LIPOSARCOMA—THE MALIGNANT TUMOR OF LIPOBLASTS*

ARTHUR PURDY STOUT, M.D

NEW YORK, N. Y.

FROM THE LABORATORY OF SURGICAL PATHOLOGY, COLUMBIA UNIVERSITY, AND THE DEPARTMENT OF SURGERY, PRESBYTERIAN HOSPITAL, NEW YORK, N. Y.

SURELY, one of the most bizarre and fantastic chapters in the story of oncology is furnished by the tumors of fat-forming cells. The strange way in which they grow, their astounding size, equalled by no other tumor, and many other peculiar features and relationships make them of great interest. A good deal of information exists about benign fatty tumors but not nearly as much is known about the malignant ones because of their rarity. For this reason it seems worth while to record the group of 41 cases of liposarcoma which have gradually accumulated in the Laboratory of Surgical Pathology of Columbia University during the past 37 years, and to integrate the information gained from them with what can be gleaned from the publications of others.

As Gideon Wells has so ably pointed out in his fascinating review, adipose tissue has been sadly neglected and fat, which is certainly a substance known to everyone, has been the subject of extraordinarily little scientific investigation. Even its histogenesis is in doubt. Wells discusses this question and the majority of modern observers will agree with him that the older conception of the fat cell as a modified fibroblast (Jacobsen) which has assumed the function of fat storage is no longer tenable. According to Hausberger, Chlopin and Burkhardt the lipoblast is a specialized cell differing from the fibroblast although derived like it from vascular mesenchyme. This difference is emphasized when the lipoblasts of a liposarcoma are grown *in vitro*. Murray and Stout have shown that they can readily be distinguished from fibroblasts. Wells is inclined to accept the work of Wassermann who derives the fat organs from special perivascular mesenchymal cells supposedly related to reticulum and thus makes fat a close relative of lymphoid tissue and the reticulo-endothelial system. Wells supports this by citing the well known interrelationships of fat and lymphoid cells in lymph nodes and thymus and the occasional finding of extramedullary hemopoiesis in fat. But such an assumption does not take into account all of the facts demonstrated by tumors. There are many lipomas, especially the deep intramuscular variety, which are not only associated with blood vessels so that in some areas they look like pure hemangiomas but also with the formation of masses of smooth muscle and there are liposarcomas in which well differentiated bone is a prominent feature (Knox; Josephson and Westberg; Dreyfuss and Lubash; Case 40). Moreover Babès found normoblasts, megakaryocytes and plasma cells in one liposarcoma reported by him. Thus,

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it seems safer to regard the lipoblast as an ordinarily specialized fat-forming mesenchymal cell which on occasion can produce a very wide variety of different and complex tissues.

Although lipomas are very common tumors; malignant fat tumors are rare. Moreland and McNamara found only nine liposarcomas among 16,000 tumors of all kinds. In the laboratories of pathology and surgical pathology of the Presbyterian Hospital there are recorded 1454 lipomas and 21 cases of liposarcoma. Since many patients with lipomas never have them removed, the incidence is probably even less frequent.

Perhaps the most sensational feature of fatty tumors is the enormous size which they may attain. Wells says that he has seen a case of liposarcoma which weighed 69 pounds (32 kilos). Other tremendous liposarcomas, are recorded by McConnell (65 lbs.), Salzer (63.8 lbs.), Vanderveer (56 lbs.), Williams (51 lbs.), Harrington (47 lbs.), Madelung (38.5 lbs.), Waldeyer (30 lbs.) and Wechsler (25 lbs.). These massive tumors were all either mesenteric or retroperitoneal, with a predilection for the perirenal zone. The record weight and size for a tumor of any kind, so far as I am aware, is held by Delamater's case. This was a fatty tumor which was retroperitoneal and protruded posteriorly outside the left labium majus and buttock so as to form a mass four feet in circumference while the circumference of the abdomen was seven feet eight inches. When she was weighed about three years before her death she registered 269 pounds, of which it was estimated that 179 pounds were tumor. Supposing that the tumor continued to grow at the same rate of speed after weighing as before, Delamater reckoned that the tumor weighed 275 pounds at death. Even if one rejects this second figure, a tumor weighing 179 pounds dwarfs any of the more recently recorded cases. Delamater's account of this woman's life history from the age of 25, when the abdominal mass was first palpated, until her death in her 36th year is detailed and most interesting, for after a preliminary period of discomfort she became adjusted to the huge mass and, except for its weight which kept her bedridden for the last four years, breathed freely, ate well with good appetite, menstruated regularly, evacuated her bowels easily and remained cheerful. Most extraordinary of all she became pregnant five years before death, although the fetus was born dead (Fig. 1).

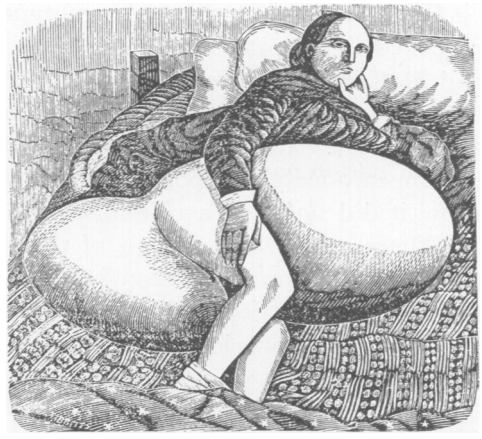

FIG. 1.—Enormous retroperitoneal lipoma weighing at least 179 pounds and possibly 275 pounds. (Reproduced from Delamater's paper in the Cleveland Medical Gazette.)

Adair, Pack and Farrior state that lipomas are more common in females (73 per cent). This sex discrepancy does not apply to liposarcomas, for in

39 liposarcomas in our own series there were 23 males and 16 females, while of 134 cases reported in the literature 71 were males and 63 females. Geographically, they are reported from Europe, Africa and the Americas. Cases from the Asiatic continent have not come to my attention.

The majority develop in the later years of life; 60 per cent of the Columbia University group were past 40 years when the tumor was first noticed, and the mean age was 53 years. Nevertheless, cases are reported in children. Fichman's case, which is somewhat questionable, was congenital, Kretschmer's case was 2 years old, Goeters' 2¾ years, Senftleben's 8 years, Sanes and Kenny's 16, while Pack and Anglem mention, without details, 13 cases under age 15. One must be prepared therefore to encounter the tumor at any age.

Trauma seems to play a very minor rôle in the etiology of this tumor. It preceded the appearance of the tumor in the thigh by three months in Jones and McClintock's case, and by a few days in Ackerman and Wheeler's second case, and accelerated the growth of a thigh tumor reported by Adair, Pack and Farrior. In Muller's case trauma to the back occurred one year before the appearance of a liposarcoma in the same locality. So far as our records show it did not play a rôle in any of the Columbia University cases.

There are certain regions of the body where liposarcomas are much more prone to develop than elsewhere. The retroperitoneal area and especially the perirenal portion of it, the mesentery and the omentum are most favored so far as cases previously reported are concerned, for nearly half come from these regions. It would seem, however, that this is due to selective reporting, for in the Columbia University group, which consists of 43 tumors in 41 patients only 7 (16.3 per cent) were in the retroperitoneal, perirenal, omental and mesenteric group. Far more common were the tumors arising in the thigh, popliteal space and gluteal region. There were 15 of these, or 35 per cent of the total. The other regions involved included the trunk 6, head, face and neck 5, inguinal canal and groin 3, leg 3, arm and forearm 3, and mammary gland 1. Other regions reported include intrathoracic (Ackerman and Wheeler; Barbier and Mollard, Chiovenda; Narr and Wells; Perkins and Bowers); meninges (Berger; Caldwell and Zinninger); spermatic cord (Kerschner; Dreyfuss and Lubash; Neal and Jolley; Marshall; Strong); bone (Barnard; Duffy and Stewart; Fender; Rehbock and Hauser; Stewart); vulva (Taussig; Kleeberg); common bile duct (Goeters); doubtful cases in the stomach by Abrams and Turberville, and in the uterus by Springer. Liposarcomas in animals are described by Haagensen and Krehbiel, and by Gavrilov and Silberfeld. Of the soft-part tumors a majority develop deeply from the inter- or intramuscular zones rather than from the subcutaneous fat where a majority of simple lipomas are located. Some tumors have been found closely attached to the sheaths of large blood vessels (Virchow 1857; Huet) but it seems very doubtful that they sprang from these sheaths. Equally open to question is the supposed relationship of lipomas and liposarcomas to nerves, inferred by Virchow 1857, Patel,

Adair, Pack and Farrior, and others. Wells discusses this question and wisely leaves it in abeyance. The development of lipomas is undoubtedly affected in some fashion by the nervous system but there exists no proof that malignant fatty tumors spring from nerve sheaths themselves.

Undoubtedly some liposarcomas develop from preexisting lipomas. This is stressed by Schiller, and Katz, and illustrated by our Case 21, where a definite liposarcoma was found completely surrounded by a simple retroperitoneal lipoma above the bladder. It is difficult to say how often it occurs because many of the tumors are composed of an intermingling of fully developed fat cells with neoplastic lipoblasts and one has no means of knowing whether or not this state of affairs existed from onset. It seems probable, however, that the large majority of malignant lipoblastic tumors are malignant from their beginning.

Wells discusses at some length the question of the availability of the lipoid in fatty tumors for use as a food in nutritional disturbances. He noted that the patient bearing the huge retroperitoneal liposarcoma, reported by Hirsch and himself, was emaciated to the maximum degree and yet the pounds of protein and fat it contained were not available to the patient. He quotes other cases of simple lipomas retaining their fat in wasting disease. None of the present group of liposarcomas demonstrated this peculiarity, but the Presbyterian Hospital records contain the description of an old woman dying in an extremely emaciated state whose entire small intestine was the seat of multiple submucous lipomas bright yellow in color and made up of solidly packed masses of normal appearing fat cells. Wells has not been able to detect any chemical difference between normal and neoplastic fat and cannot explain the phenomenon.

There is a bizarre and unexplained fact noted in connection with liposarcoma of the kidney itself. Some ten cases have been recorded (4 by Fischer and 1 each by Froug, Harbitz, Hartwig, Lubarsch, McCartney and Wynne, and Judd and Donald). The six cases of Fischer, Froug and Harbitz occurred in individuals suffering from tuberous sclerosis and adenoma sebaceum (Pringle) of the face. The records of the Squier Urological Clinic of this Medical Center contain another example of this bizarre association in a young woman who is still alive. The classical paper on the subject is by Fischer, who described other types of neoplastic malformations in the kidneys of patients with tuberous sclerosis as well as multiple lipomas and liposarcomas.

In addition to their sometimes enormous size, liposarcomas are notable for their variation in growth rate, which occasionally is very rapid and at other times exceedingly slow. An excellent example of slow growth is recorded by Martin and Colson. Symptoms commenced at 23 years when the woman began to have pains in her thigh. At 36 the thigh began to swell. At 38 a huge tumor was removed which extended from Scarpa's triangle back to the gluteal fold and forced her to keep the extremity in abduction. The mass was excised in two parts from beneath the deep fascia. Grossly, it looked

like salmon paste (laitance) and was called either round cell sarcoma or malignant lipoma. Six years later, at age 44, a recurrent mass was removed from beneath the gluteal fold which was soft, diffluent and the color of wet chamois skin. At this time roentgenograms showed rarefactions of the ischium and femur. The next operation was performed 16 years later, when she was age 60. Pieces of the tumor were removed but she died of shock. At autopsy, the tumor surrounded the hip joint, invaded the adjacent bones and passed into the pelvis through the obturator foramen. There is no mention of metastases. This story represents the probable course of a very considerable number of liposarcomas provided it is not interrupted by death or cure. It is of interest that the tumor secondarily invaded bone, because several cases reputed to have been primary in bone formed bulky extra-osseous tumors around relatively small bony lesions, and one wonders if in these cases the bony involvement may not have been secondary (L. Barnard, Fender, Rehbock and Hauser). Indeed, the whole question of the origin of liposarcomas in bone marrow needs further investigation and confirmation from other sources than the one which has sponsored either directly or indirectly almost all of the cases published. The cases originally published by Stewart were challenged by the late W. G. Barnard, and one must acknowledge that they seem different from liposarcomas arising in other tissues.

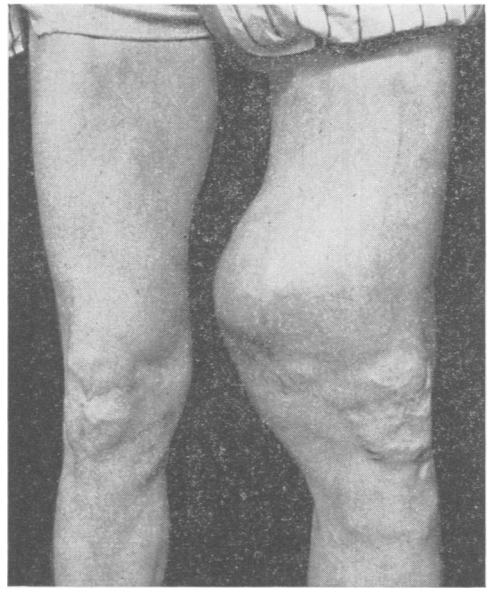

FIG. 2.—Case 7: Undifferentiated myxoid liposarcoma of thigh. A characteristic example of these bulky tumors.

Some liposarcomas pursue a much more rapid course, as exemplified by several cases in the present series, *e.g.*, Case 7 (Figs. 2 and 3), which attained a size of 24 by 16 cm. in the thigh in six months and caused death by extension and metastasis five months after amputation; Case 9, the total known duration of which was only ten months, and Case 16, which reached a size of 14 x 12 cm. in the buttock in six months and resulted in death with intra-abdominal and lung involvement in another six months. Between these extremes there are all grades of variation, but with the greater number exhibiting slower growth and with a relatively small number spreading by metastasis. Before the question of metastasis can be debated, the extremely interesting subject of the multiplicity of tumors must be elaborated for the two inevitably become confused one with the other.

It is well known that lipomas are often multiple; occasionally one or

more of these fatty tumors develop in the body and, succeeding them, many other tumors appear as if they were metastases. Lubarsch's case is representative of one type. There was a large multinodular fibrous and fatty tumor in the left perirenal region with many smaller similar foci in the kidney itself, retroperitoneal region, suprarenal gland, liver, heart, subpleura, left lung, periaortal and retro-esophageal areas, spinal vertebrae and both femora. In spite of the benign appearance he believed these small foci were metastases. Siegmund described a very similar case except that the secondary nodules

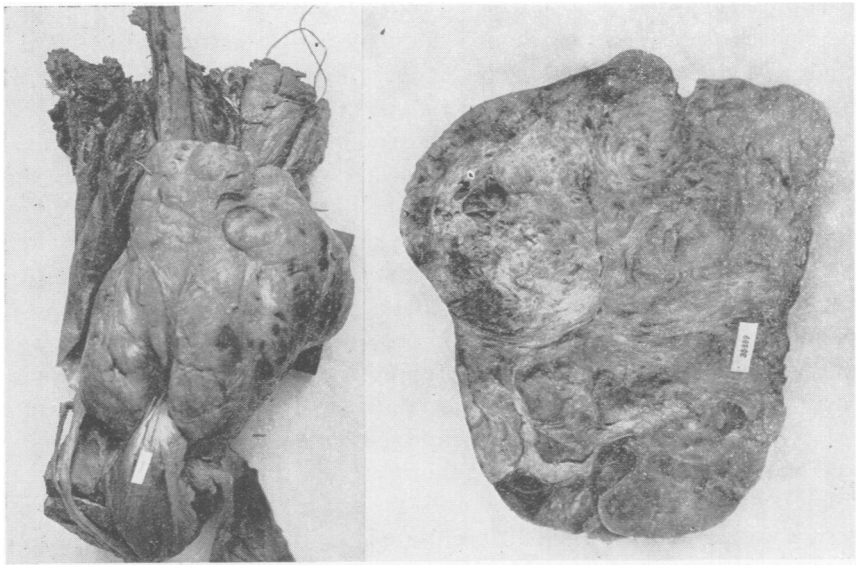

FIG. 3.—Case 7: The tumor lay deep to the sartorius, semimembranosus and vastus medialis muscles which have been dissected away to expose it. At the right the cut surface of the tumor is shown.

appeared like liposarcomas. He believed that both his own and Lubarsch's cases were examples of multiple tumors and not metastasis formation. Somewhat comparable cases have been recorded by Goormaghtigh, *et al.*, who favor the metastasis hypothesis and by Martland, Gold, and Sternberg, all of whom preferred to believe that the tumors were independent. Somewhat more frequent are instances in which a few more or less widely separated liposarcomas appear simultaneously or successively, and one must decide whether they are independent or represent metastases. An excellent example is Case 15 in the present series, previously reported by Murray and Stout. The first tumor appeared in the antecubital fossa and two and one-half years later a second tumor developed higher up in the arm. In Case 32 there were three entirely separate liposarcomas in the thigh, the popliteal space and in the pelvic retroperitoneal space. In Case 7, following amputation for a thigh liposarcoma, the patient died with tumors in the pelvis, back, gluteal region and cerebrum. The cerebral tumor must have been a metastasis but

should one accept the other three nodules as extensions, metastases or separate tumors? Similar problems arise with regard to cases reported by Hosemann and Lang, Josephson and Westberg, and Narr and Wells. It seems to the writer that in the majority of the above quoted cases one is dealing probably with multiple independent tumors. The question is of more than academic importance for it has some bearing on the choice of treatment.

The preceding paragraph indicates that there are some cases in which apparent metastases may only be multiple tumors. It should not be interpreted as meaning that metastases never occur in cases of liposarcoma, for most certainly they do. In addition to one example each by the five reporters of bone liposarcomas, unquestionable metastases are recorded by Daniel and Babès, Geschickter, Gricouroff, Harbitz, Jaffé, Lepoutre, Lifvendahl, Menne and Birge, Moreland and McNamara (2 cases), Nieuhuis, Seids and McGinnis (2 cases), Stich, Taussig, Vincent and Sénellart, Virchow (1857 and 1865), and Waldeyer. To these may be added Cases 3, 6, 7, 9, 14, 16, 26, and 34. From the data at hand, it is impossible to determine the relative frequency of metastases because there exists no series of consecutive cases followed over a long enough period to be of statistical significance. The impression one gains from the literature is that metastases are less common than with other types of sarcoma since among 134 cases there are only 24 with metastases, and if one subtracts the eight bone cases from the total then there are only 19 among 126. If one takes the Presbyterian Hospital cases, most of which have been followed, and excludes the last four which have occurred within the last two years; there remain 17 cases of which six have shown metastases. If Cases 2, 4 and 11 are also subtracted because they represent examples of the well differentiated form of liposarcoma, often called myxolipoma or some comparable name, there are then six metastatic cases among a group of 14, or 40 per cent. This figure is probably somewhere near the truth. In 60 per cent of cases metastases lodge in the lungs or pleurae, in 25 per cent in the liver, after which come bone marrow and central nervous system, with isolated examples of involvement of other scattered parts. In no single acceptable case were there widespread metastases—a further argument against the acceptance of the cases of Lubarsch and Siegmund as ones of extensive metastasis rather than multiple tumors.

The gross characteristics of liposarcomas are quite varied, but in general they form large bulky, nodular, masses of apparently encapsulated tissue which is always firmer than the adipose tissue of simple lipomas and runs a gamut of colors from orange to pale cream often with an admixture of reds caused by areas of increased vascularity or hemorrhage (Fig. 3). Somewhat more than half of them are slimy and mucoid (Fig. 4). These tumors not infrequently have areas of normal yellow fat interspersed among the sarcomatous masses. In a few tumors there are dense fibrous areas. Occasionally degeneration cysts may form but this is exceptional and even the colossal tumors usually remain solid throughout in spite of extensive areas of degeneration. Secondary or local multiple nodules are probably quite frequent and account

for the many times which local recurrences manifest themselves after attempted excision.

The microscopic features of liposarcomas are even more varied than the gross and unfortunately have given rise to a great variety of names which make for confusion and misconception. Ewing (1935) gives us a basic separation of liposarcomas into two main types: One, the myxoliposarcoma, which is vascular, myxoid and lipoblastic; the other, the granular cell lipoblastoma composed of cells resembling the foamy lipoblasts of brown fat. With this recognition of two forms of lipoblasts, all who have had any degree

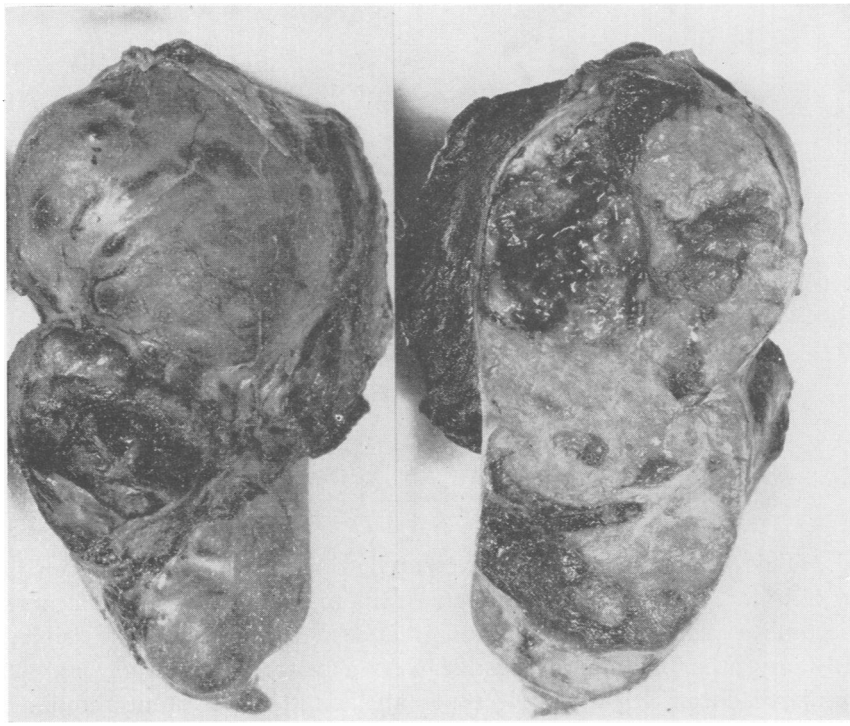

FIG. 4.—Case 12: Undifferentiated myxoid liposarcoma after its removal from within the gastrocnemius muscle. The highlights of the cut surface at the right represent slimy mucoid material.

of experience with these tumors will agree but will demand further elucidation. How, for instance, can one distinguish between what is so frequently called myxolipoma, fibromyxolipoma or some similar name and Ewing's myxoliposarcoma? The answer to this query is that one cannot, because, as Gricouroff has pointed out, the *"lipome embryonnaire"* or myxoid lipoma can behave like a malignant tumor by recurring and metastasizing. He places them between simple lipomas and atypical liposarcomas. Mucicarmine will stain the intercellular substance but never intracellular vacuoles which contain lipoid. He points out that these tumors may have areas resembling fibrosarcomas poor in collagen as well as myxoid areas. Jaffé also recognizes

these three different variants which he called respectively lipoblastomas, lipoma pseudomyxomatodes and liposarcoma but he was apparently not aware that the first tumor form might recur after excision and the second both recur and metastasize. Moulonguet and Pollosson also have three divisions of lipoblastic sarcoma which they call respectively malignant lipoma, lipoblastic myxoid sarcoma and lipo- and fibroblastic sarcoma.

This attempt to divide the malignant fat-forming tumors into three separate and distinct groups is doomed to failure, however, because when one has a relatively large group to study, such as the 41 cases in the present collection, one finds that all of the cases are not pure types but that some of them are

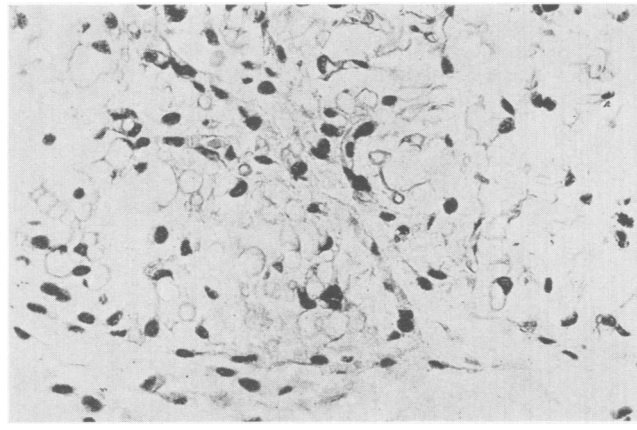

FIG. 5.—Embryonal fat from the subcutaneous layer of a supernumerary finger removed a few days after birth.

mixed. This should have been anticipated, since it has already been pointed out by Schiller, and others, that a benign lipoma can change its characteristics and become a malignant tumor, and if one such mutation is possible, theoretically any other change is possible. As a matter of fact, all combinations of the above described histologic types are found in different tumors of this series. For example, both myxoid and round cell (adenoid) areas are found in different parts of Cases 5, 8, 17, 22, 24, 28, and 29; combinations of myxoid and fibrosarcomatous areas in Case 25; myxoid, round cell and fibrosarcoma-like areas in Case 14; and areas of osseous and cartilaginous metaplasia in an otherwise myxoid tumor in Case 40. The fact that both myxoid and adenoid or round cell developments may be found in the same tumor seems to be an observation of some importance. It indicates that there are probably not two separate and distinct ancestral lipoblasts, one of which forms ordinary adipose tissue and the other brown fat, but that the same ancestral cell in the primitive mesenchyme is capable of forming either or both—certainly, Figures 11 and 12 show that the two types can be so juxtaposed in the same tumor that one can hardly credit that they were formed by two different cell prototypes. If this is true it should lead

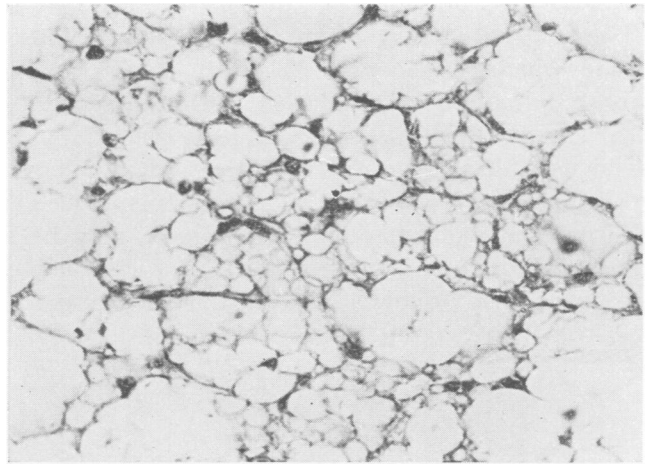

FIG. 6.—Brown fat from the deep fatty tissues of the lateral neck region of a male, age 41.

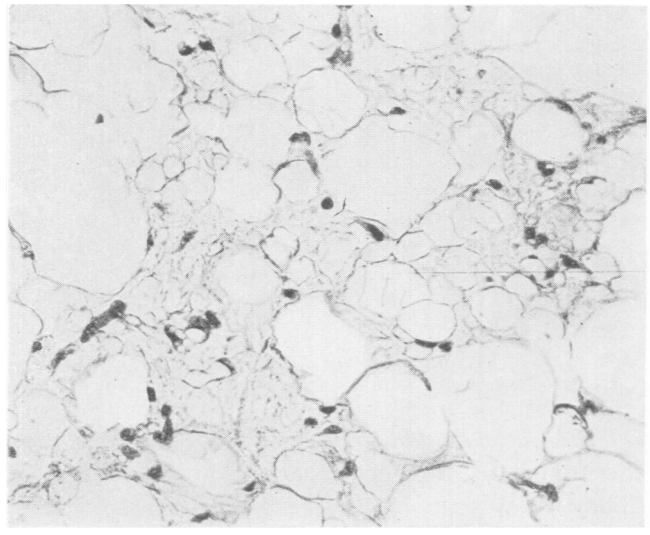

FIG. 7.—Case 19: Differentiated myxoid liposarcoma. The photomicrograph shows embryonal lipoblastic tissue, resembling the embryonal fat shown in Figure 5, mixed with adult fat cells.

us to look upon the liposarcomas not as a group of separate and distinct tumor types worthy of bearing separate names but as a single group capable of manifesting different degrees of differentiation which can be indicated by descriptive adjectives. Since this group represents the malignant form of the fat-forming tumor it is quite properly called liposarcoma. With this conception in mind, liposarcomas may be subdivided as follows:

1. *Well Differentiated Myxoid Type:* This resembles the usual type of embryonal fat (Figs. 5 and 7). It consists of adult fat cells, embryonal stellate- or spindle-shaped fat cells containing droplets of a material which can be

stained with scharlach R. or sudan III, and usually a rather rich network of capillaries. The whole mass is bound together by a loose meshwork of connective tissue which is generally, but not always, slimy and myxoid. Sometimes this slimy material can be tinted with mucicarmine and sometimes not. This characteristic picture is occasionally varied by the presence of more or less dense fibroblastic tissue with well developed collagen and reticulin fibers. The lipoblasts whether stellate- or spindle-shaped are rather small, regularly formed and, although such tumors may be enormous, it is almost impossible to detect any mitoses. It is questionable whether such tumors ever metastasize while they remain in this state of good differentiation. Cases 2, 4, 11, 19, 31, 36, 37 and 41 are examples.

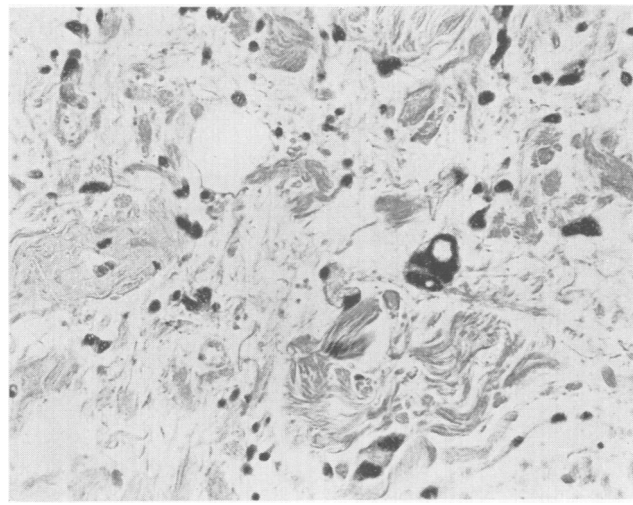

FIG. 8.—Case 10: Undifferentiated myxoid liposarcoma. The lipoblasts are bizarre with hyperchromatic nuclei. The stroma of this tumor is quite fibrous.

2. *Poorly Differentiated Myxoid Type:* This group resembles the first group, with the important difference that the lipoblasts are bizarre and often monstrous. They grow to a large size with astonishingly variable nuclear formations and the misshapen nuclei are often hyperchromatic or pyknotic (Figs. 8 and 9). As noted by Murray and Stout, such cells are usually degeneration forms and incapable of reproduction *in vitro*. The bizarre lipoblasts often dominate the picture and the amount of lipoid produced is correspondingly less. Signet-ring forms are occasionally seen. Completely differentiated adipose tissue is less or entirely absent and the number and arrangement of blood vessels so variable as to be no longer significant. Fibrosarcomatous areas are sometimes produced (Fig. 14). This poorly differentiated type is definitely malignant, difficult to eradicate, and may metastasize. It is represented in this series by Cases 1, 6, 7, 9, 10, 12, 13, 15, 18, 19, 20, 21, 23, 26, 30, 32, 33, 34, 35, and 40.

3. *Round Cell or Adenoid Type:* The characteristic lipoblast of this tumor type is rounded with centrally placed nucleus and voluminous foamy cytoplasm,

the vacuoles of which are filled with lipoid. The cells are massed together in close approximation with only a delicate fibrous framework and an inconspicuous blood supply (Figs. 10, 11, and 12). In many such tumors the cells may reach an enormous size. Jaffé measured them as large as 120 microns and the cell illustrated in Figure 13 is 126 microns in length. The hyperchromatic pyknotic nuclear material indented by the vacuoles suggests that these are degeneration forms. These tumors are not myxoid. Like the tumors of the second group they are difficult to eradicate and may metastasize. Cases 3, 16, 27, 38 and 39 are examples of this group.

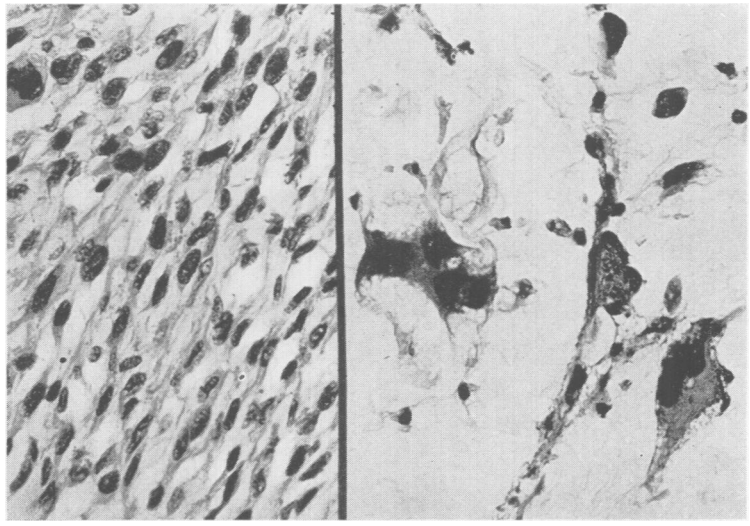

FIG. 9.—Case 35: Undifferentiated myoid liposarcoma. At the right are bizarre lipoblasts partly filled with vacuoles in a mucoid stroma. At the left, the lipoblasts are elongated, probably because there is little intercellular material and they tend to be compressed.

4. *Mixed Group:* These are the tumors composed of two or more elements of the preceding groups. They, too, are definitely malignant (Figs. 10, 11, 12, 14). Representatives are Cases 5, 8, 14, 17, 22, 24, 28 and 29.

Diagnosis of any tumor should be made with accuracy before it is treated. Liposarcomas can be suspected clinically if they have reached a very large size and with some degree of certainty at exploration if in addition the tumor is both yellow and slimy. But the only proper procedure is biopsy before treatment, confirmed by immediate frozen section if possible, if not by paraffin section. Progress in the treatment of soft part tumors will never be attained if this is not made a routine procedure instead of the all too common method of excising the whole tumor first and secondarily trying to carry out some further and more radical procedure if the growth proves to be malignant. Liposarcomas have such distinctive histology that the only tumor with which they may easily be confused is the myxoma. The myxoma has no lipoblasts and no fat is formed. The differentiation between the two is worth while because the myxoma, while it may continue to grow if not completely excised, never metastasizes, so far as this writer is aware.

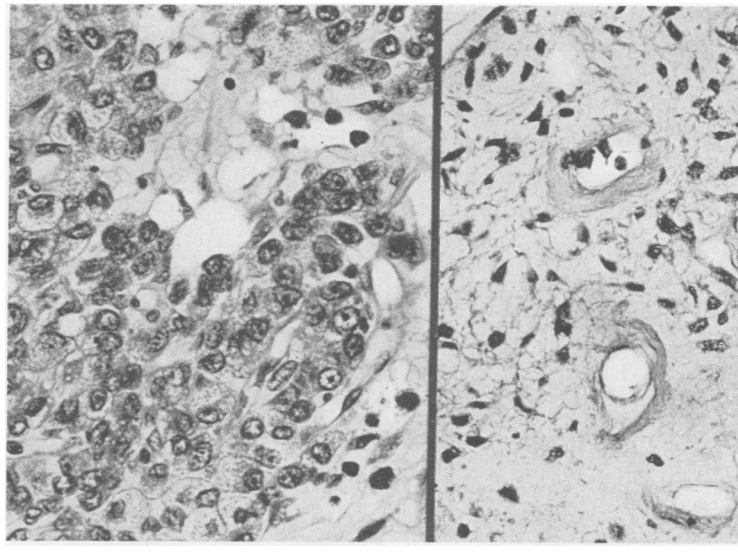

FIG. 10.—Case 24: Mixed myxoid and round cell liposarcoma. At the right a myxoid area is shown resembling the embryonal fat shown in Figure 5. At the left is the junction between a myxoid and round cell area. The rounded lipoblasts are honeycombed with tiny lipoid vacuoles.

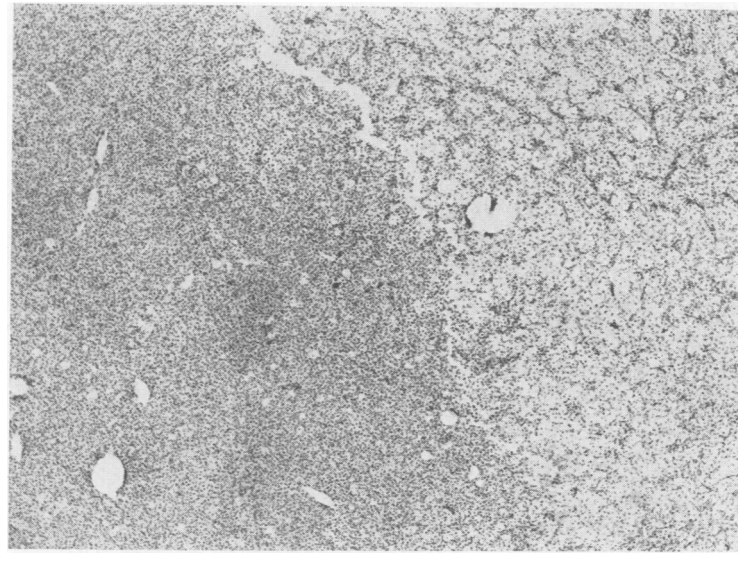

FIG. 11.—Case 8: Mixed myxoid and round cell liposarcoma. At the left is shown the solid mass of rounded lipoblasts. At the right is the loose-textured vascular myxoid portion of the tumor.

Treatment of liposarcomas is primarily surgical but it should be pointed out that some liposarcomas have proved to be definitely radiosensitive, and for this reason radiotherapy as a mode of treatment must not be neglected. Ewing (1935) has recommended that it be used before any operation. In Cases 12 and 15 of this series it was used on relatively small recurrent nodules with success lasting seven years and five months in the former and two and one-half years in the latter. Radiotherapy was used in six other Presbyterian Hospital cases either without any benefit or with only temporary effect. It should be noted that the good results were obtained with rather small recurrent masses in easily accessible situations while the failures were

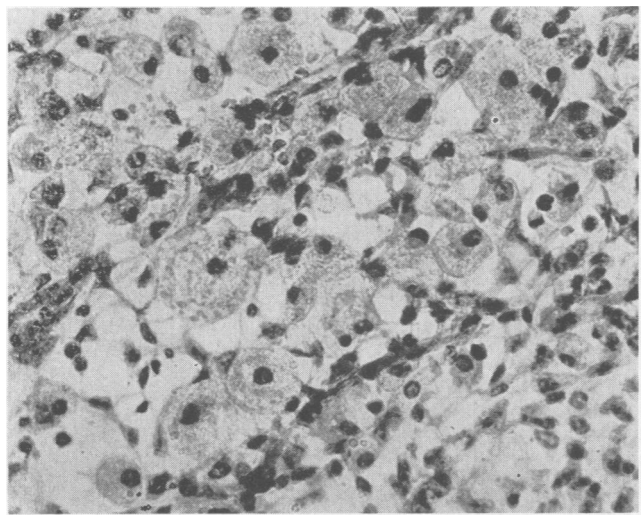

FIG. 12.—Case 8: Details from the junction of the two cell types shown in Figure 11. The rounded, finely vacuolated lipoblasts are intermingled with the stellate and elongated cells of the myxoid area.

in larger and usually deeper tumors. The details are recorded elsewhere in this paper. Reports from other clinics are discouraging. It was used postoperatively to prevent or because of recurrences by Moreland and McNamara in two cases, by De Renzi, Selman, and Seids and McGinnis in one case each, with complete failure. Another case treated by Seids and McGinnis postoperatively was without recurrence at the end of one year; too short a time to be significant. Siegmund treated some of the many tumors in his case with roentgenotherapy and reported partial and temporary regression. In spite of this, one should be encouraged to believe that since some success has been obtained at the Memorial Hospital and in this institution, this is a form of treatment which should not be abandoned.

If a tumor is a well differentiated myxoid liposarcoma, one does not need to be as radical as for the other three groups, because the worst that may be expected is local recurrence. Nevertheless, it will pay to treat even these tumors with respect and remove the entire capsule and the tissue

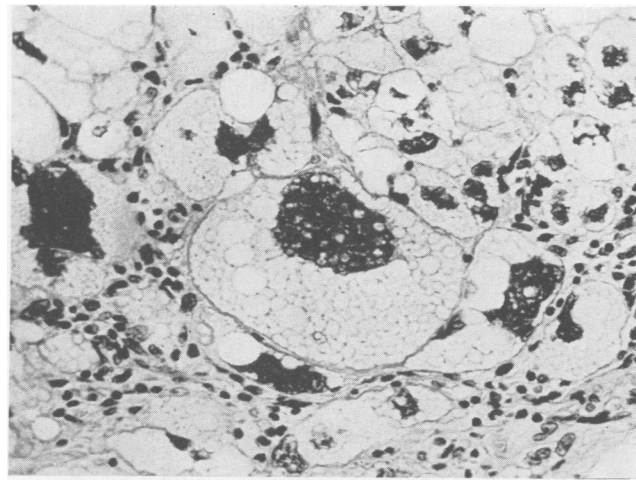

FIG. 13.—Case 27: Detail of a round cell liposarcoma showing giant lipoblasts. The large cell in the center is 126 microns in length. It is probable that these huge cells are degenerate and incapable of reproduction.

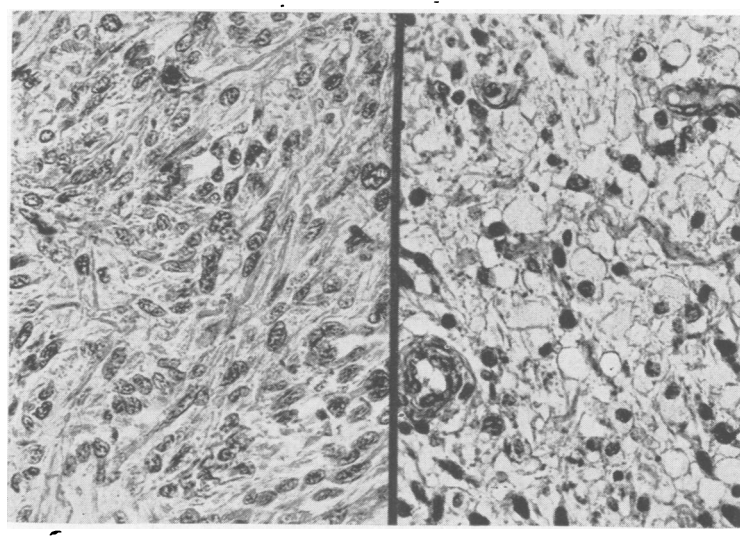

FIG. 14.—Case 14: Mixed myxoid and round cell liposarcoma. At the right a myxoid area with intermingled round cell lipoblasts. At the left an area where the cells simulated the appearance and arrangement of a fibrosarcoma.

immediately outside of it because one can never be absolutely sure that the entire tumor is well differentiated, or that a recurrence may not be less well differentiated and more malignant. The ease with which a second nodule may be overlooked is illustrated by Case 19. An apparently encapsulated tumor attached to the deep fascia was enucleated from the thigh with the diagnosis of lipoma. When the microscope showed that it was a liposarcoma, the whole area was reexcised. In the gross specimen, a second deeper entirely unsuspected nodule of similar type was discovered.

TABLE I

RECORD OF CASES*
PRESBYTERIAN AND ALLIED HOSPITAL CASES

Case No.	Sex	Age	Site	Duration Before Diag. Mos.	Size—Cm.	Type	Treatment	Result
1	F	65	Lumbar	?	?	Myxoid (undiff.)	Excision	?
2	F	43	Canal of Nuck	5	12 x 7 x 2	Myxoid (diff.)	Excision	No recur. 22¼ years
3	M	33	Retroperitoneal (psoas-iliacus musc.)	3	21 x 17 +	Round cell	Partial excision. Radiotherapy	Died 15 + months. Lung and liver metastases
4	M	38	Back of neck	12	7 x 6	Myxoid (diff.)	Excision	No recur. 17½ years
5	F	29	Back	120	4 x 2.7	Myxoid (undiff.) and round cell	Excision	No recur. Died 45 mos. myocarditis
6	F	60	Omentum	0.75	"very large"	Myxoid (undiff.)	Biopsy	Died postop. Metas. in liver and pleurae
7	M	59	Thigh	6	21 x 16	Myxoid (undiff.)	Biopsy. Amputation	Died 5 mos. Metas. to cerebrum. Tumors in pelvis, back & gluteal regions
8	F	55	Thigh	180	21 x 15 x 9	Myxoid (undiff.) and round cell	Excision. Radiotherapy	Recurred. Died 42 mos. postop.
9	M	40	Scapular reg.	3	15 x 13	Myxoid (undiff.)	Excision. Biopsy recur. Radiotherapy	Died hemorrhage 7 mos. postop. Metas. to lungs & extension to axilla
10	M	66	Cheek	24	3 x 2 x 1	Myxoid (undiff.)	Excision	No recur. 15 mos. postop. died "heart disease"
11	M (colored)	37	Temporal reg.	96	8 x 8 x 4	Myxoid (diff.)	Excision	6 years, 3 mos.—no recurrence
12	F	59	Leg (gastrocn. mus.)	7	12.5 x 6	Myxoid (undiff.)	Excision. Radiotherapy of reputed recur.	Reputed local recur. at 15 mos. 8 yrs., 8 mos. after op. no definite disease
13	F	57	Retroperitoneal	132	42 x 22 x 18 (wt. 28 lbs.)	Myxoid (undiff.)	Biopsy	Died postop. No metastases
14	M	32	Thigh	4	15 x 11	Myxoid (undiff.) with areas like fibrosarcoma and round cell	Excision. Reexcision. Radiotherapy	Died 67 mos. after 1st op. with recur. and lung metastases
15	M (colored)	64	Forearm	5	20 x 8 x 6	Myxoid (undiff.)	Excision. Excision of 2nd tumor. Radiotherapy of recur.	2nd tumor in arm and recur. in forearm after 30 mos. No evidence of tumor 60 mos. after 1st op.
16	M	74	Gluteal	6	14 x 12	Round cell	Biopsy. Radiotherapy	Died 6 mos.—lung met. and intra-abdominal tumor.
17	F	52	Thigh	3.5	16 x 16	Myxoid (undiff.) and round cell	Biopsy	Died 1 mo.—hemorrhage.
18	F	75	Perirenal	12 +	15 x 15	Myxoid (undiff.)	Excision. Nephrectomy	Died 3 mos.
19	F	46	Thigh	3	4 x 3 & 2.7 x 1.5	Myxoid (diff.)	Excision in 2 stages	Recovered
20	M	49	Thigh (intramuscular)	24	27 x 18 x 11 (wt. 7.5 lbs.)	Myxoid (undiff.)	Biopsy. Excision	Recovered
21	M	86	Retroperitoneal (above bladder)	7	8 x 8	Myxoid (undiff.) (within larger lipoma)	Excision	Recovered

TABLE I—(*Continued*)

CASES FROM OTHER SOURCES

Case No.	Sex	Age	Site	Duration Before Diag. Mos.	Size—Cm	Type	Treatment	Result
22	F	Adult	Arm	?	4 x 3 x 2	Myxoid (undiff.) and round cell	Excision	?
23	F	28	Thigh	?	Unknown	Myxoid (undiff.)	Excision	Local recur. after 4 yrs.
24	M	50±	Popliteal space	6	16 x 15	Myxoid (undiff.) and round cell	Excision	No recur. after 4 years
25	M	?	Forearm	?	Unknown	Myxoid (undiff.) with areas like fibrosarcoma	Excision	?
26	M	60	Popliteal space	24	18 x 12 x 8	Myxoid (undiff.)	Excision. Radiotherapy	Died with met. after 3 yrs., 2 mos.
27	M	62	Inguinal	2	10 x 10±	Round cell	Partial excis.	?
28	F	62	Back	3	20 x 13 x 5	Myxoid (undiff.) and round cell	Excision	?
29	M	55	Popliteal space	2	12.5 x 10 x 10	Myxoid (undiff.) and round cell	Excision	?
30	?	?	Leg	?	?	Myxoid (undiff.)	Excision	?
31	M	67	Scrotum, canal & pelvic retroperitoneum	48±	Large	Myxoid (diff.)	Excision	?
32	M	54	(1) Thigh (2) Pop. space (3) Pelvic retroperitoneum	144	(Retroperit. Weighed 1–2 kilos)	Myxoid (undiff.)	Excision of all 3	?
33	?	?	Leg	?	8.5 x 8	Myxoid (undiff.)	Amputation	?
34	F	58	Popliteal space	12	16 x 9	Myxoid (undiff.)	Biopsy. Excision	Died with metastases
35	M	50	Axilla	0.5	12 x 12	Myxoid (undiff.)	Excision	?
36	M	Adult	Cheek	?	3.2 x 2 x 1.8	Myxoid (diff.)	Excision	?
37	M	50±	Lumbar	?	?	Myxoid (diff.)	Excision	?
38	F	18	Gluteal	6±	8 x 7 x 6	Round cell	Excision. Radiotherapy	9 years no recurrence
39	M	57	Infraclavicular (also ca. mammary gland)	?	?	Round cell	Excised	?
40	M	68	Gluteal (intramuscular)	2	19 x 13 x 5.5	Myxoid (undiff.) (with bone & cartilage metaplasia)	Excised	?
41	F	50	Orbit	1	?	Myxoid (diff.)	Excised	?

*These cases have the following origins: Case 22 from Vanderbilt Clinic, New York, Dr. P. R. Turnure; Case 23 from Roosevelt Hospital, New York, Dr. W. C. White; Cases 24 and 25 from Lincoln Hospital, New York, Dr. Chester R. Brown; Cases 26, 28, 30, 31, 35, 36 from the Nix Hospital Laboratory, San Antonio, Texas, Dr. A. O. Severance; Case 27 from the New York Postgraduate Hospital, Dr. M. N. Richter; Case 29 from the Hospital for Ruptured and Crippled, New York, Dr. H. Pheasant; Case 32 from Ellis Fischel State Cancer Hospital, Columbia, Mo., Dr. L. V. Ackerman; Case 34 from Cornwall Bridge, Connecticut, Dr. W. C. Clarke; Cases 37 and 41 from the Hospital of the University of Pennsylvania, Dr. R. C. Horn; Case 38 from the Mather Hospital, Port Jefferson, L. I., Dr. Ethel Trygstad; Case 39 from Bellevue Hospital, New York, Dr. W. G. von Glahm; Case 40 from Vassar Bros. Hospital, Poughkeepsie, N. Y., Dr. Elizabeth Heath.

DETAILS OF CASES TREATED WITH RADIOTHERAPY

Case 3.—One month after operation six radiotherapy treatments were given in the course of two weeks. Factors unknown. No effect.

Case 8.—Immediately after operation eight treatments were given during a period of three and one-half months through anterior and posterior 15 x 20 cm. fields to thigh and hip, totalling 2300 r. with the following factors: 200 kv, 50 cm. skin distance, 8 ma., 1.86 mm. cu. + 1 mm. al. Sixteen months later after the tumor had reappeared, 16 more treatments were given to 20 x 25 cm. anterior and posterior thigh and hip fields, totalling 4800 r. The factors were: 195 kv, 50 cm. skin distance, 8 ma., 1.86 mm. cu. + 1 mm. al. Eight years before operation the original tumor had been treated elsewhere with roentgenotherapy without effect. The treatment of the recurrence had no effect.

Case 9.—The treatment given was to a large rapidly growing local recurrence and axillary extension. 2790 r. was first given to the recurrent mass. Factors: 200 kv, 30 ma., 50 cm. skin distance, filter ½ mm. silver and 1 mm. of aluminum. This caused some shrinkage. Three months later, using the same factors, 1860 r. were given through anterior and posterior fields to the axilla. This was supplemented after 3 months with 4900 mg. hrs. of radium in 3.5 cm. radium needles. The effect was slight and probably did not retard the fatal termination.

Case 12.—When a 2.5 x 2 cm. mass appeared in the scar 15 months after excision this was assumed to be a recurrence. This was treated through two 8 x 10 cm. fields, a total of 6000 r. in 40 days was given. Factors 200 kv, 25 ma., skin distance 50 cm. filter 2 mm. cu. + 1.25 mm. al. This caused complete disappearance of the mass and it has not reappeared in the succeeding 7 years and 5 months.

Case 14.—Roengenotherapy was begun after a recurrent tumor mass was excised with resection of the sciatic nerve from the posterior thigh. During a period of 5 months through two 10 x 15 cm. and one 8 x 12 cm. fields a total of 9000 r. was given. Factors 190 kv, 8 ma., 50 cm. skin distance; 1.31 mm. cu. + 1 mm. al. filter. One year after the termination of the first course there was no local tumor in the thigh but a mass could be felt deep in the iliac fossa. A second course was begun using three 15 x 15 cm. fields in the thigh and hip regions. It was continued for 3 months, and a total of 9000 r. was given with the following factors: 200 kv, 25 ma., 50 cm. skin distance, filter 1.05 mm. cu. + 1.25 mm. al. This did not prevent the tumor from persisting and slowly filling the pelvis. Two months after the termination of the second course a little more irradiation was given to the abdomen and pelvis, totalling 975 r. All of this failed to check the progress of the disease to a fatal termination.

Case 15.—Details of radiotherapy given in paper by Murray and Stout.

Case 16.—The roentgenotherapy given in this case represents treatment of the tumor begun 3 days after biopsy. Three 10 x 15 cm. fields were used and a total of 7000 r. given in a period of 40 days. The factors were: 200 kv., 25 ma., skin distance 50 cm., filter 1 mm. cu. + 1 mm. al. The patient left the city before any more treatment could be given. It did not check the progressive growth of the tumor and the rapid fatal termination.

Case 20.—This represents postoperative prophylactic radiotherapy. Two 8 x 20 cm. and two 10 x 20 cm. fields were used and a total of 8000 r. given in a period of 54 days. The factors were: 200 kv, 25 ma., 50 cm. skin distance, filter 1 mm. al. + 1 mm. cu. The case is too recent to have any significance.

The principle of treatment for all other liposarcomas should be radical surgery, if a cure is to be attempted. Failures are bound to occur, however, in some cases, such as the retroperitoneal tumors, because their situation makes complete removal impossible, and in others because there may be undiscovered multiple tumors. In many cases this may not result in immediate death even with recurrence, because so many of these tumors progress slowly and fail to metastasize. It would seem not worth while to attempt very extensive and shocking operations in the very old and infirm because the risk of operative death may be greater than the untoward results which may follow more conservative treatment of the tumor. One cannot establish rules to govern the treatment of every individual case, because the factors are so many and so varied. One can only keep in mind the possibilities when treatment is planned.

SUMMARY

A group of 41 cases of liposarcoma has been studied in connection with 134 previously reported cases. These tumors tend to form very large bulky masses, with a predilection for the thigh and extraperitoneal tissues but with occasional appearance in many other regions as well. They exhibit great variations in growth speed, they are sometimes multiple and the more malignant forms metastasize usually either to the lungs or liver.

Grossly, these tumors are frequently mottled with yellow because of their lipoid content and are often slimy from the formation of mucoid material. Microscopically, they can be divided into one well differentiated, less malignant group, which simulates the appearance of ordinary embryonal fat and three other poorly differentiated more malignant groups resembling respectively atypical ordinary embryonal fat, atypical brown fat with the formation of rounded lipoblasts, and finally a group showing both of these elements in combination. Probably as a result of metaplasia these tumors can on occasion form other tissues such as reticulin and bone. This versatility suggests that there are probably not separate embryonal stem cells for adipose tissue and brown fat but that both spring from a common ancestor segregated from the primitive mesenchyme.

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