiomyosarcomas contained in the above-mentioned reports indicates a significantly high incidence of metastasis and death. On the other hand, the information contained in the isolated case reports of primary leiomyosarcomas involving the skin, or skin with subcutis, is insufficient in terms of total number, accurate details, and follow-up information to permit definite conclusions about the biological behavior. Adding to the confusion, the authors in many instances failed to specifically delineate the site of histologic origin or localization of the tumor relative to the skin (cutis) or subcutis. Moreover, in some reports, the tumor localization described in the title was contradicted in the text of the article or by the published photomicrographs.^{1,3,10,12,18,19,22,25}

Headington *et al.*¹³ in a report of a leiomyosarcoma of the skin described a high degree of cytologic differentiation by electron microscopy and enzymatic findings which apparently differentiated leiomyosarcoma from malignant fibrous histiocytoma.

Materials and Methods

The case material used in this study was accessioned at the Armed Forces Institute of Pathology, Washington, DC, between the years 1940 and 1972, and included military, Veterans Administration, and civilian sources. All available pathologic material, autopsy protocols, and clinical records supplemented by questionnaires were reviewed for cases which were coded as leiomyosarcoma, angioleiomyosarcoma, glomoid sarcoma, neurogenic sarcoma, fibrosarcoma, and spindle cell or undifferentiated sarcoma of the skin and subcutaneous tissue.

Eighty lesions from 79 patients with primary leiomyosarcoma were accepted for the study, and were classified according to anatomic histologic site as cutaneous or subcutaneous in origin. One patient had a leiomyosarcoma of the skin and one of the subcutaneous tissue at distant sites ten years apart. Hematoxylin and eosin (H & E)-stained sections of the skin or subcutaneous tissue with associated overlying skin structures were available for study in each case. Of the 80 leiomyosarcomas, 65 originated in the cutaneous skin and 15 were clearly of subcutaneous origin. All tumors arising from smooth muscle in the genital or mamillary skin were excluded. Also excluded from the study was a case accessioned at the AFIP previously reported by Stout and Hill²⁸ and by Stout

TABLE 3. Anatomical Distribution of Primary Cutaneous and Subcutaneous Leiomyosarcomas in 79 Patients

| Anatomic site | Cutaneous tumors | | Subcutaneous tumors | |
|-----------------|------------------|-----|---------------------|-----|
| | No. | % | No. | % |
| Lower extremity | 35 | 54 | 10 | 67 |
| Proximal | | | | |
| Buttock | 2 | | 1 | |
| Thigh | 18 | | 5 | |
| Knee | 5 | | | |
| Distal | | | | |
| Lower leg | 9 | | 4* | |
| Not specified | 1 | | | |
| Upper extremity | 20 | 31 | 3 | 20 |
| Proximal | | | | |
| Shoulder | 8 | | | |
| Upper arm | 6 | | | |
| Elbow | 1 | | 1 | |
| Distal | | | | |
| Forearm | 3 | | 1 | |
| Wrist | 1 | | 1 | |
| Finger | | | | |
| Trunk | 8 | 12 | 2 | 13 |
| Chest | 4 | | | |
| Abdomen | 2 | | | |
| Back | 2 | | 2 | |
| Face | 2 | 3 | | |
| Cheek | 2 | | | |
| TOTAL | 65 | 100 | 15 | 100 |

* One patient had had earlier primary lesion of the skin of the thigh ten years before.

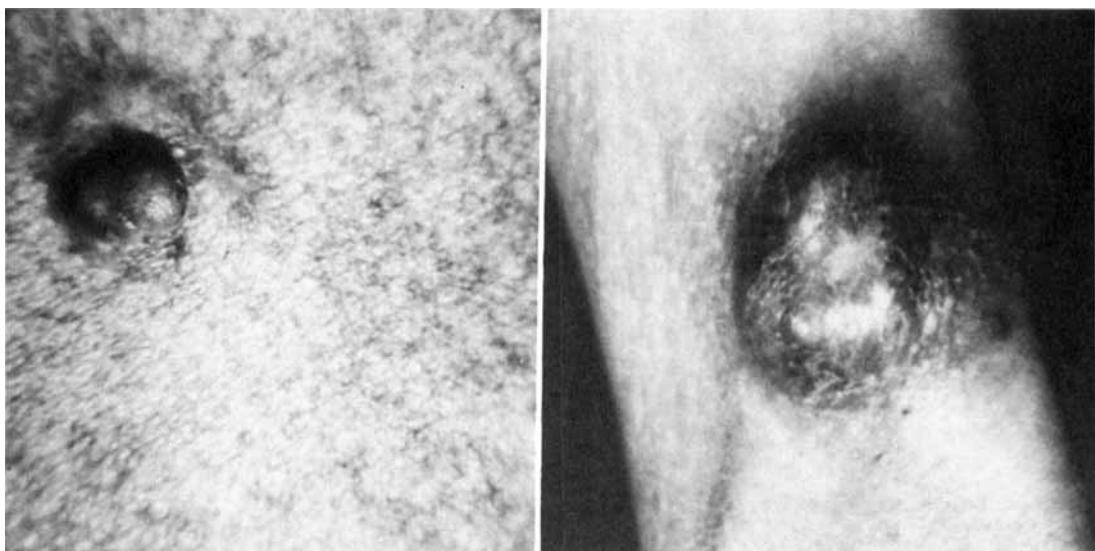


FIG. 1. (left): Cutaneous leiomyosarcoma appearing as an irregular hemispherical dermal nodule surmounting a circumscribed induration of the skin (Courtesy of Richard C. Miller, M.D.).

FIG. 2. (right): Subcutaneous leiomyosarcoma appearing as a protuding spherical tumor (AFIP Neg. 2505).

and Lattes;²⁹ this was a fungating leiomyosarcoma of the submental region histologically proliferating throughout all levels of the skin and subcutis and obscuring the exact primary site.

The histologic study included determination of the localization of the tumor relative to the papillary; upper, middle or lower reticular dermis, or the subcutis; the pattern of growth, circumscription and vascularity; epidermal alterations; and any degenerative changes. Careful attention was directed to the cytologic detail in terms of the degree of differentiation, the nuclear and cytoplasmic fine structures, and the total number of clearly recognizable mitotic figures within 50 high-power fields for each lesion. In selected cases, special stains were employed, including the Masson trichrome, Movat pentachrome, Van Gieson, elastic-Van Gieson, and phosphotungstic acid hematoxylin (PTAH). Special staining techniques were prepared,²⁰ and all pertinent information was recorded on data cards and ultimately subjected to computer analysis.

Clinical Data

Age, Sex and Race

The known ages of 63 patients with cutaneous leiomyosarcoma at the time of biopsy or excision ranged from 19 to 81 years, with a median age of 50. The ages of 15 patients with subcutaneous leiomyosarcomas at the time of biopsy or excision ranged from seven months to 74 years, with a median age of 47 years (Table 2). There were 49 male and 16 female patients

with cutaneous leiomyosarcoma; 11 male and 4 female patients comprised the subcutaneous group. The 3:1 male-to-female sex ratio reflects the usual sampling of case material at the AFIP. Separating the total number of military and Veterans Administration (assumed to be military-related) cases from those which were contributed from civilian sources revealed a ratio of six male patients to one female patient within the former group and two male to one female patients in the latter. By ethnic groups among the patients with cutaneous tumors, 50 (77%) were Caucasian, two were black, one was Cuban, and one was Venezuelan. Among patients with subcutaneous tumors, six were Caucasian, and four were black. Race was unknown for the remaining patients.

TABLE 4. Sizes of 80 Primary Cutaneous and Subcutaneous Leiomyosarcomas

| Size | Cutaneous tumors | | Subcutaneous tumors | |
|------------------|------------------|-----|---------------------|-----|
| | No. | % | No. | % |
| <1.0 cm | 11 | 17 | 1 | 7 |
| 1.0–1.9 cm | 23 | 35 | | |
| 2.0–2.9 cm | 16 | 25 | 2 | 13 |
| 3.0–3.9 cm | 7 | 11 | 4 | 27 |
| 4.0–4.9 cm | 5 | 8 | 4 | 27 |
| 5.0–5.9 cm | 2 | 3 | 1 | 7 |
| 6.0–6.9 cm | 1 | 1 | 1 | 7 |
| >7.0 cm | | | 2 | 13 |
| TOTAL | 65 | 100 | 15 | 100 |
| Smallest (cm) | 0.4 | | 0.5 | |
| Largest (cm) | 6.0 | | 13.0 | |
| Median size (cm) | 1.8 | | 3.8 | |



FIG. 3. Cutaneous leiomyosarcoma exhibiting a gray, slightly whorled cut surface (AFIP Neg. 56-17874).

Anatomic Location

Fifty-five (85%) of the 65 primary cutaneous leiomyosarcomas occurred on the extremities, with 54% of the total number located on the lower extremities and 31% on the upper extremities. Forty of the 55 lesions of the extremities occurred on the proximal portion on or above the knee or elbow (Table 3). Twenty-five of the cutaneous tumors occurred on the extensor aspect and 15 on the flexor aspect. Thirteen (87%) of the 15 subcutaneous tumors occurred on the extremities, with 67% of the total number located on the lower extremities and 20% on the upper extremities.

Signs and Symptoms

All tumors of the skin and subcutis appeared clinically as a solitary mass, except three cutaneous leiomyosarcomas which appeared as two or more circumscribed grouped nodules. The usual surface configuration of the cutaneous tumors was a round to oval, more or less hemispherical elevation of the skin ranging from 0.3 to 2.5 cm (Fig. 1). The subcutaneous tumors produced hemispherical elevations ranging from 0.6 to 5.0 cm (Fig. 2). Five of the cutaneous tumors were irregular in contour, four were pedunculated, two were umbilicated, one was mulberry-shaped, and one was described as a circumscribed induration of the skin. The skin was smooth in 13 cases, ulcerated or crusted in 10, and roughened scaling, or verrucous in nine. Discoloration of the skin was more commonly encountered with cutaneous leiomyosarcomas, and was noted in only four of the subcutaneous tumors. The color of the overlying skin was pink-red to deep red

in 20 patients, brown to bluish-black in seven, tan to yellowish in three; and hypopigmented in one.

Eleven of 43 (24%) cutaneous leiomyosarcomas were reported to be painful, and an additional 27 (63%) elicited pain on pressure. Four of nine (44%) of the subcutaneous tumors were reported as painful, and three (33%) elicited pain on pressure. Eight patients experienced pruritus, and seven complained of burning or other irritative sensations. Bleeding was reported by six patients, five of whom were in the cutaneous group.

Size and Duration

Clinically, the size (Table 4) of the tumors ranged from 0.4 to 6.0 cm in diameter among the cutaneous leiomyosarcomas (63 lesions: median size 1.8 cm). There was more variation among the subcutaneous tumors, which ranged in size from 0.5 to 13.0 cm (15 lesions: median size 4.0 cm). Both the cutaneous and subcutaneous leiomyosarcomas were usually characterized as slow growing. The initial growth rate was slow, followed by rapid growth in 13% of cutaneous and 18% of subcutaneous lesions. The median duration from onset to diagnosis of 47 cutaneous lesions was two years (range:two weeks to 40 years); of 13 subcutaneous lesions, the time was one year (range:four months to 30 years).

Clinical Diagnosis

The most commonly suggested clinical diagnoses were as follows: skin malignancy—14 (carcinoma—7, sarcoma—7); cyst—13; histiocytoma, dermatofibroma or fibroma—10; tumor or mass—5; lipoma—3; neurofibroma or neurilemmoma—2; granuloma—2; various other diagnoses—5; diagnosis not stated—10.

Possible Predisposing Factors—Trauma or Radiation Injury

Antecedent injury at the site of the tumor was reported in 15 patients and specifically denied by 27. The nature of such injury varied and included contusions, puncture wounds, tick bite, burn scar, and inoculation site. Prior exposure to ionizing irradiation was recorded by two patients with cutaneous leiomyosarcomas and specifically denied by 31 patients. None of the five patients with subcutaneous leiomyosarcomas for whom information regarding exposure to radiation was known were exposed.

Pathologic Data

Gross Observations

Cutaneous leiomyosarcomas developed either a circumscribed nodular, lobulated, or pedunculated tumor,

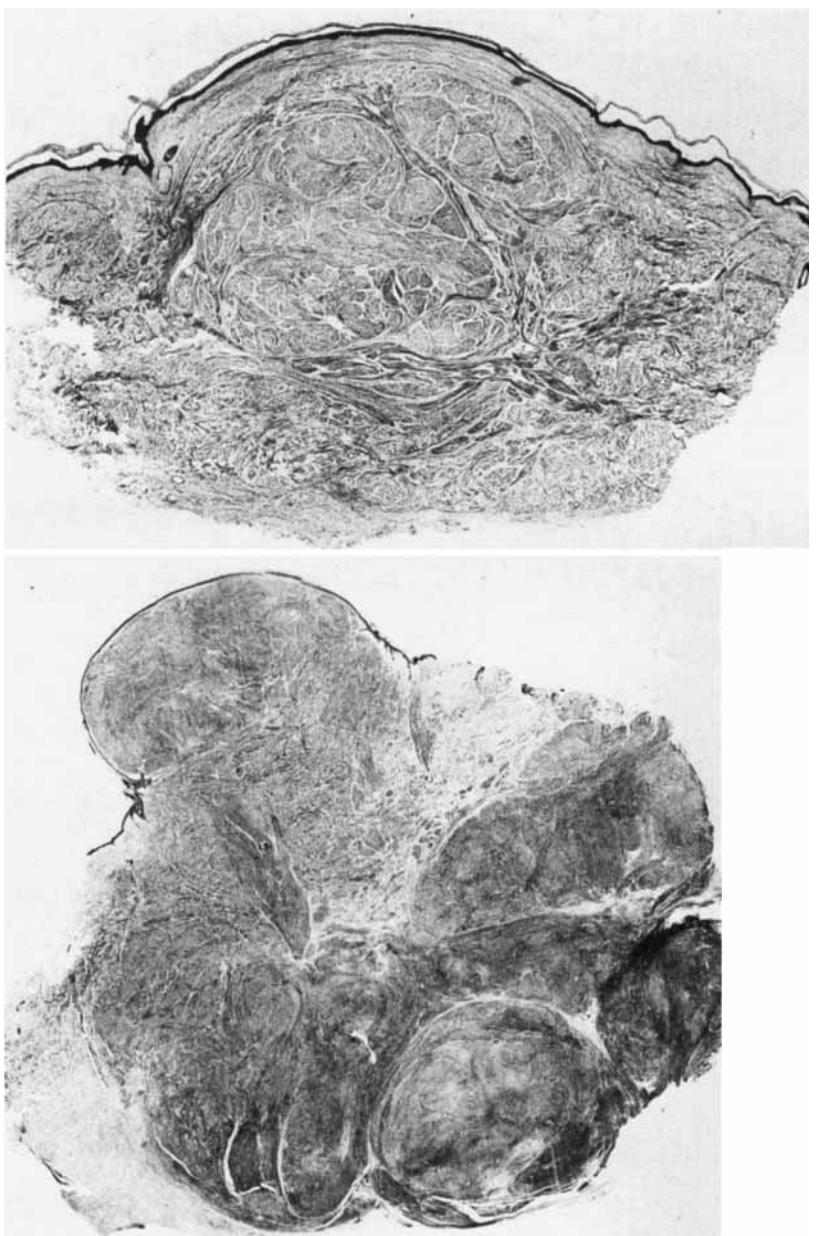


FIG. 4. (top): Cutaneous leiomyosarcoma composed of sweeping, irregularly interlacing bundles of atypical leiomyomatous cells (H & E, $\times 12$; AFIP Neg. 72-1072).

FIG. 5. (below): Exophytic cutaneous leiomyosarcoma composed of nodules and irregular fascicles of atypical smooth muscle cells (Masson trichrome, $\times 5$; AFIP Neg. 72-1054).

or a poorly defined induration of the skin. The cut surfaces exhibited a translucent white, grayish-white, or pale tan to yellowish-white color and a fibrous, whorled appearance (Fig. 3).

Subcutaneous leiomyosarcomas were circumscribed round to oval or lobulated and rubbery hard. The cut surfaces appeared gray-white to yellow and glistening.

Microscopic Observations

Primary cutaneous leiomyosarcomas. The lesions varied from moderately well- to poorly delimited intradermal tumors that elevated the epidermis and

sometimes penetrated the subcutis. The thickened dermis was occupied by sweeping bundles or discrete rounded nodular elements of abnormal smooth muscle tissue which appeared more compact and more deeply eosinophilic than the surrounding connective tissue (Figs. 4, 5). In well-differentiated lesions, the fascicles of tumor cells appeared to interlace or intersect (Fig. 6). In less well-organized lesions, narrow sinuous bands of atypical smooth muscle cells or foci of pleiomorphic cells proliferated in a disordered pattern (Fig. 7). Twenty-five of the cutaneous tumors were histologically confined to the dermis and 40 were localized predominantly to the dermis but extended

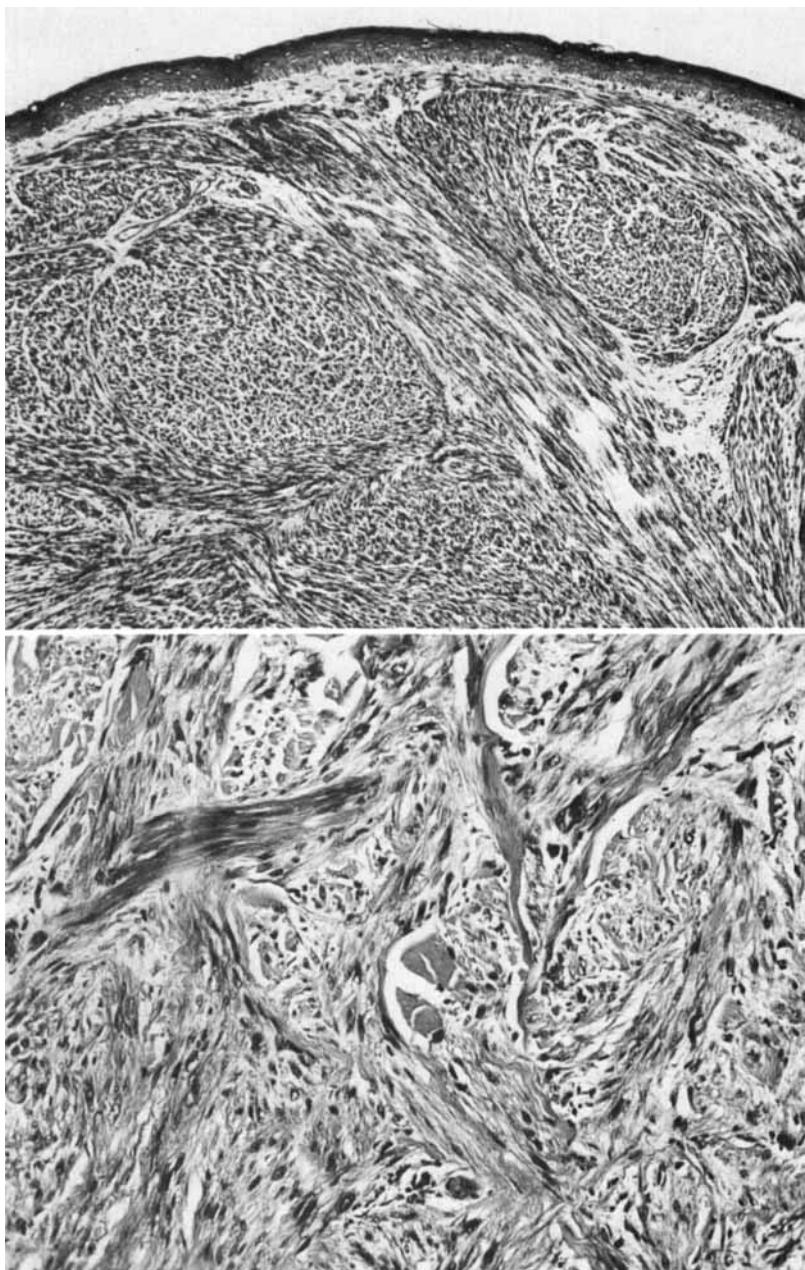


FIG. 6. (top): Cutaneous leiomyosarcoma with interwoven fascicles of atypical smooth muscle. The rete ridges are effaced and a grenz zone of uninvolved collagen is present (Masson trichrome, $\times 80$; AFIP Neg. 72-11851).

FIG. 7. (bottom): Cutaneous leiomyosarcoma showing narrow sinuous bands of atypical spindloid myomatous cells resembling arrectores pilorum muscles (H & E, $\times 115$; AFIP Neg. 71-11330).

into the superficial subcutis (Fig. 8). Marginally irregular strands of atypical smooth muscle usually extended between collagen bundles. Some lesions showed expansile tumor nodules compressing the stroma laterally and pushing aside the skin appendages. The latter were either absent or entrapped within the tumors.

The most frequent epidermal change, noted in 30 lesions, was mild to moderate acanthosis. Effacement of the rete ridges with epidermal thinning was seen in 24 lesions, erosion was present in five and ulceration in four. A thin to wide subepidermal grenz zone was identifiable in virtually all lesions. Inflammatory

cells, mostly lymphocytes and histiocytes, with lesser numbers of plasma cells were seen around the periphery of 34 lesions. Mucinous changes in the stroma were observed in four lesions.

At high magnification, the neoplasms were composed of spindle shaped or ribbon-like cells possessing elongated nuclei with blunt ends which in their long axes tended to align in a tandem arrangement suggestive of palisading. The better-differentiated cells possessed long, narrow nuclei with a well-formed nuclear membrane, a small nucleolus, and finely dispersed nuclear chromatin (Fig. 9). The more atypical nuclei were elongated, somewhat plumper, and con-

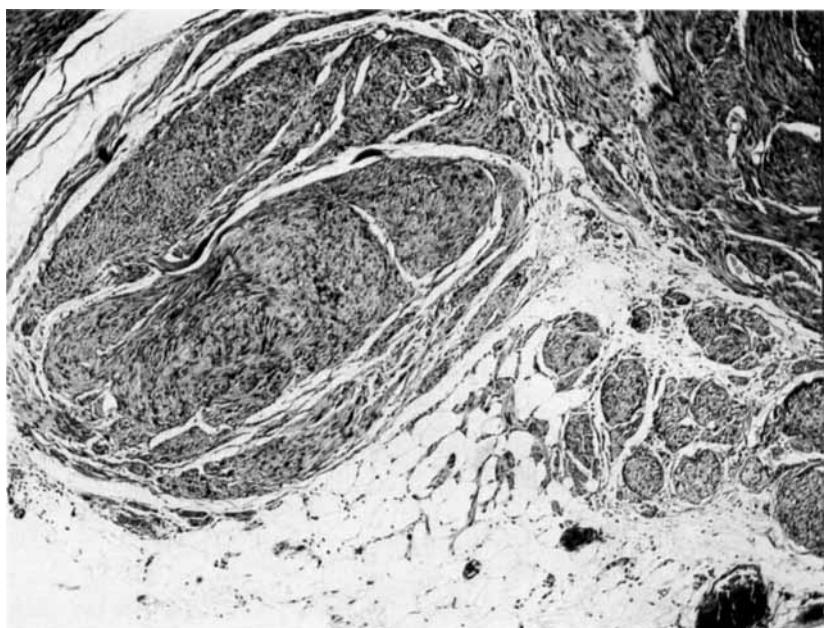


FIG. 8. Cutaneous leiomyosarcoma with tumor fascicles bulging into the subcutis and infiltrating between fat cells (H & E, $\times 50$; AFIP Neg. 72-10524).

tained prominent nucleoli. All lesions displayed anisocytosis and poikilocytosis, varying numbers of bizarre, multinucleate giant cells containing abundant deeply basophilic coarse chromatin, and anaplastic multinucleate giant and bizarre monster cell forms (Fig. 10). Twelve cutaneous leiomyosarcomas exhibited abnormal tripolar or quadripolar mitoses. The mitotic frequency is tabulated in Table 5.

Despite the presence of dysplastic or anaplastic foci, an interwoven fascicular pattern and cytologic features in all lesions afforded a recognition of smooth-muscle differentiation. The relation of cutaneous leiomyosarcomas to arrectores pilorum muscles is suggested by the presence of myomatous structures resembling the configuration of arrectores pilorum muscles running in various directions and the intimate association of hair follicles in some instances.

Differential stains such as the Masson trichrome, Van Gieson, or Movat pentachrome revealed varying quantities of collagen between the around smooth muscle cells or bundles of cells. Both collagen bundles and elastic fibers were scanty within the central tumor masses, and the latter was present only in the broader connective tissue bundles. The tumor cells individually, in groups, or in bundles, were enmeshed in a delicate reticulum network with fine fibers running parallel to the long axes of tumor cell nuclei (Fig. 11). With good fixation, longitudinal intracytoplasmic myofibrils could be visualized in H & E- or trichrome-stained sections, but they were generally better discerned in the PTAH preparations, where they appeared as purple intracellular threads (Fig. 12). In bundles of tumor cells cut on their short

axes, the presence of perinuclear clear spaces, apparently caused by condensation of the cytoplasm toward the periphery of the cells, aided in their recognition as smooth-muscle cells. This feature is especially striking in trichrome, pentachrome, or PTAH preparations.

Recurrent cutaneous leiomyosarcomas. Ten cases



FIG. 9. Well-differentiated cutaneous leiomyosarcoma composed of spindle-shaped cells with blunt-ended nuclei, finely dispersed nuclear chromatin, occasional bizarre nuclei ad mitotic figures (H & E, $\times 300$; AFIP Neg. 71-11339).

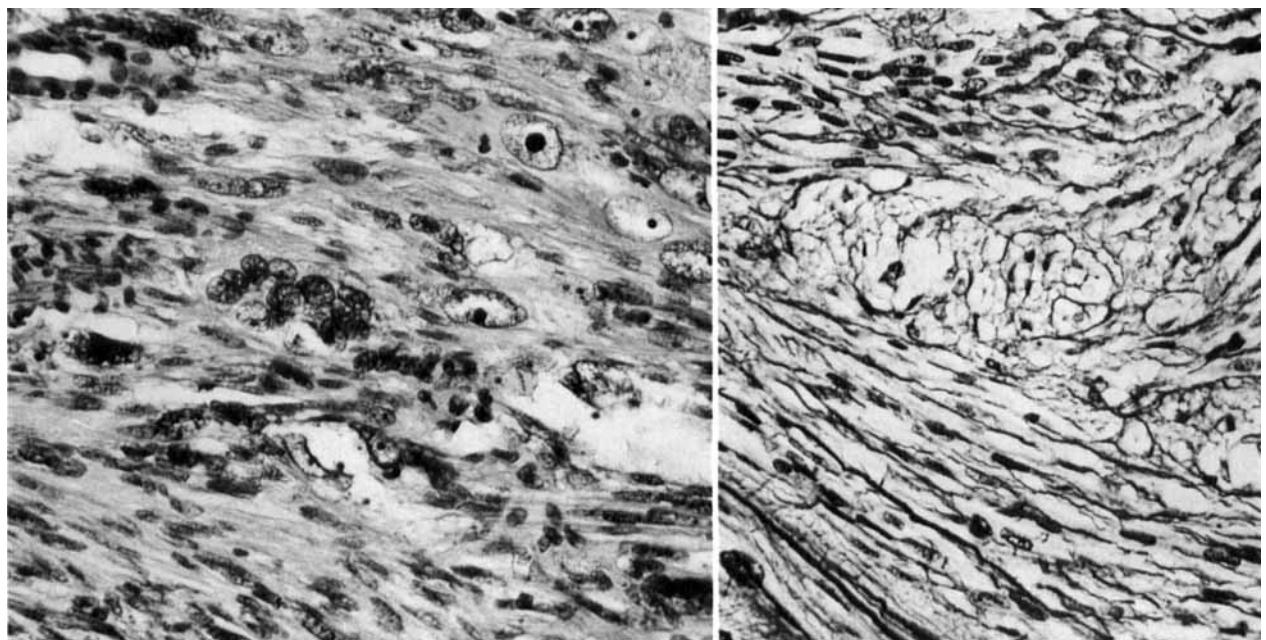


FIG. 10. (left): A highly cellular cutaneous leiomyosarcoma showing pleomorphic cells containing plump nuclei with deeply basophilic coarse chromatin and prominent nucleoli (H & E, $\times 300$; AFIP Neg. 71-11338).

FIG. 11. (right): Cutaneous leiomyosarcoma with a delicate reticulum network surrounding tumor cells (Snook, $\times 300$; AFIP Neg. 71-11337).

were available for study of one or more recurrent tumors along with the earlier cutaneous primary lesion. In half of the examples, recurrent tumors measured about twice the size of the original lesion and were histologically deeper in the dermis or tended to involve deeper levels of the subcutis than the corresponding primary lesion. In the single example of cutaneous leiomyosarcoma which recurred four times, the last recurrence appeared in the subcutis exclusively. Seven recurrent tumors exhibited greater numbers of mitoses than the primary, and in two instances, atypical mitotic figures were observed in recurrences while none were seen in the primary lesions.

Primary subcutaneous leiomyosarcomas. This group of 15 tumors occurred in the superficial subcutaneous

region as solitary, circumscribed, smooth, spherical to lobulated nodules. Eight tumors were covered by uninvolved skin; one tumor adhered to the overlying cutis; and in the remaining six examples, the tumor histologically invaded the dermis by direct extension (Fig. 13). Most did not extend above the lower one-third of the dermis; however, one lesion originating in the subcutis recurred in the subcutis and involved the skin up to the mid-dermis level. Degenerative changes were encountered in subcutaneous tumors measuring 4.0 cm or more in diameter. Fibrosis was noted in five examples, necrosis in four, hemorrhage in two, and focal calcification in one. Because of degenerative changes, the bulk of the well preserved smooth muscle tissue was seen at the periphery of the tumor.

Subcutaneous leiomyosarcomas regularly appeared surrounded by a compressed rim of connective tissue. Irregular aggregates of atypical myomatous spindle cells intertwined haphazardly without the distinct fascicular pattern that characterized the cutaneous counterparts. A vascular pattern was another conspicuous feature of subcutaneous leiomyosarcomas. Especially at the periphery but throughout the tumors, endothelial-lined thin walled vessels with variously shaped lumens of differing dimensions surrounded by smooth muscle cells, were present (Fig. 14). Blood vessels with walls of medium thickness composed of

TABLE 5. Frequency of Mitoses per 50 High-Power Fields in 80 Primary Cutaneous and Subcutaneous Leiomyosarcomas

| No. mitotic figures | Cutaneous tumors | | Subcutaneous tumors | |
|---------------------|------------------|-----|---------------------|-----|
| | No. | % | No. | % |
| 1-9 | 13 | 20 | 5 | 33 |
| 10-24 | 18 | 28 | 1 | 7 |
| 25-49 | 18 | 28 | 1 | 7 |
| >50 | 16 | 24 | 8 | 53 |
| TOTAL sections | 65 | 100 | 15 | 100 |

circularly disposed smooth muscle fibers were observed in some lesions, and occasionally continuity of the vascular smooth muscle with the tumor could be demonstrated. These tumors were composed of spindle-shaped cells with cytoplasmic myofibrils, and nuclei which tended to be smaller and shorter than those seen in the tumors derived from the arrectores pilorum muscles (Fig. 15). Five of the lesions exhibited tripolar or quadripolar mitotic figures. The mitotic frequency is tabulated in Table 5.

Treatment and Follow-up

Cutaneous leiomyosarcomas in this series were generally managed by excisional or incisional biopsy followed by conservative or wide local surgical excision with primary closure or skin grafting of the defect. A large *en bloc* resection of the skin, subcutaneous tissue, and gastrocnemius muscle group was performed following the biopsy diagnosis of cutaneous leiomyosarcoma in one patient, and another involving the chest was radically re-excised along with portions of the rib and sternum. Prophylactic regional lymph node dissections were performed in two other cases.

Three cutaneous leiomyosarcomas were treated during the course of several recurrences with radiotherapy, including supervoltage cobalt therapy in one patient. In each instance, surgical intervention was necessary because of subsequent recurrence.

Follow-up information was available in 59 patients with cutaneous leiomyosarcomas ranging from two months to more than 30 years (median interval three years, nine months). In this group, data regarding incidence of recurrence were available in 55 patients. The overall recurrence rate totaled 42%. Recurrences were encountered in approximately one-third (32%) of the cutaneous leiomyosarcomas which appeared histologically confined to the dermis, and in almost half (47%) of those which exhibited microscopic extension into the subcutis. Recurrences were recorded in primary tumors which ranged in size from 0.8 to 5.0 cm, whereas those which did not recur ranged from 0.4 to 6.0 cm. Likewise, there was no association between recurrences and mitotic counts. As determined from the interval following initial surgery to treatment of recurrences, most of the recurrent lesions developed slowly over a one- to five-year period.

Each of the subcutaneous leiomyosarcomas was treated initially by local excision. Follow-up information was available in 12 patients ranging from five months to more than seven years (median interval—two years, one month). Seven patients (58%) developed recurrence, metastases, or both. Recurrent tumors



FIG. 12. Cutaneous leiomyosarcoma showing longitudinal myofibrils staining as purple intracellular threads (PTAH, $\times 650$; AFIP Neg. 72-1841).

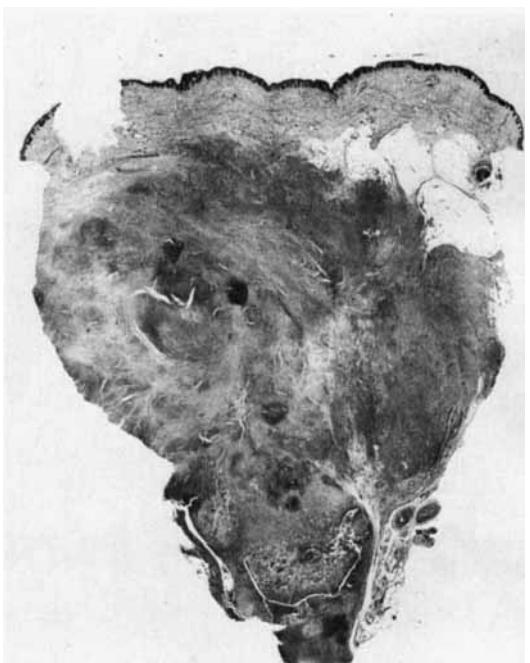


FIG. 13. Subcutaneous leiomyosarcoma with dense proliferation of atypical smooth muscle tissue encroaching upon the overlying dermis (H & E, $\times 4$; AFIP Neg. 72-11558).



FIG. 14. Subcutaneous leiomyosarcoma showing poorly defined intertwining bands of smooth muscle and large irregular thin-walled vessels (H & E, $\times 50$; AFIP Neg. 72-10522).

were documented in six patients (50%) within four to 18 months of initial diagnosis. One patient was free from recurrence after surgical excision and super-



FIG. 15. Subcutaneous leiomyosarcoma showing individual spindle-shaped cells with elongated, blunt-ended hyperchromatic nuclei (Masson trichrome, $\times 300$; AFIP Neg. 71-11335).

voltage cobalt therapy. Two patients were successfully treated by amputation of portions of their affected extremity. Metastases occurred in four patients (33%) and caused death in three. The cause of death in one additional patient was attributed to recurrent leiomyosarcoma. Two patients with tumors of 15 years duration developed generalized metastases within four months following primary excision, an occurrence suggesting that surgical intervention enhanced the spread of tumor. There was no association between tumor size or presence of necrosis and biological behavior. Recurrences followed removal of a primary lesion as small as 0.5 cm and metastasis occurred in tumors ranging from 3 to 13 cm in diameter.

Discussion

Although the reputed statistical incidence of superficial leiomyosarcomas has varied from 2.3 to 5.3% of malignant soft tissue tumors^{5,28} and from 4.0 to 6.5% of soft tissue sarcomas,^{8,11} these are rare, especially those related to the skin. The literature contains only 19 adequately documented case reports of leiomyosarcomas of the skin or superficial subcutis. Leiomyosarcomas of these areas may occur at any age, but are encountered most often in the middle years of life. The youngest patient with a cutaneous leiomyosarcoma in this study was 19 years of age. One patient in this study had a subcutaneous leiomyosarcoma present at birth, as did one other published in the literature.¹² The overall sex incidence in the present series follows a 3:1 ratio of males to females, but in the civilian group there is a male to female preponderance of 2:1. The latter figures are in agreement with those reported by Dahl and Angervall,⁵ but are at variance with those of Stout and Hill,²⁸ who reported that 64% of superficial soft tissue leiomyosarcomas occurred in female patients. The lesions occurred more commonly in Caucasians than in any other racial or ethnic group.

Leiomyosarcomas may occur at any anatomic site. The majority (85%) of the primary cutaneous or subcutaneous leiomyosarcomas in the present series developed on the extremities, chiefly the lower extremities. The cutaneous lesions occurred more commonly on the proximal than the distal portion of the upper extremities, whereas both cutaneous and subcutaneous lesions exhibited a predilection for the proximal portion of the lower limbs, coincident with the distribution reported by others.^{5,25} Cutaneous leiomyosarcomas also occurred more frequently on the extensor than the flexor aspects of both the upper and lower extremities, an expected distribution pattern in view of the apparent greater density of hair structures (arrectores pilorum muscles) on the extensor

surfaces of the legs and arms. Similarly, Stout remarked that more than half of the solitary leiomyomas which he studied developed on extensor surfaces²⁷ and about one-third more of the multiple cutaneous leiomyomas reported by Fisher and Helwig⁹ occurred in the extensor surfaces than on the flexural aspect.

Antecedent traumatic injury, ionizing irradiation, or other pre-existing lesions may serve as a predisposing influence for the development or accelerated growth of a leiomyosarcoma. In the present study, some form of mechanical injury was reported by 15 patients, two of whom developed cutaneous leiomyosarcoma at the site of superficial x-ray therapy. From the literature, a cutaneous leiomyosarcoma on the nose arose at the site of a lupus vulgaris lesion treated previously with x-ray, and two other superficial leiomyosarcomas reported developed in lupus vulgaris lesions.¹⁴

In two of our patients the primary cutaneous smooth muscle neoplasm was objectively called a leiomyoma and the recurrent tumor met the histologic criteria for leiomyosarcoma, an experience which parallels that of three other authors.^{19,25,30} Others⁶ have interpreted origin of leiomyosarcoma from leiomyoma on the basis of histologic foci of dysplastic and well-differentiated smooth muscle tissue existing in the same lesion. Although we observed the same phenomenon in many of our study lesions, we do not believe that the finding justifies the interpretation that all such leiomyosarcomas arose from pre-existing leiomyomas, but rather that there are varying degrees of differentiation within a single leiomyosarcoma.

Pain occurring spontaneously or upon the application of pressure is the most frequently encountered symptom. It occurred in 97% of our patients with cutaneous leiomyosarcoma, exceeding the 80% frequency reported in solitary superficial leiomyomas by Stout,²⁷ and approaching the 100% frequency reported by Fisher and Helwig⁹ for multiple cutaneous leiomyoma. Pain occurring spontaneously or induced by pressure was encountered in 77% of our patients with primary superficial subcutaneous leiomyosarcoma, in contrast to only two symptomatic cases of the 36 superficial soft tissue leiomyosarcomas reported by Stout and Hill.²⁸

Correlating the median duration from onset to diagnosis with the median size (diameter and skin surface elevation), it appears that subcutaneous leiomyosarcomas attain a median size about twice that of cutaneous leiomyosarcomas during a median growth period that is half as long. The apparent difference in growth rate seems real in view of the probability that a lesion situated in the subcutaneous region would arouse attention later than a lesion growing in the more superficial dermis.

The diagnosis of leiomyosarcoma, which is rarely suspected on clinical grounds, requires histopathologic examination. Other spindle cell lesions most often considered in the differential microscopic diagnosis include dermatofibrosarcoma protuberans, nodular fasciitis, fibrosarcoma, malignant Schwannoma, fibroma or dermatofibroma, neurofibroma, rhabdomyosarcoma, atypical fibroxanthoma, malignant fibroxanthoma, and synovial sarcoma.

A combination of several criteria is used to determine that a spindle cell tumor is basically leiomyomatous. Those tumors which develop within the skin, presumably from the arrectores pilorum muscles, exhibit a fascicular, infiltrative peripheral growth pattern and a less common nodular, expansile pattern. At least some of the cells show the cytologic appearance of smooth muscle cells. Bundles of pleiomorphic smooth muscle cells may be located contiguous with the margins of hair follicles and merged with larger masses of tumor.

In contrast, the subcutaneous leiomyosarcomas are apparently vascular in origin and occur in the adipose tissue at or below the cutis-subcutis junction. Although they may encroach upon the cutis by compression or infiltration, unlike most of the cutaneous leiomyosarcomas, they display a pattern of circumscription, and are formed of narrow, poorly defined irregular aggregates of myomatous spindle cells intertwining or growing haphazardly. The tumors often include a vascular pattern with channels ranging from capillary dimension to larger lumens.

At least some of the cells of the leiomyosarcoma show the cytologic appearance of smooth muscle cells. The nuclei are elongated with blunt ends and the cells are aligned somewhat in a tandem when cut on their long axes and exhibit a perinuclear clear space when cut on their short axes. With adequate fixation using H & E, trichrome, or PTAH staining methods, longitudinal myofibrils are visualized within the cytoplasm. In each of 20 cases with PTAH stains myofibrils are identified.

The histologic criteria for malignancy of cutaneous and subcutaneous leiomyosarcoma are identical with those of soft tissue leiomyosarcoma, namely a high degree of cellularity, pleomorphism, bizarre giant cells, and increased number of mitotic figures. The atypical myomatous cells possess large nuclei which vary in size and shape from elongated to plump to oval and contain abundant basophilic chromatin with a prominent nucleolus. Bizarre myomatous cells associated with a conspicuous number of mitotic figures, generally the equivalent of one or more per ten high-power fields, constitute the minimum histologic criteria for leiomyosarcoma. Typically, those lesions exhibit rare to

numerous multinucleated, giant, or anaplastic tumor cells, but those are not considered a prerequisite for diagnosis.

Effective treatment of cutaneous leiomyosarcomas consisted of local surgical excision including adequate histologic borders of uninvolved tissue. Our data indicate that residual or recurrent cutaneous leiomyosarcomas which were subsequently excised widely enough to require skin grafting for closure of the defect generally did not recur. As evidenced by the necessity for subsequent surgical intervention in the three cases treated by x-ray therapy, this modality is of no value. Follow-up information of 59 patients revealed a higher incidence of recurrence in the tumors which extended into the subcutis than in those which remained confined to the dermis. Although up to four recurrences were recorded, none of the cutaneous leiomyosarcomas metastasized.

According to Stout and Hill,²⁸ one of the most significant histopathologic features reflecting the malignant potential of superficial soft tissue leiomyosarcomas is the mitotic frequency as determined by counting the numbers of mitoses in 50 high-power fields. Their histologic criterion for smooth muscle tumors which were "almost certainly malignant" included those with an average rate of one or more mitotic figures per five high-power fields; those which were considered "certainly malignant with a poor chance for cure" included tumors which exhibited an average of one or more mitotic figures per high-power field. Of the primary cutaneous leiomyosarcomas in our study, 80% exhibited ten or more mitoses per 50 high-power fields (2 or more/10 high-power fields), and 24% exhibited 50 or more mitoses per 50 high-power fields (ten or more per ten high-power fields). Our results show that this previously published criterion for malignant behavior in soft tissue leiomyosarcoma is invalid for and must not be employed in the prediction of the biological behavior of cutaneous leiomyosarcomas as defined in this study.

The circumscribed configuration of subcutaneous leiomyosarcomas constitutes a pitfall in their management, tempting one to enucleate or conservatively shell them out. On the contrary, these tumors should be excised early and with wide surgical margins. More extensive surgical procedures are called for in recurrent subcutaneous leiomyosarcomas. According to the follow-up data available in 12 patients, recurrences developed in 50% and hematogenous metastases occurred in 33% with the lung as the most frequent organ involved. Our figures fall within the previously reported 40 to 60% range of recurrences and the 27 to 56% range for metastases^{5,28} in soft tissue leiomyosarcoma.

Of the subcutaneous leiomyosarcomas 67% exhibited ten or more mitoses per 50 high-power fields (two or more per ten high-power fields), and 53% exhibited 50 or more per 50 high-power fields (ten or more per ten high-power fields). The number of mitoses in 50 high-power fields varied from 30 to 139 in the tumors that metastasized or killed, and from 78 to 150 in those that only recurred. Of the eight tumors known to have recurred, metastasized, or killed, one exhibited the equivalent of six mitoses, seven exhibited 15 or more mitoses, and five exhibited 20 or more mitoses per ten high power fields. In contrast, three subcutaneous leiomyosarcomas which did not metastasize, recur, or kill exhibited less than four mitoses per ten high-power fields. One exceptional case which caused no complication during 14 months of follow-up exhibited 22 mitoses per ten high-power fields. Although these data tend to confirm the validity in subcutaneous leiomyosarcomas of the criterion of high mitotic frequency as an index of malignant behavior established by Stout and Hill²⁸ for leiomyosarcomas of the superficial soft tissue, one cannot rely totally on mitotic counts to predict recurrence or metastasis.

Leiomyosarcomas that can be determined microscopically as cutaneous, although histologically malignant, may undergo multiple local recurrences, but are otherwise biologically benign. In contrast, leiomyosarcomas primary in the superficial subcutaneous tissue are fully capable of malignant behavior with the potential to metastasize or kill in about one-third of the patients.

REFERENCES

1. Bartkowiak Z. Ein fall von sarcoma leiomyoblasticum der haut. *Zentralbl Allgemeine Pathologische Anatomie* 1936; 65:179-180.
2. Charlton CAC. Leiomyosarcoma of the external auditory canal. *Br J Surg* 1964; 51:24-25.
3. Chaves E, Sa HH, Gadelha N, Vasconcelos E. Leiomyosarcoma in the skin. *Acta Derm Venereol* 1972; 52:288-290.
4. Conway H, Hugo NE, Tulenko JF. Sarcoma of the skin. In: *Surgery of tumors of the skin*, 2nd ed. Springfield: Charles C Thomas, 1966:336-338.
5. Dahl I, Angervall L. Cutaneous and subcutaneous leiomyosarcoma—A clinicopathologic study of 47 patients. *Pathologia Europaea* 1974; 9:307-315.
6. Daoud R, Mascaro JM. Leiomyosarcome primitif de la peau — Rapport d'un cas personnel. *Bull Soc Fr Dermatol Syphil* 1962; 69:526-533.
7. Duperrat B, Gueguen H, Maruelle J. Leiomyosarcome cutane. Tumor unique à évolution lente. *Bull Soc Fr Dermatol Syphil* 1973; 80:462-464.
8. Ferrell HW, Frable WJ. Soft part sarcomas revisited. Review and comparison of a second series. *Cancer* 30:475-480, 1972.
9. Fisher, WC, Helwig EB. Leiomyomas of the skin. *Arch Dermatol* 1963; 88:510-520.
10. Haim S, Gellei B. Leiomyosarcoma of the skin—Report of two cases. *Dermatologica* 1970; 140:30-35.
11. Hare HF, Cerny MJ Jr. Soft tissue sarcoma. A review of 200 cases. *Cancer* 1963; 16:1332-1337.
12. Heieck JJ, Organ CH, Jr. Leiomyosarcoma of the scalp in a newborn. *Arch Dermatol* 1970; 102:213-215.

13. Headington JT, Beals TF, Niederhuber JE. Primary leiomyosarcoma of skin: A report and critical appraisal. *J Cutan Pathol* 1977; 4:308-317.
14. Hietanen A, Sakai Y. Leiomyosarcoma in an old irradiated lupus lesion. *Acta Derm Venereol* 1960; 40:167-172.
15. Jansen LH. Leiomyomata Cutis. *Acta Derm Venereol* 1952; 32:40-50.
16. Jansen LH, Driessen FML. Leiomyoma Cutis. *Br J Dermatol* 1958; 70:446-451.
17. Jain SP. Leiomyosarcoma in the skin—A case report. *Indian J Surg* 1969; 31:638-641.
18. Kilgour CS. Cutaneous leiomyosarcoma. *Br J Plast Surg* 1955; 8:144-146.
19. Levack J, Dick A. Cutaneous leiomyosarcoma with lymphatic spread—A report of two cases. *Glasgow Med J* 1955; 36: 337-342.
20. Manual of Histologic Staining Methods of the Armed Forces Institute of Pathology. 3rd ed. Luna LG ed. New York: The Blakiston Division, McGraw-Hill Book Co, 1968.
21. Montgomery H, Winkelmann RK. Smooth-muscle tumors of the skin. *Arch Dermatol* 1959; 79:32-41.
22. Panabokke RG, Attygalle LS. Leiomyosarcoma of the skin (letter to the editor). *Br J Dermatol* 1967; 79:305-306.
23. Pense AK, Saxena O. Superficial leiomyosarcoma—Report of a case. *Indian J Pathol Bacteriol* 1969; 12:120-121.
24. Phelan JT, Sherer W, Mesa P. Malignant smooth muscle tumors (Leiomyosarcomas) of soft tissue origin. *N Engl J Med* 1962; 266:1027-1030.
25. Rising JA, Booth E. Primary leiomyosarcoma of the skin with lymphatic spread. *Arch Pathol* 1966; 81:94-96.
26. Smith LJ Jr. Tumors of the corium. In: Helwig EB, Mostofi FK, eds. The Skin, International Academy of Pathology Monograph. Baltimore: Williams and Wilkins, 1971:533-557.
27. Stout AP. Solitary cutaneous and subcutaneous leiomyoma. *Am J Cancer* 1937; 24:435-469.
28. Stout AP, Hill WT. Leiomyosarcoma of the superficial soft tissues. *Cancer* 1958; 11:844-854.
29. Stout AP, Lattes R. Tumors of Soft Tissues, Second Series, Fascicle 1. In: Atlas of Tumor Pathology. Washington, D.C.: Armed Forces Institute of Pathology, 1967:127-133.
30. Tappeiner J, Wodniansky P. Solitaires Leiomyom-Leiomyosarkom. *Hautarzt* 1961; 12:160-163.