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Luis Requena

## Anatomy and Histology of Normal Subcutaneous Fat, Necrosis of Adipocytes, and Classification of the Panniculitides 419

Sonia Segura and Luis Requena

The panniculitides comprise a group of heterogeneous inflammatory diseases that involve the subcutaneous fat. Histopathologic study is required for the specific diagnosis of these disorders, because different panniculitides usually show the same clinical appearance, which consists of erythematous nodules on the lower extremities. The histopathologic study of panniculitis is difficult, however, because of an inadequate clinicopathologic correlation and the changing evolutive nature of the lesions. Some cutaneous lymphomas may simulate panniculitis, both from clinical and histopathologic points of view, and for that reason are included in this article despite the fact that they are not inflammatory processes but authentic lymphocytic neoplasms involving subcutaneous tissue.

## Erythema Nodosum 425

Luis Requena and Evaristo Sánchez Yus

Erythema nodosum is the most frequent clinicopathologic variant of panniculitis. The process is a cutaneous reaction that may be associated with a wide variety of disorders, including infections, sarcoidosis, rheumatologic diseases, inflammatory bowel diseases, medications, autoimmune disorders, pregnancy, and malignancies. Histopathologically, erythema nodosum is the stereotypical example of a mostly septal panniculitis with no vasculitis. The composition of the inflammatory infiltrate in the septa varies with age of the lesion. Treatment of erythema nodosum should be directed to the underlying associated condition, if identified.

## Erythema Induratum of Bazin 439

José M. Mascaró, Jr. and Eulalia Baselga

Erythema induratum of Bazin is a chronic, nodular eruption that usually occurs on the lower legs of young women. It has been regarded as a manifestation of tuberculin hypersensitivity, a type of tuberculid occurring on the legs, whereas nodular vasculitis represents the nontuberculous counterpart. The number of reports of erythema induratum of Bazin is decreasing in most developed countries in accordance with the decreased incidence of tuberculosis. The etiopathogenesis of erythema induratum of Bazin and its relation to tuberculosis are still controversial, because mycobacteria cannot be cultured from the skin lesions. Most authors currently consider erythema induratum of Bazin (nodular vasculitis) a multifactorial disorder with many different causes, tuberculosis being one of them.

**Alpha-1-Antitrypsin Deficiency Panniculitis**

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Ricardo Valverde, Belén Rosales, Francisco Javier Ortiz-de Frutos, José Luis Rodríguez-Peralto, and Pablo L. Ortiz-Romero

Alpha-1-antitrypsin deficiency is a congenital error of metabolism linked to pulmonary (emphysema) and liver (cirrhosis) disease. Since 1972, panniculitis has been associated with this deficiency, initially related to Weber-Christian syndrome and finally as a differentiated entity. Clinical manifestations typically consist of wide nodular lesions on the trunk and proximal extremities that evolve to ulceration and drainage. Histopathologically it presents as a mixed septal-lobular panniculitis pattern with some typical findings referred. Differential diagnosis from other types of panniculitis and neutrophilic dermatosis must be established. Different treatments, including tetracyclines, dapsone, and alpha-1-antitrypsin repositioning, have shown variable efficacy in controlling this disease.

**Lupus Erythematosus Panniculitis**

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Javier Fraga and Amaro García-Díez

Lupus erythematosus panniculitis is an uncommon variant of lupus erythematosus characterized by a specific involvement of the subcutaneous fat. It is a panniculitis with peculiar clinical features and histopathologically characterized by a mostly lobular panniculitis. It may appear in patients with discoid lupus erythematosus and systemic lupus erythematosus, but also as the unique manifestation of lupus erythematosus, and in the latter cases the diagnosis may be problematic. Histopathologic differential diagnosis with subcutaneous panniculitis-like T-cell lymphoma may also be extremely difficult. This article reviews the salient clinicopathologic features and treatment of lupus erythematosus panniculitis, with special emphasis on the histopathologic features.

**Pancreatic Panniculitis**

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Diana García-Romero and Francisco Vanaclocha

Pancreatic panniculitis is an uncommon complication of pancreatic disease, most frequently pancreatitis and pancreatic carcinoma. The pathogenesis of the process remains unknown, but possibly the release of pancreatic enzymes may induce permeability of the microcirculation and cause fat necrosis. Clinically, pancreatic panniculitis presents with tender, ill-defined, red-brown nodules in the lower extremities that may ulcerate and drain an oily substance and usually precedes pancreatic disease. The histopathologic picture consists of a mostly lobular panniculitis without vasculitis, with the presence of the typical ghost cells that correspond to necrotic and calcified adipocytes. Treatment should be directed at the underlying pancreatic disease.

**Infective Panniculitis**

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Yolanda Delgado-Jimenez, Javier Fraga, and Amaro García-Díez

Infective panniculitides are infections of the subcutaneous fat induced by any kind of micro-organism. They have rarely been considered as an entity within the spectrum of the panniculitis. Because of the increase in the immunosuppressive population, cutaneous infections' incidence is growing and atypical clinical presentations can be found. In this article, we analyze the etiology, clinical picture, histopathologic findings, diagnostics tools, and treatment of the more relevant infective panniculitis. We divide them according to the causative micro-organisms in bacterial, mycobacterial, fungal, and viral panniculitis.

**Traumatic Panniculitis** 481

Abelardo Moreno, Joaquim Marcoval, and Jordi Peyri

Traumatic panniculitis refers to changes in the subcutaneous fat related to physical or chemical agents. The clinical picture of traumatic panniculitis is nonspecific. Cutaneous lesions are indurated, warm, red, subcutaneous plaques or nodules not necessarily related to the intensity of the injury. The histologic picture includes fat microcysts surrounded by histiocytes, collections of foam cells, and inflammatory cells. Late lesions may show fibrosis, lipomembranous changes, or dystrophic calcic deposits. Traumatic panniculitis is usually a self-limiting disorder and requires only symptomatic treatment.

**Cold Panniculitis** 485

Alicia Quesada-Cortés, Lucía Campos-Muñoz, Rosa M. Díaz-Díaz, and Mariano Casado-Jiménez

Cold panniculitis has been described in children and young women following cold exposure. Histopathologically, cold panniculitis shows a mostly lobular panniculitis, which consists of an infiltrate of lymphocytes and histiocytes in the fat lobules. Usually, the dermis shows a superficial and deep perivascular infiltrate mostly composed of lymphocytes, with no vasculitis. Inflammation is most intense at the dermal-subcutaneous junction. Differential diagnosis of cold panniculitis should be established with subcutaneous fat necrosis of the newborn, sclerema neonatorum, poststeroid panniculitis, chilblains, and frostbites.

**Panniculitis in Children** 491

Antonio Torrelo and Angela Hernández

The panniculitides include a group of disorders of varied etiology that manifest as inflamed nodules in the subcutaneous tissue. They are rarely seen in infants and children. The panniculitides of the newborn represent a unique response of the infant's fat to different injuries, and are a specific type of panniculitis that is only seen in neonates and very young infants. These specific panniculitides of children include subcutaneous fat of the newborn, poststeroid panniculitis, sclerema neonatorum, and cold panniculitis. This article reviews in detail the specific types of panniculitis of the newborn and discusses the pediatric aspects of the panniculitis that is often seen in adults.

**Sclerosing Panniculitis** 501

Celia Requena, Onofre Sanmartín, and Luis Requena

Sclerosing panniculitis is a chronic panniculitis characterized by skin induration and hyperpigmentation of one or both legs that often occurs in patients who have venous insufficiency. The indurated plaques are often painful and the legs frequently have a characteristic "inverted wine bottle" appearance. Histopathology is characterized by mostly lobular panniculitis with necrosis of fat and without vasculitis, and in fully developed lesions by septal sclerosis and membranocystic changes. Treatment of sclerosing panniculitis includes compression therapy with graded stockings and anabolic steroids.

**Sclerosing Postirradiation Panniculitis** 505

Luis Requena and Carlos Ferrándiz

Sclerosing postirradiation panniculitis is an unusual variant of panniculitis that appears as a complication of megavoltage radiotherapy. Most patient are women

with a history of breast cancer who develop nodular lesions on the anterior chest skin several months after receiving megavoltage therapy for breast carcinoma. Sclerosing postirradiation panniculitis is an unusual cutaneous complication of megavoltage radiotherapy that should be distinguished from subcutaneous metastatic disease, cellulitis, and connective tissue diseases involving the subcutaneous fat. The differential diagnosis can be established on the basis of the characteristic histopathologic features.

### **Lipomembranous Fat Necrosis of the Subcutaneous Tissue**

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Sonia Segura and Ramon M. Pujol

Lipomembranous fat necrosis (LMFN) is a special subtype of fat necrosis characterized by the development of pseudocystic cavities lined with hyaline-crenulated membranes. This regressive degeneration or localized destruction of adipose tissue has been reported as a focal phenomenon or, rarely, as an extensive one in several pathologic conditions of the subcutaneous tissue. LMFN is frequently observed in patients who have chronic sclerotic infiltrated plaques or tender subcutaneous nodules on the lower extremities, often diagnosed as lipodermatosclerosis. There is increasing evidence that it is a morphologic feature that cannot be related to any particular clinical setting, however. Multiple local or systemic events causing a compromise in the blood supply of the subcutaneous tissue have been incriminated. The current knowledge of the different disorders associated with LMFN is reviewed. The different postulated pathogenic mechanisms leading to LMFN are also discussed.

### **Factitial Panniculitis**

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Onofre Sanmartín, Celia Requena, and Luis Requena

Factitial panniculitides are subcutaneous tissue injuries produced by external agents or actions. In most cases, factitial panniculitis is caused by self-injection of different substances. Factitial panniculitis can also appear as an iatrogenic consequence of injections of drugs or immunization agents. The clinical features of factitial panniculitis are quite variable, depending on the inciting agent. The histopathology of factitial panniculitis usually shows a pattern of an acute lobular panniculitis associated with fat necrosis and an abundant inflammatory infiltrate predominantly composed of neutrophils.

### **Subcutaneous Panniculitic-Like T-Cell Lymphoma and Other Primary Cutaneous Lymphomas with Prominent Subcutaneous Tissue Involvement**

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Fernando Gallardo and Ramon M. Pujol

The concept of subcutaneous T-cell lymphoma defines a reduced group of primary cutaneous lymphomas characterized morphologically by a prominent or exclusive subcutaneous tissue involvement. Subcutaneous panniculitic-like T-cell lymphoma is a rare subtype of primary cutaneous T-cell lymphoma clinically mimicking panniculitis. The clinical course is usually protracted with recurrent cutaneous lesions but rarely with early extracutaneous dissemination. The clinical, histopathologic, immunophenotypic, and evolutive features of this heterogeneous and rare group of primary cutaneous lymphomas are reviewed.

### **Subcutaneous Sweet Syndrome**

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Guillermo Guhl and Amaro García-Díez

Neutrophilic panniculitis encompasses a heterogeneous group of diseases histopathologically characterized by an inflammatory infiltrate in the subcutaneous fat

mainly composed of mature neutrophils. This group of panniculitides includes  $\alpha_1$ -antitrypsin deficiency, infectious panniculitis, factitious panniculitis, subcutaneous Sweet syndrome, neutrophilic/pustular panniculitis associated with rheumatoid arthritis, erythema nodosum–like lesions of Behçet disease, bowel bypass panniculitis, and iatrogenic panniculitis. This article reviews subcutaneous Sweet syndrome, which is a rare idiopathic panniculitis characterized by a dense neutrophilic infiltrate in the subcutis and is often related to hematologic malignancies. The relationship of subcutaneous Sweet syndrome and erythema nodosum is discussed as well as the differential diagnosis with other neutrophilic panniculitis.

### Subcutaneous Sarcoidosis

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Joaquim Marcoval, Abelardo Moreno, Juan Mañá, and Jordi Peyri

Subcutaneous sarcoidosis has been reported to occur in 1.4% to 6% of patients with systemic sarcoidosis. Most reported cases are in women, most often in their fifth and sixth decades, and appear as multiple, asymptomatic, hardly indurated subcutaneous nodules without changes in the overlying epidermis. The lesions are characteristically located in the upper extremities, mainly in the forearms, and usually are bilateral and asymmetric. In most cases the lesions appear at the beginning of systemic sarcoidosis and are not associated with chronic fibrotic disease. Histopathologically, sarcoidosis is characterized by noncaseating naked granulomas involving fat lobules, with minimal to no septal involvement.

### Calciphylaxis

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Esteban Daudén and María-Jesús Oñate

Calciphylaxis is defined by the presence of calcium deposits within the wall of small and medium-sized vessels. It is classically considered a life-threatening disease in patients with end-stage renal disease under dialysis. Clinically, it is characterized by the presence of painful plaques surrounded by a reticulate purpura that progresses to nonhealing ulcers, predominately in the lower limbs. It is associated with elevated parathyroid hormone levels and a dysregulation of the calcium/phosphate metabolism. In the absence of renal disease, normal parathyroid hormone levels, and calcium/phosphorus product, a good prognosis and the observation of similar calcium deposits associated with different conditions or even an epiphenomenon in diseases with well-known diagnosis leads one to consider the term calciphylaxis controversial.

### Lipodystrophy Syndromes

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Pedro Herranz, Raul de Lucas, Luis Pérez-España, and Matias Mayor

Lipodystrophy syndromes comprise a group of rare, heterogeneous disorders characterized by progressive loss of fat tissue, mainly from subcutaneous compartment and occasionally affecting visceral fat. Lipoatrophy may be partial, localized, or generalized. The latter cases are usually accompanied by metabolic-related disorders, including insulin resistance, diabetes mellitus, hyperlipemia, progressive hepatic disease and anabolic state. Treatment for lipodystrophy has increased interest in recent years because a new lipoatrophic population—patients who have HIV-associated lipodystrophy—is much more numerous than the whole number of patients affected by classic lipodystrophy entities.

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