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CUTANEOUS LEIOMYOMATA WITH UTERINE LEIOMYOMATA

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Abstract. Leiomyomas of the skin may be associated with leiomyomas of the uterus. This is an autosomal dominant trait. Two families are reported. One young patient had a leiomyosarcoma of the uterus and a hypernephroma of the kidney.

There have been previous reports of the association of cutaneous and uterine leiomyomas (1–8). Three of these included family studies (1, 7, 8) that suggest an autosomal dominant inheritance. Identical twins have been reported with this association (4). We are reporting two families with members who have had both cutaneous and uterine leiomyomas—an association that has not been appreciated in the dermatological literature.

CASE REPORTS

Family I

A 20-year-old girl entered St. Joseph's Hospital because of severe lower quadrant pain. She had had normal menstrual periods until one year previous, when her periods became irregular, and she had missed her last period before hospitalization. She stated that she had never had sexual intercourse, and this was confirmed by pelvic examination.

A large mass was palpated in the area of the uterus. Intravenous pyelography showed a mass in the pelvis and an abnormal calcific lesion in the left flank displacing the left kidney. She underwent surgical exploration of the uterine tumor, and a lobulated 370 g mass was shelled away from the myometrium and removed. On pathological examination the tumor was found to be a spindle cell neoplasm occurring in strands of cells that tended to interweave with one another. The cells showed considerable variation in size. In some portions the nuclei were thin and elongated, while in other portions they were quite plump and showed irregularity in staining and in chromatin content (Fig. 1). The diagnosis was leiomyosarcoma, and this was confirmed by independent pathologists. The results of pulmonary and skeletal surveys were negative for metastases.

The patient has multiple small reddish tumors on her arms, chest, neck and legs (Fig. 2). She had been diagnosed as having Neurofibromatosis although she had no cafe-au-lait spots. Her brother, age 25, has several large areas of leiomyomata (Figs. 3, 4, 5). The results of his intravenous pyelography appeared normal, and there were no masses on his testes. Both the girl, her younger sister, and her elder brother developed their skin lesions at puberty. They have two normal sisters, one aged 16 with no skin lesions and one aged 7, thus far with no evidence of skin lesions. The mother has uterine leiomyomata.

About 6 weeks after the myomectomy, the girl underwent left nephrectomy. The kidney measured $4 \times 4.5 \times 10$ cm and the mass contiguous with it measured 5×7 cm. Together the kidney and the mass weighed 295 g (Fig. 6). The tumor surface was irregularly lobular and cystic, with the cysts and lobules varying in greatest dimension from 0.15 cm to 5 cm. When sectioned, the tumor appeared to originate from and be contiguous with the renal cortex. The tumor was variegated, in part solid and in part cystic (Fig. 7).

The pathological diagnosis was hypernephroma, based on the characteristic configuration and cytology of the solid portions, consisting of small nests of cuboidal cells with abundant foamy cytoplasm and centrally placed nuclei which varied moderately in size and shape (Fig. 7).

The patient's uterus was removed at the same time because of the earlier diagnosis of leiomyosarcoma, and the uterine corpus showed invasion by the hypernephroma.

Family II

A 50-year-old woman was seen in the office for an early seborrheic keratosis on her neck. She also had numerous large leiomyomata, grouped on the right arm and many small lesions on the abdomen (Fig. 8) and left leg (Fig. 9) which she stated had been present since age 17. Microscopic examination of these lesions led to the pathologic diagnosis of leiomyoma, probably derived from the arrectores pilorum muscles. The lesions were virtually asymptomatic, causing only some pruritus with exposure to cold.

She had had a hysterectomy for multiple benign uterine leiomyomata at age 35. She had no children. The patient's mother had identical skin lesions on her arms and legs, and the patient reported that her mother too had had a hysterectomy, at age 30. She had only the one daughter, the patient. The mother had five sisters and four brothers. Two of her sisters had had "partial hysterectomies" at ages 27 and 28. Another sister reportedly had a huge, fast-growing ovarian tumor removed when she

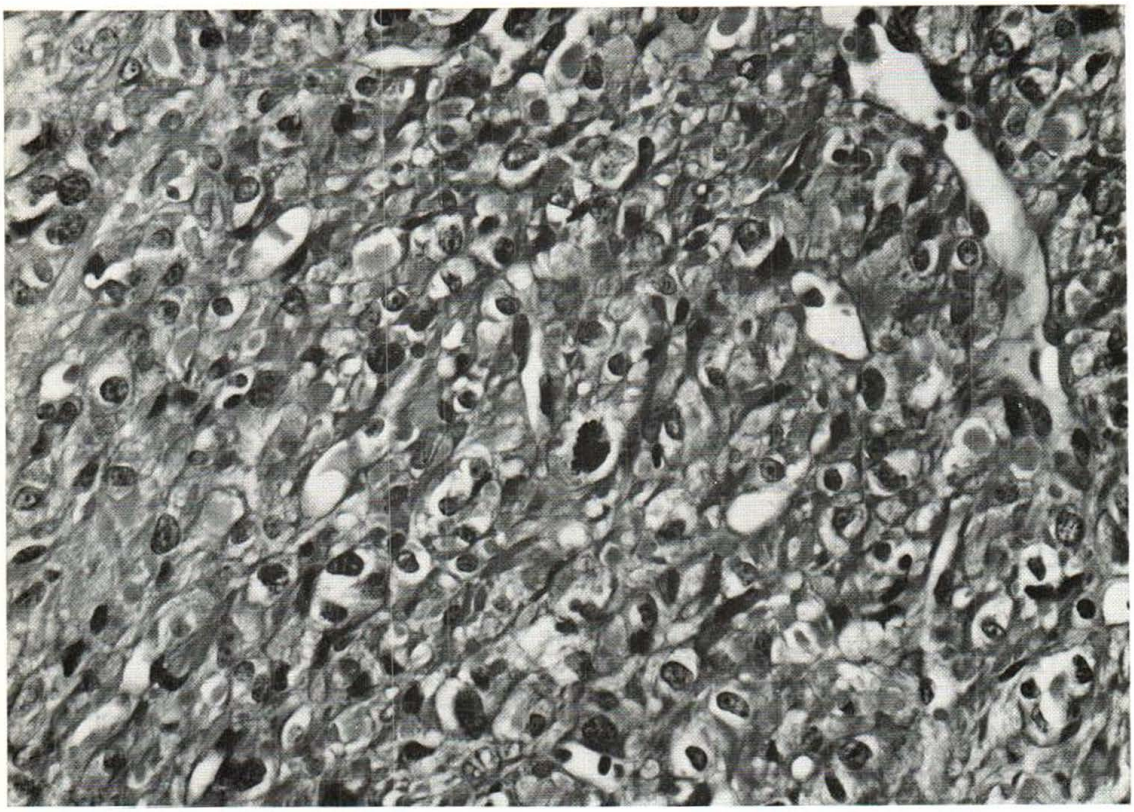

Fig. 1. High-power photomicrograph of the uterine leiomyosarcoma, composed of irregularly interlacing bundles of spindle cells showing moderate pleomorphism. (Hematoxylin and eosin, × 135.)

was age 35. None of these aunts of the patient were known to have any cutaneous tumors.

DISCUSSION

Leiomyomas of the uterus (sometimes designated as fibroids and fibromyomas) are well-circumscribed tumors which consist mainly of muscle but with a variable fibrous connective tissue component and which occur in about 25% of all women (9). Uterine leiomyomas are more common in Negro than in Caucasian women. Theories of histogenesis are varied, but all involve some type of connective tissue cell, either immature or mature, within the uterine wall or its blood vessels. Hysterectomy is often required for these women at an early age, because of degeneration or growth of the tumors, sometimes both.

In those patients with tumors of the skin whom we have had the opportunity to examine histopathologically, the tumors appear to arise from the arrectores pilorum musculature, not from the blood vessels. This probably accounts in part for the milder symptoms of the associated cutaneous leiomyomas.

The first case of multiple cutaneous and uterine leiomyomas was described by Blum and associates in 1954 (2). The second patient was presented at the Eleventh International Congress of Dermatology in Stockholm in 1957 (Case 42) (3). That 35-year-old patient developed nodular lesions on her right cheek and left arm at age 24. At age 30 her uterus was removed because of a myoma that histologically was highly cellular and was interpreted as early malignant. That patient and the patient described here in Family I are the only ones reported with malignant leiomyosarcomas.

There have been three families described that are similar to those discussed in this report, and together these suggest an autosomal dominant inheritance with incomplete penetrance (1). Rudner and colleagues reported identical twin sisters

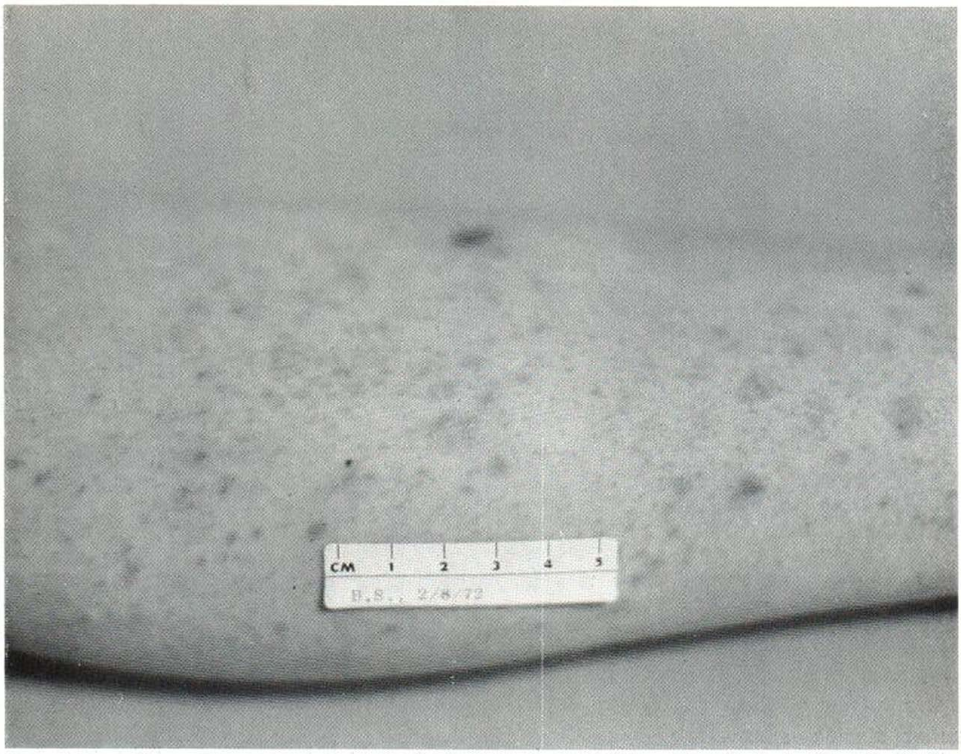

Fig. 2. Multiple small skin tumors on the legs which had been diagnosed as neurofibromas, but on histopathological examination proved to be leiomyomas.

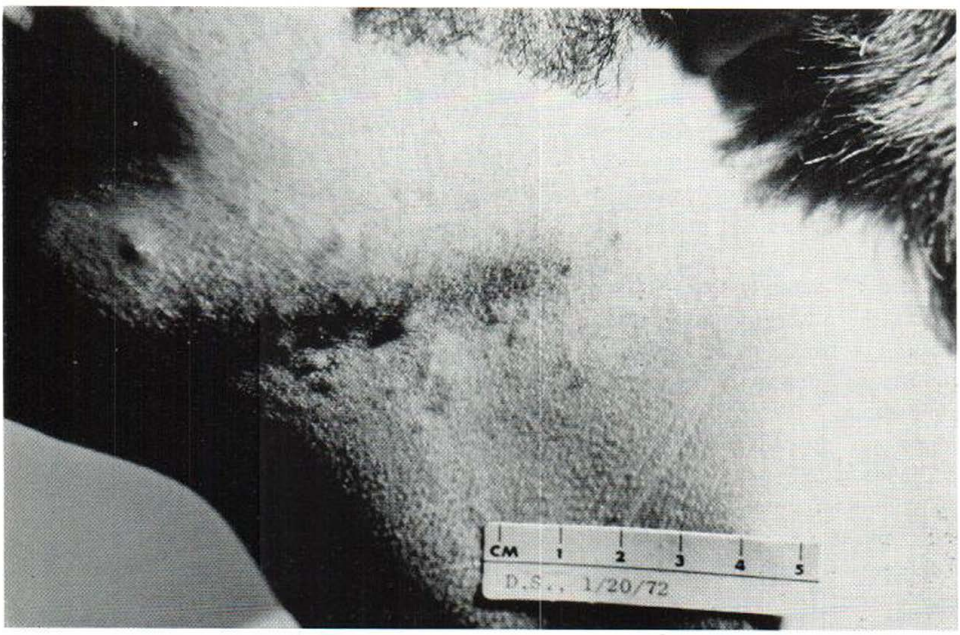

Fig. 3. Multiple leiomyomas on the face of the brother.

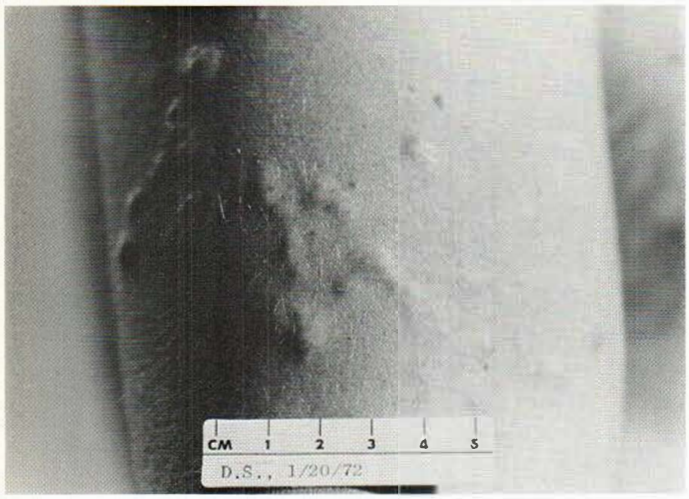

Fig. 4. Large leiomyomas on both arms in the brother.

both with hysterectomies (at age 29 and 40) for fibroid tumors. Gerardi described (as we have) a mother and daughter with both tumors (7).

Mezzadra (1) reported a large four-generation Italian family with members of three generations having cutaneous or uterine leiomyomas, sometimes both. Three sisters in one sibship had both tumors and all three required hysterectomy. Their aunt and a first cousin had hysterectomies for uterine tumors but had no skin lesions, while two male relatives had cutaneous tumors.

Our patient in Family I had three tumors at age 20: cutaneous leiomyomas, a uterine leiomyosarcoma and a hypernephroma. Her older brother and second sister had cutaneous leiomyomas but normal kidney study, and their younger sister so far has no cutaneous or uterine abnormalities. Neither their father nor mother, both examined, has any evidence of skin tumors but mother has uterine tumors.

In a large study of 38 patients described by Fisher & Helwig (10), there were no skin tumors associated with the uterus. However, an autosomal dominant inheritance was definitely shown for the cutaneous leiomyomas.

Their report does not state whether uterine tumors were even investigated.

Every female patient with cutaneous leiomyomata should be examined for the presence of uterine tumors. In contrast with the usual age (35 to 45) of patients with "fibroid" tumors with hysterectomies, our patients and those reported in the literature have had earlier hysterectomies and two have had malignant tumors removed at ages 32 and 30.

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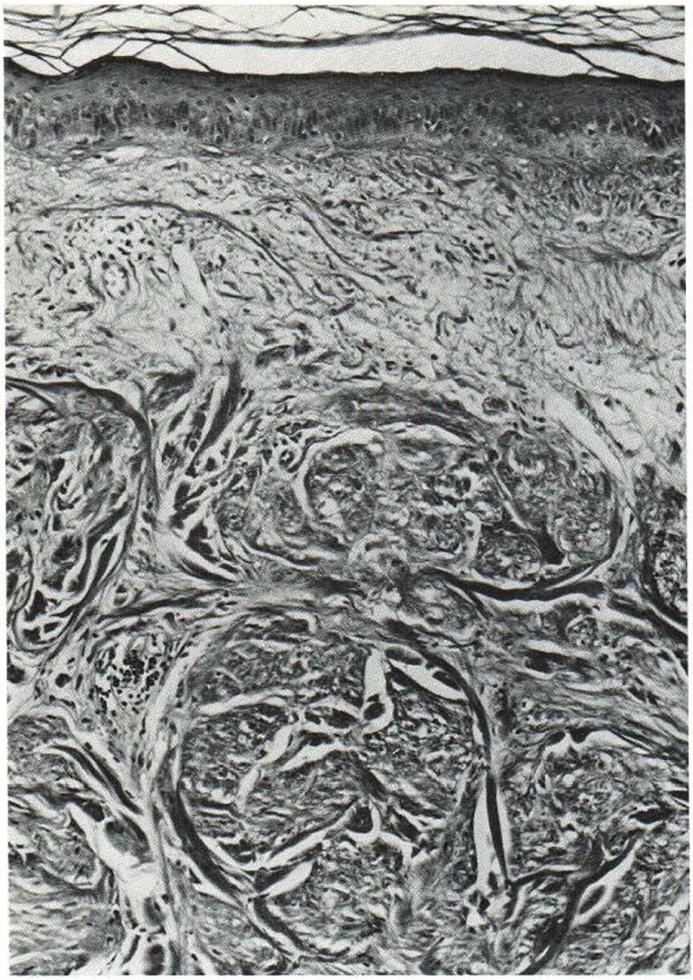

Fig. 5. Photomicrograph of segment of skin with intact and unremarkable epidermis. In the underlying dermis is a benign myoma, composed of irregularly interlacing bundles of smooth muscle cells. (Trichrome, × 120.)

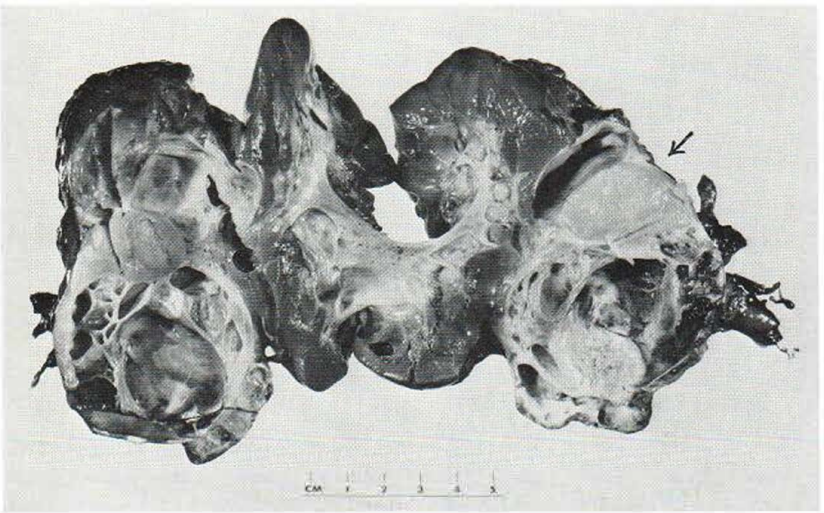

Fig. 6. Hypernephroma (adenocarcinoma) of the kidney invading from the cortex.

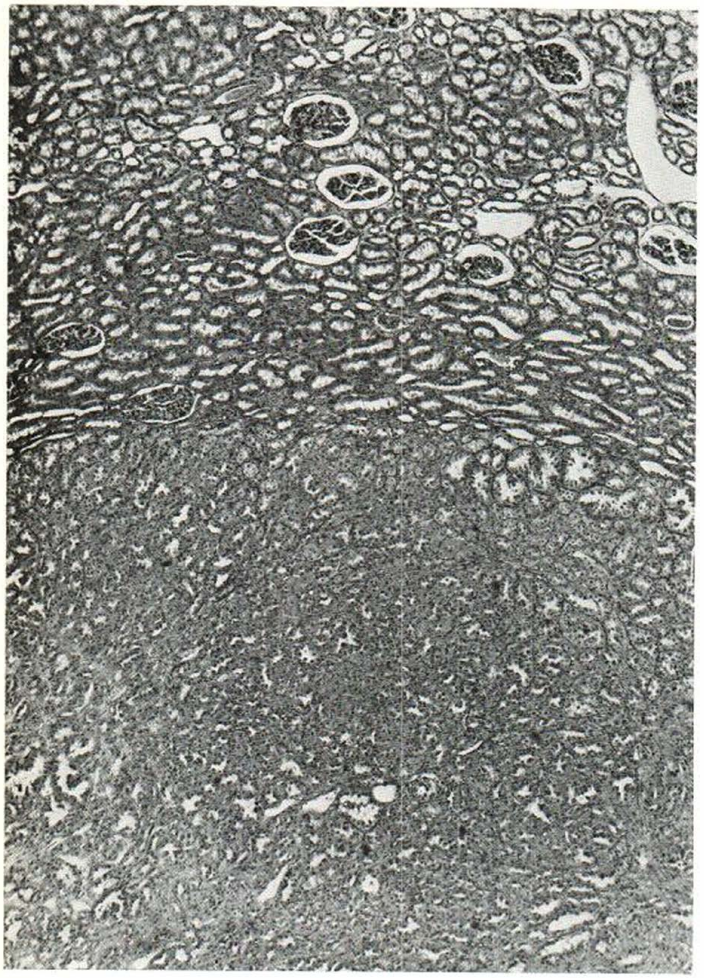

Fig. 7. Low-power photomicrograph of kidney showing the junction between the normal renal parenchyma and renal adenocarcinoma (hypernephroma). (Hematoxylin and eosin, × 30.)

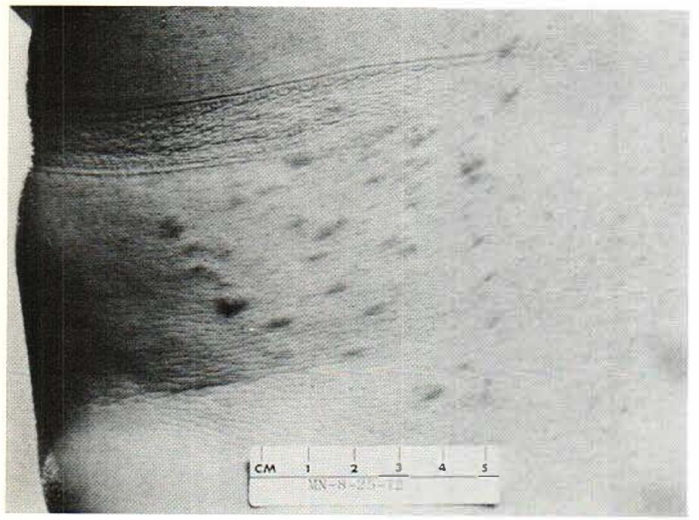

Fig. 8. Leiomyomas of the abdomen. These lesions are slightly uncomfortable despite tight-fitting clothing.

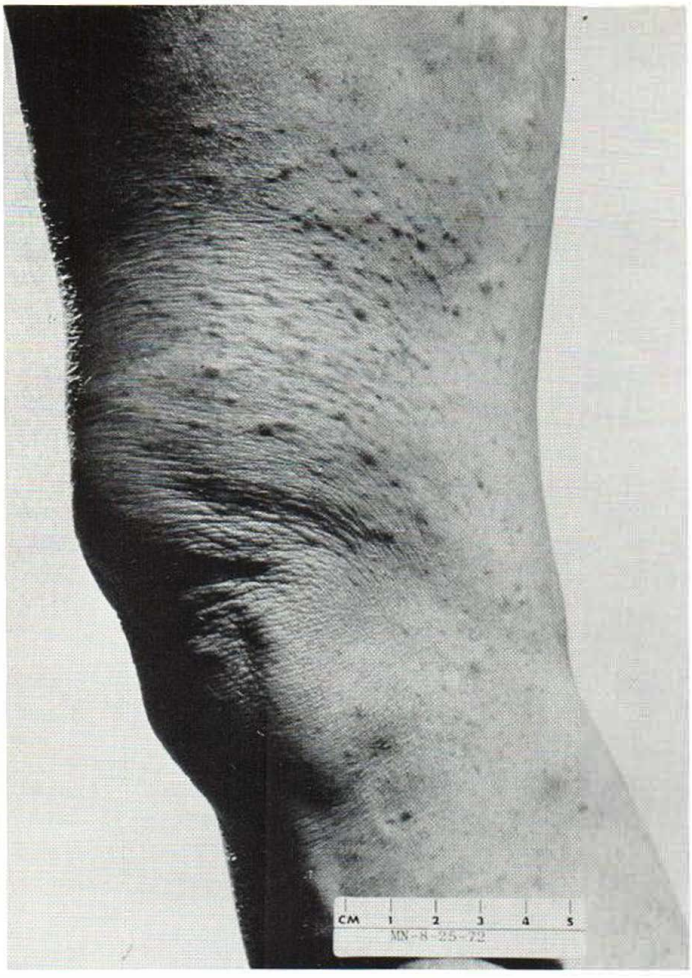

Fig. 9. Multiple miliary-sized leiomyomas of leg.