

Lipomatous Lesions of the Uterus

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Summary. Four lipomatous lesions of the uterus are reported and the available literature from 1965 to 1976 is reviewed. It is suggested that these lesions result from metamorphosis of uterine smooth muscle which can proceed to form localised or diffuse mature adipose tissue in a leiomyoma or in the myometrium.

Three terms are suggested for the nomenclature of the various morphological types of lipomatous lesions of the uterus: diffuse lipomatosis in a leiomyoma, circumscribed lipomatosis in a leiomyoma and uterine lipoma.

Key words: Uterus — Smooth muscle — Lipid metamorphosis — Lipid metaplasia — Uterine lipoma.

Introduction

The so called lipoma of the uterus, which was first described by Lobstein in 1816, is thought to be rare. Since then sporadic cases have appeared in the literature and the first review was written by Saydel (1903) who summarised 11 cases. Further reviews were published by Petersen (31 cases) in 1923, Kase-man (70 cases) in 1943, Brandfass and Everts-Suarez (96 cases) in 1955 and Barbanti-Silva (131 cases) in 1966. The nature of these lesions is still obscure and there is no over-all agreement about their histogenesis and nomenclature.

In this paper we review the literature from 1966 to 1976, report four new cases and characterise their lipid content histochemically. A new nomenclature for these lesions is suggested.

Material

The material for this study is obtained from the files of the Histopathology and Cytology Department of Falun Central Hospital from the year 1965 to 1976. During this period four lipomatous lesions of the uterus were diagnosed and the presentation, clinical findings, management and outcome is summarised in the following case reports.

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Case Reports

Case 1. G.S.; a 56-year-old unmarried, nulliparous woman who presented in 1966 with menorrhagia and metrorrhagia. On clinical examination the uterus was found to be enlarged and the lumen was irregular. Histological examination of curettings in 1966, 1968 and 1971 showed benign endometrial and cervical polyps. A total hysterectomy was performed in August 1972.

Case 2. L.L.; a 47-year-old married woman (V-gravida, IV-para) who complained of pain in the lower part of the abdomen, particularly the left iliac fossa, and the lower part of the back for several years. No bleeding, discharge or pain in the perineum were noted. Clinical examination in October 1972 revealed a tumour in the lower part of the abdomen about 15 cm in diameter. Uterine curettings in November 1972 showed a normal endometrium in the late secretory phase of the cycle. In January 1973 a hysterectomy and appendectomy were performed.

Case 3. R.J.; a 64-year-old unmarried, nulliparous woman in menopause for 6 years. During a routine gynaecological examination in 1976 a pelvic mass, about 14 cm in diameter was discovered. The mass was freely mobile, had a smooth surface and was thought to be attached to the uterus or arise from it.

Aspiration cytology from the mass in July 1976 showed benign epithelial elements and connective tissue but no conclusive diagnosis was made. Uterine curettings showed atrophic endometrium and normal cervical mucosa. In June 1976 total hysterectomy, bilateral salpingo-oophorectomy and appendectomy were performed.

Case 4. G.W.; a 61-year-old, married woman (II-gravida, II-para) in menopause for 5 years. She has been receiving thyroid substitution therapy for hypofunction for the last 30 years.

Early in 1977 she presented with vaginal bleeding and on examination a mass was felt in the anterior wall of the uterus. Hysterectomy and bilateral salpingo-oophorectomy was performed.

All patients are alive and well 6, 5, 2 and 1 year respectively after hysterectomy.

Methods

Tissues from all cases were fixed in 10% neutral buffered formalin, processed in routine fashion, paraffin sections were cut at 5 µm. In addition to haematoxylin and eosin staining, sections were stained with Sudan black B, periodic acid-Schiff (PAS), diastase digestion followed by PAS (D/PAS), Bests' Carmine and van Gieson methods.

Frozen sections were also studied with a battery of lipid stains including: Oil-red-O (ORO), Sudan black B, Luxol fast blue and Baker's acid haematein method with and without pyridine extraction.

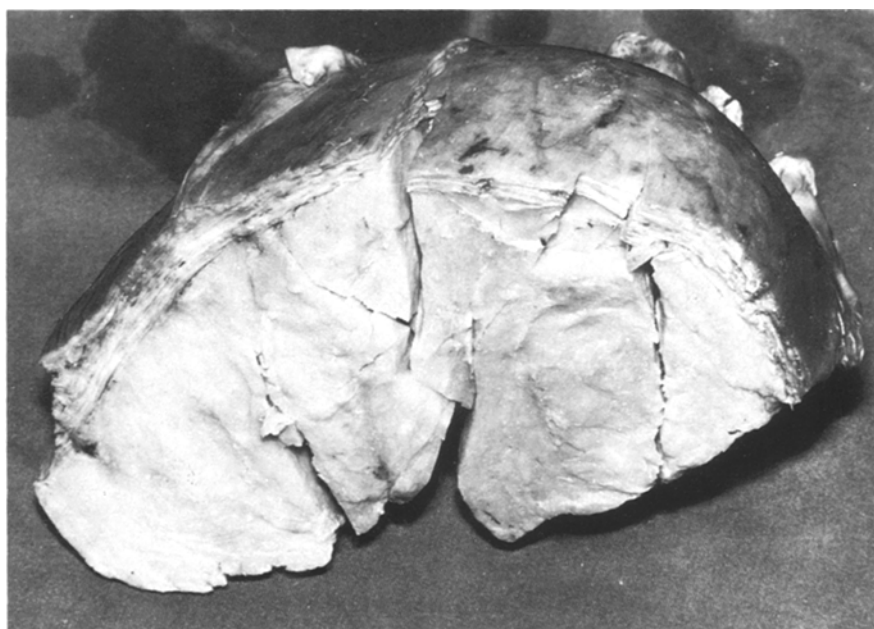
Results

Macroscopic Appearance of Tumours

Table 1 summarises the macroscopic appearance of the hysterectomy specimens. In all cases the tumour masses were well circumscribed and had a distinct rim of normal tissue around the whole circumference. In case 1 the mass was mainly brownish grey and white with yellow areas intermingled haphazardly all over the cut surface. In case 2 the yellow areas were more localised and patchy against a greyish white background. The mass in the third case was formed of coarsely lobulated, fatty tissue without any brownish grey com-

Table 1. Macroscopic characteristics of the hysterectomy specimens

Case	Site	Size	Weight	Consistency	Colour of cut surface
I (G.S.)	Intramurally in fundus	8.0 cm diam	700 g	Firm with fatty areas	Whitish yellow
II (L.L.)	Left lateral wall	8.0 cm diam	690 g	Firm with yellow resilient parts	Myoma with ordinary white colour with yellow areas
III (R.S.)	Anterior wall	18 × 14 × 14 cm	1500 g	Soft and fatty	Yellow with white streaks
IV (G.W.)	Anterior wall, subserosal in the isthmus/cervix region	7 × 4 × 6 cm	650 g	Firm	White pinkish

**Fig. 1.** The cut surface of the uterine lipoma in case 3 showing lobulated, well circumscribed adipose tissue with a pseudocapsule

ponents but only a few, very thin whitish strands in the periphery (Fig. 1). In the region of the isthmus there was a small subserosal leiomyoma measuring 1.5 cm in diameter with the typical whorled, greyish white cut surface. The mass in the 4th case was situated subserosally in the anterior part of the area between the isthmus and cervical canal. The cut surface of the tumour was

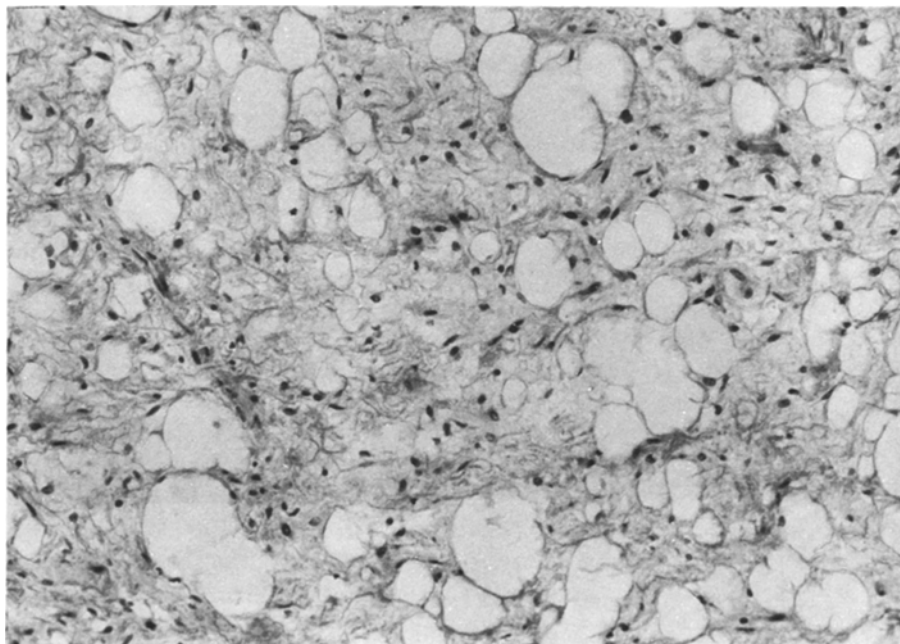


Fig. 2. Low power field from case 1 showing adipose tissue diffusely inter-mingled with the leiomyomatous structures, H & E, $\times 150$

whorled, greyish pink and firm. No necrosis or myxomatous change was noted in any of these four tumours.

The Histological Appearance of the Tumours

Section from cases 1 and 4 showed a rather compact fibro-leiomyomatous tissue admixed with irregularly arranged aggregates of adipose tissue (Figs. 2 and 3). The whole mass was richly supplied by thin-walled blood vessels and in places there was round cell infiltrate composed mainly of lymphocytes, a few plasma cells, many eosinophil leucocytes, histiocytes and some mast cells. This infiltrate was mainly around small blood vessels.

The endometrium in case 1 showed normal proliferative glands. Apart from the tumour the myometrium did not show any other abnormality. The cervix showed moderate chronic cervicitis with retention cysts and areas of reserve cell hyperplasia. Both tubes were normal and both ovaries were atrophic. The endometrium in case 4 showed postmenopausal atrophy and the cervix, tubes and ovaries were normal.

Sections from the second case showed a completely different picture. Parts of the tumour were typically those of a leiomyoma with focal hyaline degeneration and hyalinized fibrous tissue but no fatty tissue at all. Other areas were formed mainly of adipose tissue mixed in places with strands of fibrous tissue and smooth muscle (Fig. 4). In both the leiomyomatous and lipomatous parts

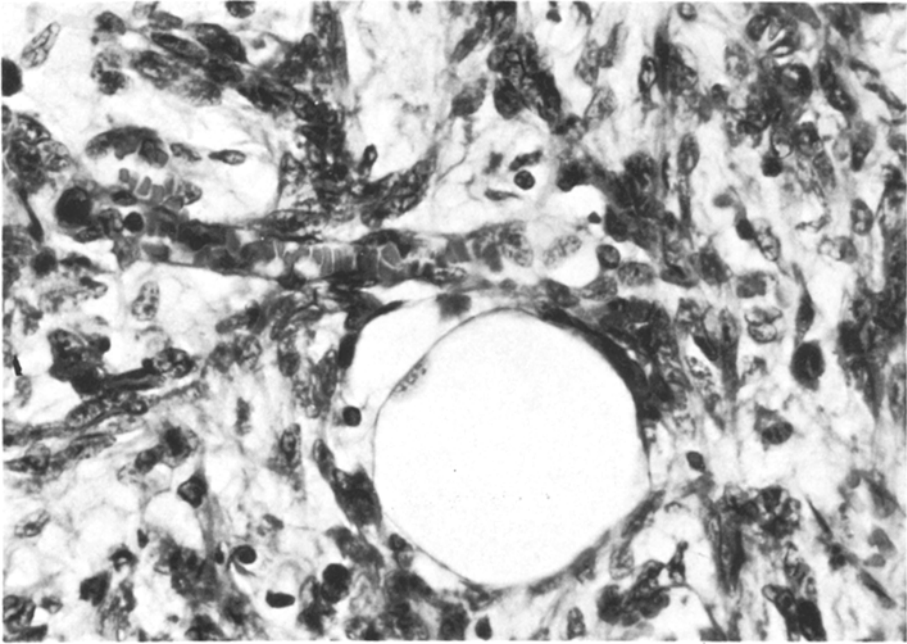


Fig. 3. Higher magnification of the diffuse lipomatosis in a leiomyoma from case 4, showing a single fat cell with the surrounding tissue rich with capillaries, lymphocytes, plasma cells and mast cells, H & E, $\times 570$

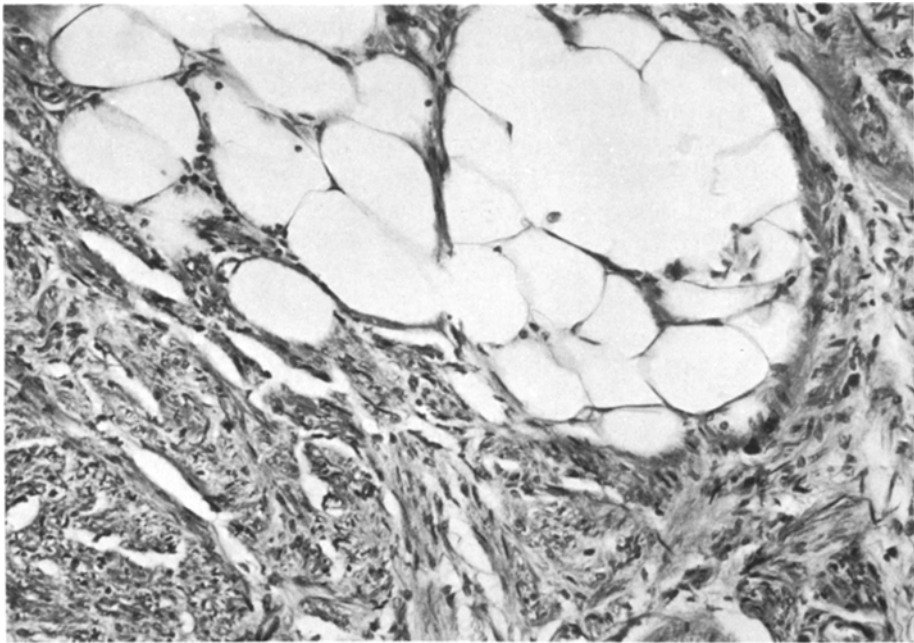


Fig. 4. Circumscribed lipomatosis in a leiomyoma from case 2; showing fairly well circumscribed fatty tissue surrounded by bundles of smooth muscle. H & E, $\times 225$

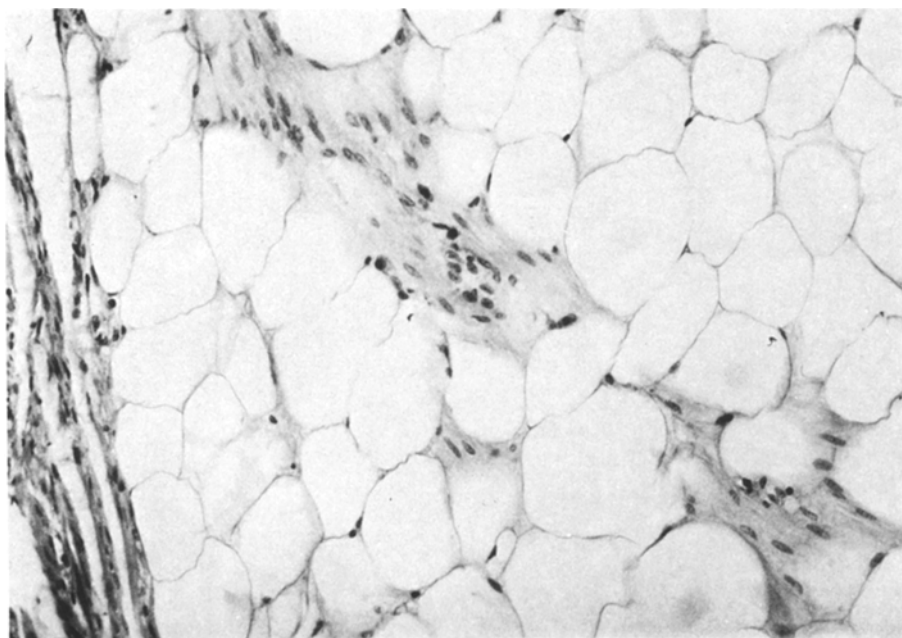


Fig. 5. The uterine lipoma of case 3 showing encapsulated adipose tissue with some strands of smooth muscle fibers in the periphery. H & E, $\times 225$

of the growth there was perivascular cell infiltrate more marked in the adipose areas. The endometrial glands were of normal proliferative type.

The third case showed a still different picture from the other three cases. The mass was formed mainly of adipose tissue with only very little smooth muscle and fibrous tissue strands scattered irregularly on the surface of the tumour between groups of fat cells (Fig. 5). The tumour was well circumscribed and outlined by a capsule of hyalinized fibrous tissue with an underlying layer of smooth muscle. The adipose tissue was rich in thin blood vessels and contained focal inflammatory cell infiltrate as in the other three cases, although this was less marked. The muscle fibres in the lipomatous growth were seen mainly in its periphery and became scanty on approaching the center, from which they were absent. The small subserosal leiomyoma in the isthmus did not show any adipose tissue.

Histochemical Studies of the Tumour

Table 2 summaries the results of staining of the tumours from the four cases with special histochemical lipid methods. All tumours proved to contain neutral lipids but case 3 contained significant amounts of Sudan black B positive material in frozen sections only. Sudan black B stains phospholipids, glycolipids and all hydrophobic unsaturated lipids.

Table 2. Lipid histochemical studies of the reported cases

Method	Type of fat	Result			
		Case 1	Case 2	Case 3	Case 4
1. Oil-Red-O	Neutral fats	Pos.	Pos.	Pos.	Pos.
2. Sudan black B	Phospholipids	Neg.	Neg.	Pos. (frozen sections) Neg. (paraffin sections)	Neg.
3. Copper phthalocyanin (luxol fast blue)	Phospholipids (myelin and other hydrophilic lipids)	Neg.	Neg.	Neg.	Neg.
4. Baker's Acid Hematein method	Phospholipids (Lecithin and sphingomyelin)	Neg.	Neg.	Neg.	Neg.
5. Diastase/PAS	Glycolipids	Neg.	Neg.	Neg.	Neg.

Discussion

Table 3 summarises the clinical data and the histological findings of 21 cases of the so-called lipoma of the uterus, reported in the literature between 1965 and 1976. Earlier literature was efficiently reviewed by Barbanti-Silva (1966). In our laboratory 1959 cases of uterine leiomyoma were diagnosed during the period of study and thus the incidence of these lipomatous lesions is 0.20%. The incidence of such lesions as reported in the literature varies from 0.03% as stated by Robertson and Barber (1953) to 0.12% in the series studied by Salm (1973). However, our impression is that these lesions are more frequent than actually reported as previously suggested by Jacobs et al. (1965). The low incidence could be attributed to the fact that the lipomatous change is not always fully manifested or does not affect large areas of the leiomyoma and is therefore not easily spotted macroscopically.

Some workers have reported the association of lipomatous change of the uterus with polypi (Vandory, 1969; Salm, 1973), adenocarcinoma or adenoacanthoma (Tlolká-Pluszezyk, 1968) as well as cervical cancer (Poniatowska, 1965). In our four cases the lesions were only accompanied by leiomyoma.

As in earlier reports the patients in the present series were in late middle age or older (Brandfuss, 1955; Salm, 1973). Two of the patients were unmarried and nulliparous. The third was V-gravida, IV-para and the fourth II-gravida, II-para. The first patient was completely asymptomatic and the enlarged uterus was discovered on a routine examination. In the second patient, pain in the left iliac fossa was the initial symptom and a uterine tumour was discovered on vaginal examination. In the third and fourth cases the patient presented with long-standing vaginal bleeding and enlarged uterus. This is in complete

Table 3. Reported cases of uterine lipoma 1965–1976

Author/Year	Age (Year)	Uterus	Lipomas		Associated disease	Amount of muscle tumour fibres in the mass
			site	size		
Poniatowska, 1965	60	—	Fundus	5 cm in diameter	Cervical ca.	None – lipoma
	63	—	All corpus	18 × 24 × 26 cm	Leiomyoma	None – lipoma
Bouda, 1965	61	14 cm in diameter	Back wall	10 cm in diameter	Leiomyoma	None – lipoma
Carli, 1966	45	—	“voluminous”	“voluminous”	—	Large
	43	—	“voluminous”	“voluminous”	—	Large
Gentili et al., 1967	61	1800 g	Fundus	20 × 18 cm	—	Moderate
Tlolká-Pluszczyk et al., 1968	59	13 × 6 × 7 cm	Corpus	5 × 3 cm	Endometrial adeno- carcinoma	Small
Vandora et al., 1969	66	330 g	Fundus	“small mandarine”	Polyps	None – lipoma
Cognat et al., 1969	63	“small melon”	Corpus	—	—	None – fibro lipoma
Krausová, 1970	57	2020 g	Corpus	15 cm in diameter	—	Small
Bhaskaran, 1972	55	small 8 × 4 cm	Corpus, lateral wall	4.5 cm in diameter	Cervicitis	None – lipoma
Salm, 1973	80	small, 105 g	Fundus	4 cm in diameter	—	Moderate
	87	11 cm, 170 g	Lat. wall	2 cm in diameter	—	Small
	71	Small, 100 g	Fundus	2.5 × 1.5 cm	Endomet. Fibroids	Small
	32	—	Pedunculated cervical polyps	4 × 3.5 × 2.5 cm, 21 g	adenoca.	Large
	64	1100 g	Post. wall	13 × 12 × 11 cm	Fibroids	Some
	88	Small	Left corner	3 × 2 cm	—	Some
	84	1100 g	Ant. wall corpus	3.5 × 3 × 2.5 cm	Mult. fibroids + endomet. polyp.	Large
Chengal, 1974	60	12 cm	Corpus	6 × 5 cm	—	None – lipoma
Meinhof et al., 1975	48	“child head” 7 cm	Central	—	Myoma	Small to large
Tureczuk-Bierla, 1976	63	—	Central	7 cm diameter	Fibrothecoma of the ovary	Lipoma, small at periphery

agreement with the generally accepted mode of presentation which simulates that of ordinary uterine fibroids (Salm, 1973; Brandfass and Everts-Suarez, 1955).

Three out of four women had gall bladder disease with cholelithiasis and cholecystectomy was performed in cases one and two. In the third case, during the hysterectomy a stone was palpated in the gall bladder. All four women were noticed to be overweight for their age and height but chemical analysis did not reveal hypercholesterolaemia or other abnormality of fat metabolism. A search of the available literature did not reveal a similar association of lipoma or lipomatous change of a leiomyoma with gall bladder disease.

Both macroscopically and microscopically our third case fits the description of a pure lipoma of the myometrium (uterine lipoma) whereas the three other cases represent lipomatous transformation or metamorphosis in pre-existing leiomyoma. We reserve the term "diffuse lipomatosis in a myoma" for the picture described in the first and fourth cases. The second case shows a more localised fatty aggregation for which we find the term "circumscribed lipomatosis in a myoma" most suitable. Adipose tissue, whether diffuse or circumscribed and in a myoma or in the myometrium, contained rather thin walled blood vessels and slight focal infiltration by lymphocytes, plasma cells, histiocytes and mast cells. Smooth muscle fibres were seen admixed with the lipomatous elements in both the diffuse and circumscribed lipomatosis in myomas but not in the uterine lipoma. In this case the muscle fibres were seen in the periphery as if they were lying in the pseudocapsule of the tumour, but were absent centrally. The presence of mast cells in these lipomatous structures has been previously described (Jacobs et al., 1969) but its significance remains undetermined.

Histochemical analysis of material from all four cases showed that three of them contained neutral fat only but that the uterine lipoma contained Sudan black B positive material in frozen section in addition, which may reflect the presence of phospholipids. Angervall et al. (1965) studied the lipid content of lipomata chemically and found that they contain neutral fat with minimal amounts of cholesterol (0.02–0.05%) and phospholipids (0.11–0.28%).

The origin of these lipomatous lesions of the uterus has been the subject of much speculation. Brandfass and Everts-Suarez (1955) summarised the various theories concerning the histogenesis of such lesions, suggesting the following as possible alternatives: misplaced embryonic fat cells, metaplasia of muscle or connective tissue cells into fat cells, lipocytic differentiation of a specific primitive connective tissue cell, perivascular fat cells accompanying the blood vessels into the uterus, inclusion of fat cells into the uterine wall during surgery or fatty infiltration or degeneration of connective tissue in the uterus. They favoured origin from misplaced embryonic cells, or metaplasia of muscle or connective-tissue cells into fat cells. The fact that smooth muscle fibres in leiomyoma (Linder and Gather, 1965) and in arteriosclerotic lesions (Bendit and Bendit, 1973) are monoclonal and the presence of neutral fat in uterine muscle in toxæmia of pregnancy (Haust et al., 1977) and atheromatous plaques (Gear and Haust, 1972; Bendit and Bendit, 1973) led us to consider fatty metamorphosis of the smooth muscle cells of leiomyomata as a possible aetiological factor

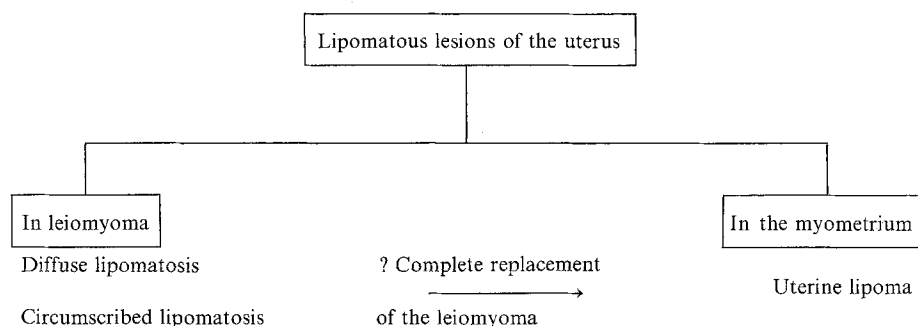


Fig. 6. Schematic representation of the evolution of the lipomatous lesions of the uterus

in the formation of adipose tissue. It is also possible that if this process continues it might lead to a complete replacement of leiomyoma by fat cells, thus forming the uterine lipoma. Whether fat metamorphosis or fat metaplasia occurs exclusively in smooth muscle cells of leiomyomata or also in the cells of ordinary myometrium is a matter for further studies. Haust et al. (1977) reported fat metamorphosis in toxæmia of pregnancy and suggested that this could be caused by hypoxia. In our three cases of localised and diffuse lipomatosis the fat cell aggregates were irregularly distributed. Furthermore, those aggregates were seen both near to blood vessels and far from them. It is thus difficult to accept the theory of hypoxia as the sole causative factor in fatty metamorphosis although it is accepted that ischaemia and necrosis are common features in leiomyomata.

It seems that once the metaplastic or metamorphic process is completed the newly formed fat cells may take one of three pathways (Fig. 6). They may remain dormant and become admixed with the preexistent fibroleiomyomatous structures, forming diffuse lipomatosis in a leiomyoma. The fat cells can also multiply in a more localised manner and partly replace the fibroleiomyomatous elements to form circumscribed lipomatosis in a leiomyoma. In the fully developed uterine lipoma it is difficult to state whether the lesion originally arose in a leiomyoma and eventually replaced it completely, or developed *de novo* in the myometrium itself.

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