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Lipogranulomatosis Circumscripta (Panniculitis Non Suppurativa)

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Summary. Four cases of nodular lipogranulomas in the breast, the arms and in the omentum are discussed.

Nodular lipogranulomas develop from single fat cells, the fat of which is enclosed and phagocytized by lipophages. The small areas grow and become confluent into larger granulomas, which become scars by the formation of reticulin fibers. The rosette-like pattern, the primary degenerative alteration of the fat cells and the progression of the lesion all suggest insufficient blood supply. Inflammation is secondary and appears only occasionally.

Key words: Lipogranulomatosis – Panniculitis – Weber – Christian – syndrome – Rothmann – Makai – syndrome

Circumscribed nodular necroses of the fat tissue are called Rothmann-Makai-Syndrome when they appear without general symptoms, and Pfeifer-Weber-Christian-Disease when combined with fever and other clinical symptoms. They are move frequent than described in the very few reports in German medical literature (Schulz et al. 1972). The Anglo-Saxon literature contains several observations and in Japan 135 cases were reported between 1951 and 1972 (Matsukake et al. 1973). Knowledge of the diseases is based on the descriptions of Pfeifer (Germany 1892), followed 30 years later by the American authors Weber and Christian, who completed the clinical picture.

The clinical significance of focal necrosis of fat tissue consists in its misinterpretation, as it often develops in the breast it may be operated on as carcinoma (Coren et al. 1974). Actually these local processes have a spontaneous tendency to heal after weeks or months forming a subcutaneous scar.

The clinical problem is the episodic progress of the disease which relapses, in some cases over years, forming new nodules with new localisations.

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Other than breasts (Bässler 1978; Leonhardt 1961; Borrie 1971; Oppermann et al. 1964; Fischer 1961) there are concentrations other regions, e.g. the extremities (Pfeifer 1892; Makai 1928; Lever 1967) the trunck, (Moschos and Palimeris 1976) and in the fat tissue of inner organs (Schulz et al. 1972; Leonhardt 1928; Matsukake et al. (1973); Mostofi and Engleman 1947). Christian (1928), as well as Moschos and Engleman 1947 depicted the episodic character especially, they were able to observe up to ten attacks during long periods which were accompanied by fever, heavy general symptoms and development of new nodes. Doerr et al. (1971) published an unusual case in which there existed many subcutaneous nodes as well as lung focuses, the histological analysis of which revealed partial granulomas, and tumor like reticulosis. Examination of enzymes showed a specific pattern of tumor which led the authors to the opinion that the changes began as a panniculitis and continued as a tumor.

During the time period of a single year we had the opportunity to explore histologically 4 separate cases, which had been surgically operated on under the suspicion of being malignant.

Case 1

H.J., a 54 year old female with diabetes, hypertension (RR 200/120 mm Hg) and obesity. She had been suffering for weeks with 2 nodules in her right breast and 1 in her left. Clinically, there was reddening and venous dilatation of the skin on the nodules, which were firm in consistancy; the skin being easily shiftable. Mammography revealed the suspicion of carcinoma and an excision was therefore recommended.

For histological examination there was removed a walnut-sized piece of tissue from the left breast, as well as a some what larger piece from the right, these revealed tiny white spots in the form of lime-splashes.

Case 2

M.R., a 51 year old female with obesity and hypertension (220/130 mm Hg). Previously, a tumor had been removed from her right breast. Histological: fat tissue including focal necrosis. For a number of weeks she had noticed the development of a new node in the right breast; it appeared firm and was not painful. Hospitalization was recommended in order to investigate possible malignancy. There appeared to be no fever or other general symptoms. The exision of the tumor was not followed by complications.

Two years later another nodule was discovered in the same breast, localized more medially in the voluminous fat. This nodule revealed only local symptoms and was removed without complication. The fatty tissue showed tiny white nodes, including a number of cysts (the largest being about pea-size) filled with a white oily fluid.

Case 3

K.H.P., a 37 year old male, noticed after about 3 weeks the growth of a painless tumor in his left upper arm, he had suffered from no previous trauma. Clinical exploration led to the discovery of a circumscribed infiltration of the skin with a slight reddening of the upper scaly epidermis. The extricated tumor was localized in the subcutaneous tissue. The wound healed without irritation or recurrence. Some nodular ping-pong ball sized tissue pieces were sent for further examination, revealing irregular gray-white confluent spots each as large as peas.

Case 4

A.B., a 69 year old male, suffering for a number of weeks from intermittent abdominal pain and nodular resistance near the navel. A diagnostic x-ray was performed as there was suspicion of the presence of a tumor in the transverse colon. Laparotomy demonstrated indurated plates

of the omentum and concretions with colon compression, however no tumor was found. Pancreatitis was then suspected. A cherry-sized yellow sprinkled, very firm piece of the omentum was excised for histological exploration.

Histological Examinations

In all the above cases there were tiny scattered, partially confluent foci which could be described as miliary granulomas. Frequently they were arranged in garlands with a central complex of unchanged fat cells surrounded by a circle of small nodules (Fig. 1). These foci showed different stages of lipophagocytosis with large histiocytes or macrophages, which invaded the fat cells from the periphery (Fig. 2a–c). First they grew along the membrane of the cell until they enclosed the reduced drop of fat (Fig. 2d, e). The structure of these drops resembled a honeycomb pattern. Later on these cells fill the whole lumen. Polynuclear giant cells of Tuton type appeared (Fig. 3), the membrane of the fat cells being well preserved, as proved by fiber staining (Gomori) (Fig. 2f, g). Necrosis of fat cells similar to those of pancreatitis were never discovered.

In a later stage reticulin fibers appeared in the fat cells. There grew in number and size until they formed a fine network (Fig. 2g). The orininal membranes of the cells were still identifable at this stage, later they became emeshed in the continuously condensing granuloma, until the picture of granuloma was complete.

In those foci the alteration of neighbouring fat cells was not developing at the same rate. There was early cell proliferation and a progressed fibrosis, which leads to the conclusion that they must be of different age. During

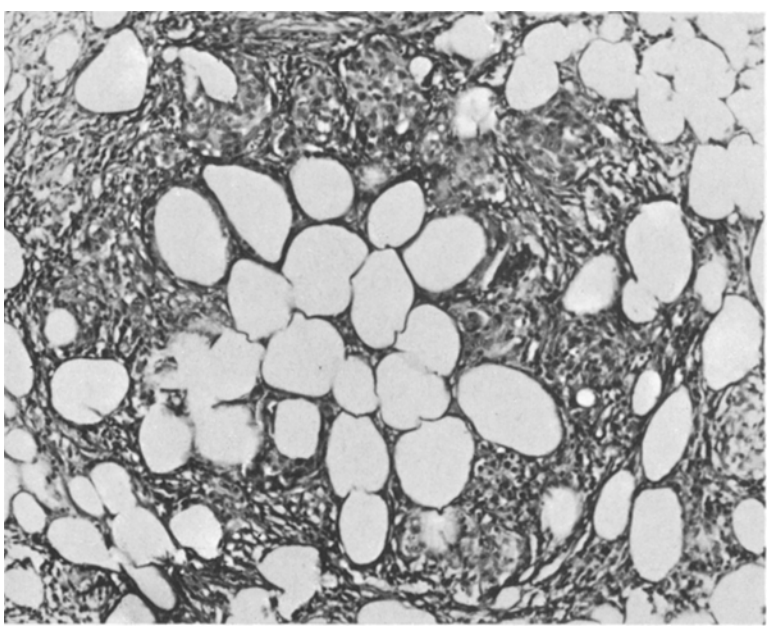

Fig. 1. Lipogranuloma with a rosette-like pattern. Haem. + Eos. × 100

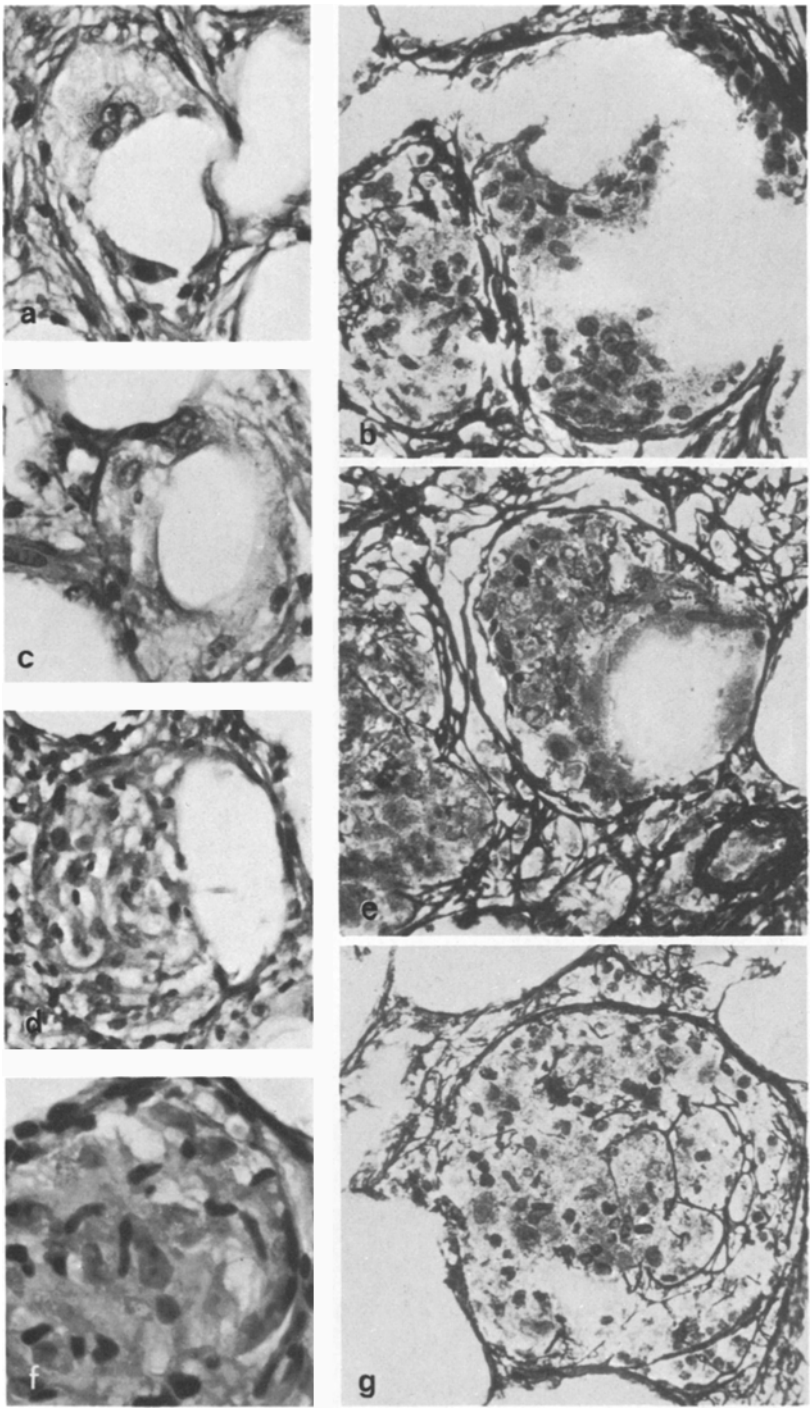

Fig. 2a–g. Development of a lipogranuloma in the fat tissue (**a**) beginning of a cell proliferation at the membrane and growing into the lumen. Haem. + Eos. × 300. **b** Gomori. × 300. **c** Inclusion of the remaining fat drop by circular cell proliferation. Haem. + Eos. × 360. **d** Half moon-like proliferation of lipophages. Haem. + Eos. × 240. **e** Preserved contour of the fat cell. Gomori. × 300. **f** Obliteration of the fat cell by lipophages. Haem. + Eos. × 360. **g** Development of tiny reticulin fibers. Gomori. × 300

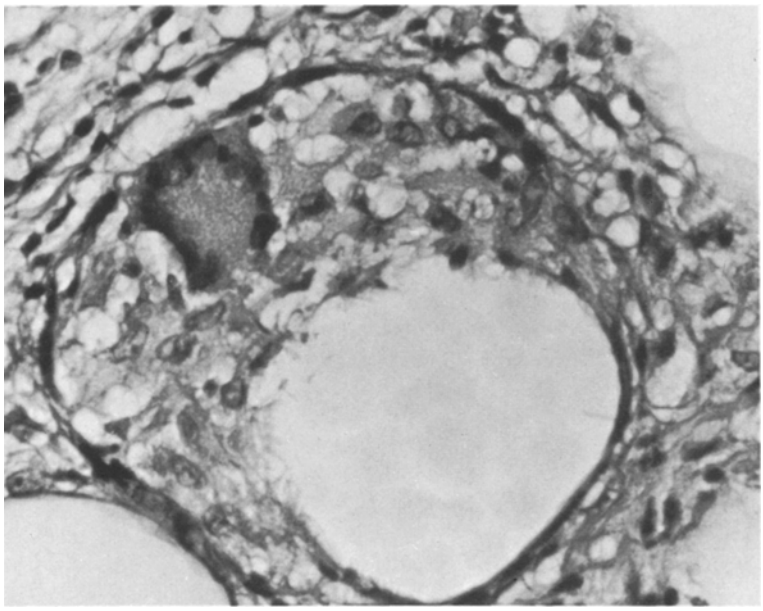

Fig. 3. Granuloma with lipophages and giant cell of Tuton type enclosing a fat drop. Haem.+ Eos. ×380

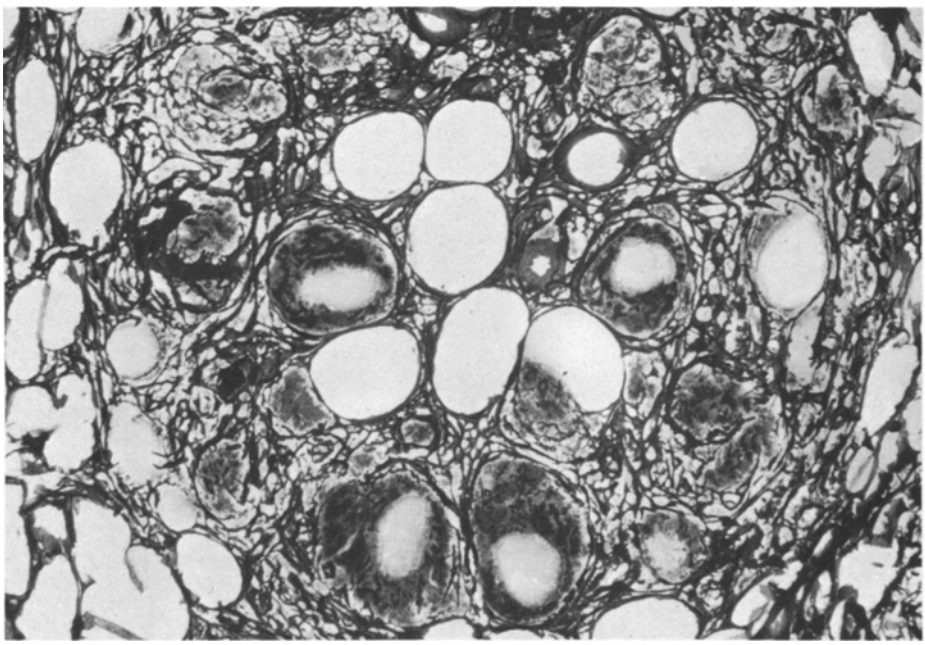

Fig. 4. Lipophagic granulomas of different age. In the center younger stages with enclosed fat drops, surrounded by reticulin fibers. Gomori. ×100

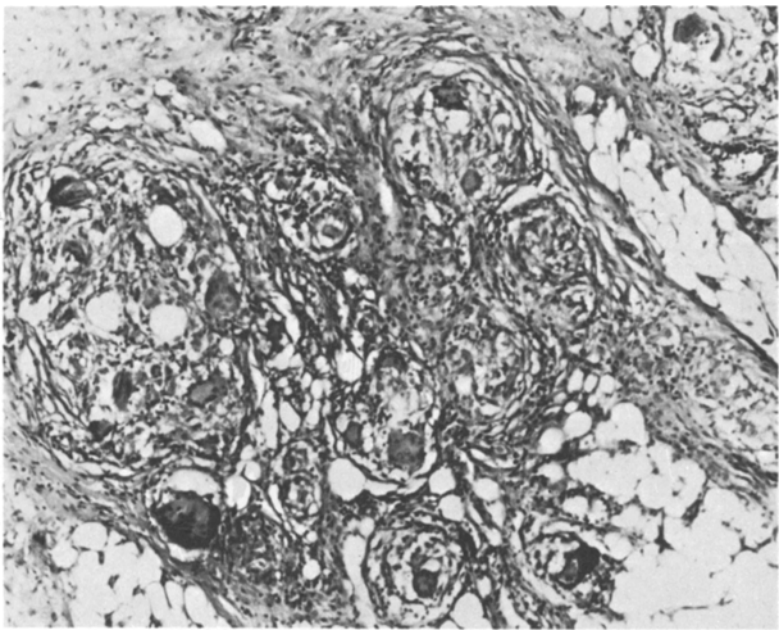

Fig. 5. "Tuberculoid" granuloma with lipophages and giant cells of Tuton type. Haem. + Eos. × 70

the development of the granuloma leukocytes, lymphocytes and plasma cells could be occasionally found. This could be interpretated as an accompanying inflammation, because the granulomas were already more or less developed. In very early stages there were no leukocytes at all. (Fig. 2). The nodules containing more reticulin fibers, which we would say are the older foci, showed a tendency to be confluent, forming larger macroscopically visible granulomas, similar to a tuberculoid pattern so that sarcoidosis had to be considered in the differential diagnoses. (Fig. 5).

Discussion

Although the existence of lipogranulomatosis has been known for sometime it remains a puzeling disease. There exist two clinical variations with identical morphology which progress without any affect on the general status (Rothmann-Makai-Syndrome) or which occur with the development of isolated, demarcarted nodes combined with general symptoms such as fever and a reduced general feeling of well-being. Occasionally there are relapsing attacks (Pfeifer-Weber-Christian-Syndrom). In Anglo-saxon medical literature the changes are called panniculitis nonsuppurativa since Weber (1925) and Christian (1928) who inferred an inflammatory etiology from the clinical symptoms. We would prefer the term lipogranulomatosis, taking the specific morphology into consideration.

In our examples the clinical findings are nodular indurations in fat under the skin with local redness and teleangiectasies, without further symptoms.

The histological changes correspond to lipophagic granulomas with proliferation of histiocytes, giant cells partially of Tuton-type and – when the foci are in early stage – with moderate evidence of inflammation.

Contrary to the clinical impression, the nodes are not, at least in the beginning compact, but consist of many microscopically tiny nodules, which later on merge. Discreet nodules remain. The granulomas occupy the fat tissue as a network.

The etiology is unknown. Earlier experiments with bacteriological culture (Christian 1928) were negative. Rheumatic factors (Leonhardt 1968), allergic-hyperergic reactions (Schulz et al. 1972), autoimmune processes (Leonhardt 1968; Oppermann et al. 1964) were taken into consideration and finally vascular diseases were considered, but none of these possibilities was considered to be a sufficient explanation. Occasionally our cases revealed cellular reactions within the small blood vessels, however they were of secondary type.

It is noteworthy that the foci prefer to grow in the fat of the breasts, trunk and thighs. All our patients suffered from obesity and were in period of life when fat deposits usually enlarge. Fat tissue is poorly vascularized, its progressive enlargment must result in disproportion between tissue and nutrition, i.e. a vascular deficiency arises. Because of its bradytrophia necrosis will not develop. Even in giant lipomas necrosis is not seen, although the preconditions are surely existant (comparable with large myomatas or other tumors). Our cases with lipogranulomatosis also revealed no necrotic fat cells, but structural cell alterations with net-like changes of the fat substance. Obviously the fat undergoes chemical transformation when insufficiently supplied with blood. Metabolites are produced, which induce cell proliferation, predominantly histiocytes, as is known from the development of tuberculoid granulomas.

These cell proliferations grow into the large fat cells, as can be identified by the still existing cell membranes; they there reabsorbe fat. In this manner foam cells and fat loaden giant cells arise, the well known pattern of lipophagic granuloma.

The dispersion of the granulomas in form of microfoci is caused by poor blood supply. The pattern is the same as that of microangiopathies of the subcutis, however, in our observations the alterations of blood vessels are not the cause, but the consequence of the changes. Later on the nodules join, this explains the clinical findings. In further stages new fibers continue growing in the granulomas, the process then heals, leaving a small scar.

Lever (1967) reported that the beginning of the process is characterized by a leucocytic stage of such a short duration, that it could scarcely be observed. Schnyder (1979) adopts this theory, but shows a figure of a fresh "steatonecrosis" with so-called "Wucheratrophie" without leucocytes. Our histological observations always show degenerative alteration of the fat cells at the beginning, which induces a resorption by histiocytes and giant cells. Leucocytes and other inflammatory cells are – when present – of minor importance. This finding is independent of the age of the process, we were able to observe new changes without leucocytes in progredient granulomas.

Prevous authors (Rothman 1894, Pfeifer 1892) did not lend particular importance to inflammation. The structural development of the lipogranulomas discriminates this entity from calcinosis lipogranulomatosa (Teutschländer 1949), defined as a Lipothesaurismosis with primary deposits of cholesterol followed by nodular calcification (Schnyder 1979).

If our opinion of the genesis is correct there is no need for further investigation of potential inflammatory causes, of bacteriological, rheumatic or other origin. Different stages of progression within the same focus contradict a singular event chemical or traumatic cause. Finally, the uneventful course of healing, leaving only a small scar points to moderate damage, which might be supposed to be due to poor blood supply. The disease could be integrated into the group of changes due to hypoxia.

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