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Review Article

Myospherulosis ☆

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ABSTRACT

Myospherulosis is a rare tumor caused by interaction of extravasated erythrocytes and exogenous or endogenous lipids. Fifty-nine articles presented 181 patients with myospherulosis since first description in 1969. Myospherulosis seems to occur in any age and in any part of the body; however, most frequent sites are paranasal sinus and subcutaneous tissue. In most cases, exogenous lipids from postoperative packing are damaging the erythrocytes, but also spontaneous cases are described. Diagnosis is made by histology but can be already suggested by radiographic imaging. Differential diagnoses include infections by fungi or algae due to histopathologic similarity. Besides that, radiographic imaging and morphology can wrongly be interpreted as carcinomas, metastases, osteofibrosis, or echinococcosis. Myospherulosis is a benign process, with symptoms deriving from the space occupying character and surgical excision can bring cure. We discuss the clinical presentation, diagnosis, and treatment and provide a systematic review of the literature on myospherulosis.

1. Introduction

Myospherulosis is a rare interaction of extravasated erythrocytes and lipids, forming histologic typical saccular parent bodies containing variable numbers of approximately 4- to 7-μm large spherules [1,2]. In most cases, myospherulosis is caused by iatrogenic exposure to petroleum-based material; however, rare cases without exogenic lipid exposure have been described [3–9]. Several cases have been sporadically reported, most frequently in the paranasal sinus but also in other parts of the body. We describe clinical appearance including macroscopic and microscopic findings as well as etiopathogenesis and epidemiology of this rare disease. We report the published knowledge of basic research, clinical case reports, and information crucial for optimized diagnosis, including possible differential diagnosis.

2. Search strategy and selection criteria

A literature search was performed including the databases of the Web of Science (1945-present), Current Contents Connect (1998-present), BIOSIS Citation Index (1926-present), BIOSIS Previews (1926-present), and MEDLINE (1950-present) using the key words myospherulosis, spherulocytosis, and spherulocystic disease. Furthermore, bibliographies of published literature on myospherulosis were searched. All articles were screened, and articles describing at least 1 human case of myospherulosis were included. The search was carried out without language restriction. The last search date was May 5, 2012.

3. Discussion

Myospherulosis was first described by McClatchie et al in 1969 [10]. They reported 7 cases from Kenya with unusual soft tissue nodules and named it myospherulosis because some of their cases involved the muscles (myo) and histology of all cases showed characteristic spherules. Another name for this disease—subcutaneous spherulocystic disease—was suggested by Hutt et al [11] in 1971 because none of his cases involved muscles. Although this would be the more precise term, myospherulosis (seldom spherulocytosis) is more common.

For almost 10 years, the origin of myospherulosis has been a matter of debate [12,13]. Initially, McClatchie et al [10] assumed "that this disease agent may spend only part of its life cycle in the human being or is perhaps a parasite which does not normally attack human beings." In addition, endosporulating fungi were taken into account due to histopathologic similarity [10]. In 1977, Kyriakos [14] was the first who suggested an iatrogenic etiology and reported 16 cases of patients with myospherulosis following ear, nose, and throat surgery with wound packing using gauze impregnated with petrolatum and tetracycline ointment. This theory was supported by De Schryver-Kecskemeti and Kyriakos in animal experiments and the pathogenesis of the disease was finally confirmed as erythrocytes damaged by lipid material by the experimental formation of saccules by incubation of erythrocytes with lanoline or petrolatum in vitro [2,15–18]. Travis et

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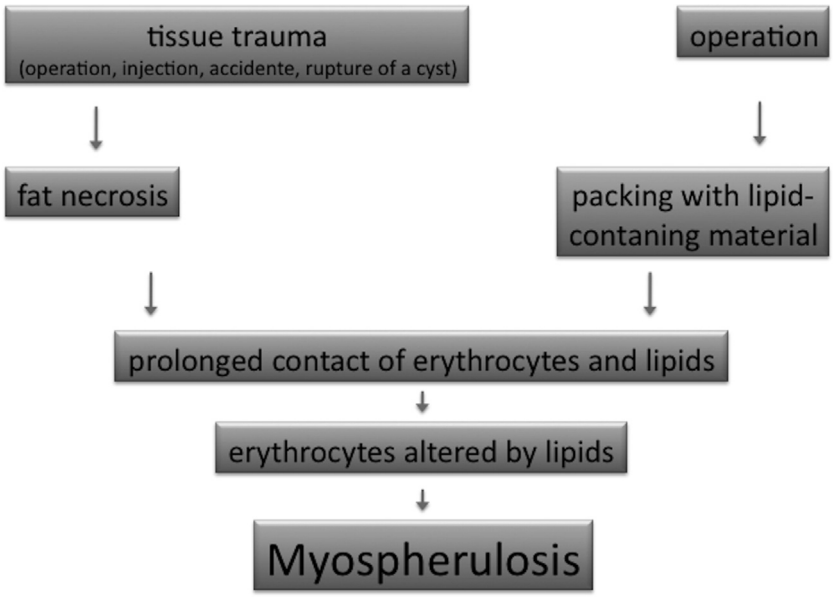

Fig. 1. Schematic diagram of pathogenesis of myospherulosis modified according to Nissen RL [39].

al [19] and Shimada et al [20] confirmed the presence of damaged erythrocytes by immunostaining for hemoglobin level. Therefore, myospherulosis is a foreign body–like interaction of erythrocytes and lipid containing material where the oily material and the extravasated erythrocytes constitute an emulsion resulting in the degeneration of erythrocytes. The damaged erythrocytes are subsequently enclosed by a lipid membrane, and the saccular structures are phagocytosed by histiocytes as part of the lipogranulomatous reaction (Fig. 1).

Histologically, myospherulosis is characterized by saccular structures (parent bodies), which contain numerous 4- to 7-μm empty spherules (endo bodies) (Fig. 2) [1,2]. Bremner first described this picture as "partly filled bags of marbles" [10]. These parent- and endo bodies are often surrounded by a foreign body–type reaction. Different stains, including Masson trichrome (Fig. 3), Giemsa, Papanicolaou (Fig. 4), and alizarin red S for hemoglobin, are typically positive in myospherulosis [20]. Immunohistochemical investigations display positivity for hemoglobin (glycophorin A, glycophorin C, carbonic anhydrase 1, agglutinin-1), peroxidase, and lipofuscin as a correlate of erythrocytes altered by a foreign substance [1,2,4,19–21].

Macroscopically, myospherulosis is characterized by "dilated pseudocystic spaces of varying sizes that, when numerous, give a Swiss cheese-like appearance" [21–23]. Cystic spaces are often filled with white to gray-white, light tan to dark brown, or yellowish, ointment-like material (Fig. 5) [11,14,24,25]. The lesions are usually small (few millimeters to few centimeters) but can also reach a size of more than 10 cm [9,10,25,26].

Within the last 43 years since the first description of myospherulosis, 59 case reports including 181 patients (80 male, 99 female, 2 no information) have been reported from all over the world. The age of the patients ranged from 1 to 89 years (mean, 46.5). Table 1 gives a summary of the reported cases of myospherulosis. In most cases, the lipids damaging the erythrocytes were of exogenous origin. Most described cases occurred in orthodontia due to postoperative packing with gauze impregnated with petrolatum and antibiotics. Because myospherulosis interferes with wound healing, nowadays, the usage of petroleum-based carriers has been discouraged in ear, nose, and throat surgery [64].

Other iatrogenic causes include postoperative packing in other parts of the body, intramuscular injections of antibiotics or hormones with an oily carrier, or portal vein embolization. The period between the iatrogenic lipid exposure and the diagnosis of myospherulosis varies widely and ranges from 13 days to 45 years (Table); however, incubation of erythrocytes and emulsified human fat for only 24 hours caused myospherulosis in vitro [16].

Although myospherulosis is caused most often by exogenic lipid exposure, Wheeler and McGavran [16] demonstrated as early as 1980 that emulsified human fat can also produce myospherulosis, at least in vitro. Since then, a few cases of spontaneous myospherulosis have been published [3-8,10,22,59,61]. According to these cases, local tissue lipids can be released due to an accidental or iatrogenic trauma causing necrosis of fat tissue, membranous lipodystrophy, or arise from tumors with a high lipid content such as steatocystoma multiplex or renal carcinoma [3,5-8,16,23,65]. One spontaneous case of myospherulosis in the perirenal adipose tissue has been described in a patient with immunosuppression due to chronic lymphocytic leukemia [4]. Another case reports myospherulosis in a patient immunosuppressed due to HIV infection [42].

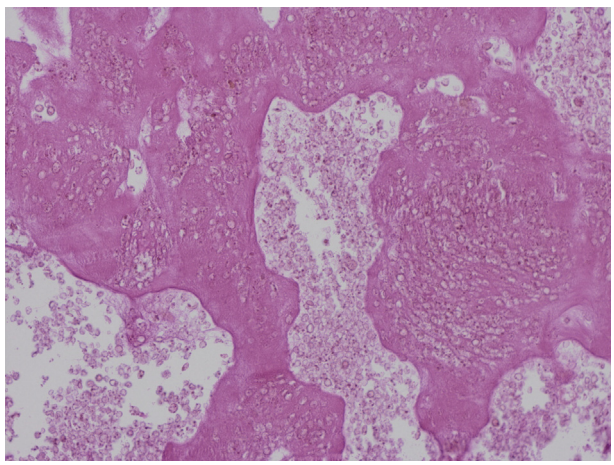

Fig. 2. Hematoxylin-eosin stain of myospherulosis, showing closely packed erythrocytes (endo bodies) within cystic spaces (parent bodies).