**CASE 1**

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**Diagnosis:** Blastic Plasmacytoid Dendritic Cell Neoplasm  

**Clinical History:** 37 year old man with 10 month history of rapidly growing left arm lesion, 5 x 6 cm purplish plaque.

**Histology:** There is a dense monotonous infiltrate of atypical cells that diffusely involves the dermis and abuts the subcutaneous fat. The epidermis is spared and a Grenz zone is present. An interstitial pattern is primarily present. On high power examination the cells are medium in size and have blast like morphology, with enlarged nuclei, increased nuclear to cytoplasmic ratios, fine chromatin and prominent nucleoli. Necrosis, apoptosis and angiocentricity are not seen. By immunohistochemistry, the cells expressed CD2, CD4, CD7, CD56, TdT, and CD123, but were negative for CD3, CD5, CD8, CD30, CD34, and myeloperoxidase.

Differential diagnosis: Entities to consider in the differential diagnosis include cutaneous involvement by acute myelogenous leukemia (AML, also known as myeloid leukemia cutis or myeloid sarcoma), B or T lymphoblastic leukemia, extranodal NK/T cell lymphoma, nasal type, and a subset of high grade B cell lymphomas. The last three entities in the differential can be eliminated via staining with pan B cell markers (PAX5, CD79a), T cell markers (CD3), and EBV in situ hybridization (these studies should all be negative). The distinction between AML involving the skin and BPDCN can be difficult. However, it has been demonstrated that the combination of expression of CD4, CD56, TCL1, and CD123 is unique to BPDCN and negativity for all of these markers essentially excludes skin involvement by AML.

**References:**

Diagnosis: Mucoepidermoid carcinoma of the external auditory canal (MEC).

Clinical History: A 62-year-old man presents with a mass in the left external auditory canal. An incisional biopsy shows a primary mucoepidermoid carcinoma, confirmed by a second opinion (MGH).

Histology: here is a malignant squamous and glandular and ductal malignant neoplasm, occupying the full thickness of the dermis and extending to the edges of the specimen. The squamoid component is syncytial-like and poorly differentiated. However, no mitoses or necrotic foci are noted. The glandular component is superficial. Both PAS+D and Alcian Blue stains confirm widespread production of mucin by tumor cells. Immunoperoxidase stains are positive for CEA (ductal component); EMA, cytokeratin 7 and high-molecular weight keratin (strong and diffuse); and low-molecular weight keratin (diffuse but weak). Cytokeratin 20 is negative. Ki-67 shows very low proliferative rate, decorating less than 5% of tumor cells. This supports that the tumor is low-grade, in spite of the greater histologic anaplasia of the squamoid portion. The overall features support a modified apocrine origin, i.e., ceruminous glands, an origin also strengthened by the location of the tumor.

Discussion: The histologic features are similar to homologous tumors in the salivary glands, conjunctiva and respiratory tract. This tumor is extremely rare in the skin. Besides the ear canal, it has been described in axilla, finger, scalp (also with nevus sebaceus) and eyelid. Rare association with extramammary Paget’s disease has been described. However, after complete removal the tumor rarely recurred.

Differential Diagnosis: It should be distinguished from the more aggressive adenosquamous carcinoma, on which the glandular component is frankly anaplastic (adenocarcinoma), unlike the almost hamartomatous and often local low-grade glandular component in MEC. When the diagnosis of MEC is established near the ear canal, a first consideration is cutaneous extension of a mucoepidermoid carcinoma from the parotid or, more rarely, a metastasis of MEC elsewhere. Low-grade tumors in the conjunctiva may resemble a mucoepidermoid papilloma. Acantholytic and adenoid squamous cell carcinomas could have areas resembling this tumor.

References:
Diagnosis: Spiny keratoderma of the palms and soles

Clinical History: The patient is a 71 year old white woman with extensive cutaneous horns less than 1 mm each on the bilateral palms. Acquisition of additional clinical information revealed that the spiny projections had been present for 2 years but seemed to be worsening recently. Similar lesions were found on both soles. The patient’s past medical history was significant for a cerebral vascular accident and squamous cell carcinoma of the lung diagnosed and treated with a right lower lobectomy 4 years ago. Physical examination showed numerous scattered cutaneous horn-like spines of less than 1 mm on the bilateral palms and soles. The remainder of the mucocutaneous examination was unremarkable. Although a CT scan of the chest was performed biannually for follow up of her pulmonary squamous cell carcinoma, the cutaneous lesions sparked further concern, and a subsequent scan showed a new mass in the right lung. A biopsy of this mass showed a moderately differentiated adenocarcinoma, presumably a second primary.

Histology: Microscopic examination showed acral skin with mild epidermal acanthosis, hypergranulosis, and compact orthokeratosis. A single distinct column of parakeratosis extended from the granular layer through and above the surrounding compact orthokeratotic stratum corneum. Underlying the parakeratotic column there was hypogranulosis but no dyskeratotic, vacuolated, or pleomorphic keratinocytes. Mild solar elastosis was present in the superficial dermis.

Differential Diagnosis: The main histological differential is with porokeratosis, particularly porokeratosis palmaris et plantaris disseminata (PPPD). While the clinical appearance of scaling annular plaques with a raised ridgelike hyperkeratotic border and central hypopigmentation and atrophy is not similar to the thin hyperkeratotic filiform projections of spiny keratoderma, the histology can be easily confused. The hallmark of the porokeratoses is the cornoid lamella, which is microscopically defined by a linear column of parakeratosis that projects through the stratum corneum and has underlying keratinocyte dyskeratosis and loss of the granular layer. The presence of an intact granular layer and the absence of dyskeratotic keratinocytes beneath the parakeratotic column are the histological features which distinguish spiny keratoderma from porokeratosis. This distinction is important as basal and squamous cell carcinomas can develop at sites of PPPD, while spiny keratoderma, in the acquired form, can be a paraneoplastic phenomenon.

References:

Diagnosis: Diffuse Dermal angiomatosis associated with calciphylaxis.

Clinical History: 71-year-old diabetic, obese patient with chronic renal failure and secondary hyperparathyroidism, who presented in 2005 with an abdominal ulcer arising over the course of three months on a purpuric area. Clinical differential diagnosis at that time was calciphylaxis, cholesterol embolization, neoplasia and infection. An excisional biopsy was interpreted as showing necrobiosis lipidica with secondary *Pseudomonas Aeruginosa* infection. After surgery, she received antibiotic treatment and was well until February of 2007, when three large ulcers developed on her right thigh and abdomen. Representative sections were available for on-line study.

Histologic: In all three specimens an extensive ulceration covered by debris and polymorphonuclears could be seen. Within the underlying viable dermis was a diffuse proliferation of small vascular spaces lined by variously prominent endothelial cells, involving also fibrous septae in the subcutis. Some endothelial cells had minute intracytoplasmic lumina. Rare small vessels featured thrombi. Scattered vascular structures (mostly arterioles and small arteries) showed calcification of their walls, with subintimal fibrosis leaving markedly narrowed lumina. Some foci of bone formation and giant cell reaction were also seen. The adipose lobules had areas of necrosis and mild inflammation.

Differential Diagnosis/Discussion: Calciphylaxis, nowadays regarded as “the skin equivalent of a myocardial infarction” (1) is characterized by cutaneous ischemia and necrosis due to calcification, intimal fibroplasia and thrombosis of pannicular arterioles (2). The clinical history in our case is rather typical for calciphylaxis, most commonly - but not exclusively- affecting patients with end-stage kidney failure and secondary hyperparathyroidism. From a clinical standpoint, the differential diagnosis includes vasculitis, infection, ischemic injury and cholesterol embolization, as well as other entities. (3) Rather surprisingly, such a florid accompanying reactive vascular proliferation in the setting of calciphylaxis has only recently been reported (4). In a review of 11 biopsy-proven cases of calciphylaxis, all specimens showed some degree of diffuse proliferation of blood vessels. The histopathologic pattern of this vascular proliferation fits the diffuse dermal angiomatosis group within the cutaneous reactive angiomatoses classification put forward by Rongioletti and Rebora (5). The histopathologic differential diagnosis involves other benign and malignant vascular proliferations. The presumed pathogenesis (a response to hypoxia) is shared by other angiomatosis allegedly secondary to ischemia, either of arteriosclerotic origin (6,7) or related to iatrogenic arteriovenous fistulas (8). Since most patients with calciphylaxis present clinically at a non-ulcerated stage (9), awareness of the clinical appearance of erythematous, tender plaques due to dermal angiomatosis may help identify patients at risk for impending calciphylaxis.
References


Notes:
Diagnosis: Primary cutaneous neuroendocrine cell carcinoma (Merkel cell carcinoma) in association with Basal cell carcinoma.

Clinical History: An 88-year-old man, who was healthy, presented an ulcerated tumor with 2 cm of diameter on the glabella for months. Multiple actinic keratosis, two Basal cell and one Squamous cell carcinomas were present on his face. Regional lymphnodes were not involved. Laboratory and imaging investigations, including computed tomographic scan of the thorax, showed no involvement of internal organs, namely lung.

Histology: The histopathological examination of a broad local excision revealed an ulcerated infiltrating tumor involving entire dermis and extending into subcutis and muscle tissue. It consisted of nests and lobules of pleomorphic medium-sized cells with scanty cytoplasm and hyperchromatic nuclei. Apoptosis was very prominent and mitotic figures were numerous. There was focal perineural extension as well as presence of tumor cells in the wall of a medium vessel. There was also another tumor towards one of the edges of that lesion composed of basaloid cells arranged in small nests connected to the epidermis, and with peripheral palisading and clefting between tumor nests and adjacent stroma suggestive of Basal cell carcinoma. There was no evidence of transition between those two components. By immunohistochemistry the cells of the main tumor were positive for AE1/AE3, NSE, Synaptophysin, Chromogranin A, and were negative for CK20, CK7, EMA, CAM5.2 and thyroid transcription factor-1 (TTF-1).

Differential diagnosis: The main differential diagnosis of Merkel cell carcinoma (MCC) is with other tumors that have a small round blue cell appearance: small cell carcinoma of the lung (SCCL), lymphoma, Ewing`s tumor and metastatic neuroendocrine carcinoma from a visceral site for example lung. This separation, based on morphological criteria alone is not possible being crucial the utilization of a panel of immunohistochemical markers. MCC exhibits both epithelial and neuroendocrine differentiation with positivity for NSE, NF, Chromogranin A, Synaptophysin as well as shows perinuclear staining, either as distinctive perinuclear dot or crescent, with low molecular weight keratins, EMA and most characteristically with CK20. However 10-20% of MCC have been reported to be negative for CK20. TTF-1 is expressed in a high percentage of SCCL and not seen in MCC being a sensitive and specific marker for SCCL.

References:

Notes:
Clinical information: Male, 56 years old; periocular symmetrical yellowish macules to plaques, developing since some years; no arthralgia, no lipid abnormalities, no paraproteinemia

Diagnosis: Early necrobiotic xanthogranuloma

Clinical History:
- Elder patients (>50 years), no sexual predilection
- Yellowish disfiguring macules and plaques around eyes, in axilla, groins, elsewhere
- No serologic lipid abnormalities
- Some (not all) cases with paraproteinemia including MGUS & plasmocytoma ("paraneoplasia")
- Progressive clinical course not parallel to underlying lymphoma (indicating a collision phenomenon)

Histology:
- Bland epidermis and grenz zone
- Diffuse dermal to subcutaneous infiltrate of xanthomatized macrophages besides vacuolated and spindly cell types
- Geographical degenerated collagen with palisading macrophages
- Characteristic bizarre giant cells of foreign body type with myriads of nuclei & cholesterol clefts
- Detection of remnants of spirochetes by focus-floating microscopy

Differential diagnoses:
- Xanthogranuloma family including xanthelasma: no palisading granulomas (no "necrobiosis")
- Eruptive xanthomas: lipid anomalies & extracellular lipid

References:
CASE 7

Carlos Monteagudo

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Diagnosis: Fibrofolliculoma in Birt-Hogg-Dubé syndrome

Clinical data: A 60-year-old male with a history of spontaneous pneumothorax at age 56. Physical examination revealed several small (2-5 mm) dome-shaped skin-colored papules on the nose, cheek and neck.

Histology: Microscopic evaluation shows distorted hair follicles with few long thin anastomosing epithelial strands or cords, extending outward from the follicular epithelium into a perifollicular fibrovascular connective tissue containing variable amount of mucin.

Differential diagnosis: Birt-Hogg-Dubé syndrome (BHD) is an autosomal dominant condition, caused by germline mutations in the FLCN (folliculin) gene, and characterised by cutaneous fibrofolliculomas, multiple lung cysts, spontaneous pneumothorax, and renal cancer. Cutaneous lesions in family members can lead to diagnosis. Fibrofolliculomas (FF) and trichodiscomas (TD) in BHD and angiofibromas in tuberous sclerosis complex (TSC) have overlapping features. Histologically, the coarser quality of the collagenous stroma and the presence of stellate fibroblasts as well as the lack of an epithelial component are helpful in distinguishing angiofibromas from FF. Immunoreactivity for CK15, CD34, and factor XIIIa is not very useful since all three markers are detected in FF, TD and angiofibromas as well as in the perifollicular fibroma type of fibrous papule. Since CK15 is expressed by undifferentiated sebocytes of the mantles and hair follicle bulge stem cells, its detection in the epithelial component of FF support the concept that these lesions are mantleomas. In FF, TD and angiofibromas the perifollicular stroma typically includes numerous CD34-positive spindle cells and scattered factor XIIIa-positive cells. These findings suggest that the three lesions may have a common histogenesis such as abnormal function of hair follicle bulge cells. BHD syndrome has a tendency to show multiple FF and TD, while tuberous sclerosis tends to manifest multiple angiofibromas, caused by the germinal mutations in the FLCN gene and TS-1/TS-2 genes, respectively. Interestingly, recent investigations revealed that FLCN and TSC proteins may function within a common pathway. Lastly, superficial angiomyxoma should be included in the differential diagnosis with fibrofolliculoma and trichodiscoma since they have in common the presence of a mucinous stroma associated with epithelial elements. In contrast with superficial angiomyxoma, however, FF and TD are usually purely dermal and do not have a tendency for local recurrence.
References


Notes:
Diagnosis: Epithelioid Cell Histiocytoma (ECH) Composed of Granular Cells

Clinical Impression: Intradermal nevus versus hemangioma, doubt dysplastic nevus

Histology: Well-circumscribed, polypoid lesion composed of a uniform population of epithelioid cells having large, vesicular nuclei, small nucleoli, and abundant, granular, eosinophilic cytoplasms; centered in the superficial dermis, with effacement of the overlying rete; focally infiltrated by T-lymphocytes; accompanied by a rich network of small blood vessels; bordered by an epidermal collarette.

Immunohistochemistry: The primary epitheliod cell population demonstrates weak to moderately intense staining with antibodies to factor XIIIa and CD68, and does not stain with HMB 45 or with antibodies to S-100 protein, MART-1, tyrosinase, broad-spectrum cytokeratins MNF116, or h-caldesmon. The epithelioid cells are accompanied by numerous dendritic cells that stain with antibodies to factor XIIIa with much greater intensity than the factor XIIIa staining of the epithelioid cells, and by sparse S-100-positive dendritic cells and CD68-positive histiocytes. The lesion demonstrates variably dense infiltration by CD3-positive T-lymphocytes. Antibodies to CD31, CD34, and smooth muscle actin stain a rich vascular network, but not the primary cell population.

Differential Diagnosis: Epithelioid cell histiocytoma (ECH) is believed to represent a variant of benign fibrous histiocytoma that can mimic a variety of melanocytic and histiocytic lesions. The current lesion is a classic ECH except for the intracytoplasmic granules seen throughout the primary epithelioid cell population. To the best of my knowledge, this is the second granular-cell ECH to be reported. Many cutaneous and non-cutaneous neoplasms may demonstrate intracytoplasmic granules that appear to correspond to accumulation of secondary lysosomes. Cells with granular cytoplasms may be a focal finding in lesions such as fibrous papule, basal cell carcinoma, atypical fibroxanthoma, dermatofibroma, leiomyoma, and leiomyosarcoma, lesions that may be specifically diagnosed on the basis of their otherwise typical histological features. The primary differential of cutaneous lesions composed entirely of epithelioid cells with intracytoplasmic granules includes conventional, "classic" granular cell tumor, which is thought to exhibit neural crest differentiation and stains with antibodies to S-100 protein and to lysosome markers such as CD68 and NKI-C3, and (primitive polypoid) nonneural granular cell tumor, which does not appear to demonstrate a clear line of differentiation, and which stains with lysosome markers, but not with antibodies to S-100 protein. Rare malignant "classic" granular cell tumors may demonstrate a variety of atypical histological features including large vesicular nuclei with large nucleoli, high nucleus to cytoplasm ratio, nuclear pleomorphism, and increased mitotic rate. Cases of (primitive polypoid) nonneural granular cell tumor have not as of this writing been reported to act aggressively even though some examples have worrisome histological features including nuclear atypia and increased mitotic activity, but several cases with lymph node metastases have been described.
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Clinical Summary: The patient is a 14 year-old female with small follicular and non-follicular pustules which coalesce into diffuse erosive erythematous plaques in neck and scalp, axilla, groin, perianal region, and vulva

Microscopic Features:
1) Subcorneal and intraepidermal pustules
2) Epidermal spongiosis
3) Dermal perivascular neutrophilic and lymphocytic infiltrate.
4) Special stains for fungal, bacterial and mycobacterial infection were negative

Discussion and differential diagnosis: In the early nineties at the French Society of Dermatology Crickx and colleagues described the first two cases of amicrobial pustulosis of the fold in two young female with systemic lupus erythematosus (1). Other names given to this entity include: amicrobial pustular dermatosis of cutaneous folds associated with auto-immune disorder, amicrobial pustular dermatosis with immunological abnormalities, amicrobial pustulosis of the folds associated with systemic lupus erythematosus and other auto-immune disease, and amicrobial pustulosis of the folds with neutrophilic gastro-intestinal involvement in systemic lupus erythematosus. Clinically, it affects predominantly females with an age range from 14 to 66 year-old. Amicrobial pustulosis of the folds presents with relapsing small follicular and non-follicular pustules which coalesced to form erosive areas with crusts or exudative erythematous plaques affecting the folds, vulva, perianal region, external auditory canal and scalp. Onychodystrophy has been observed when toes are affected. Isolated pustules are also found on various sites of the body, especially the extremities. Most of these patients suffer of an auto-immune disease or immunological abnormalities. The most common associations are systemic lupus erythematosus, celiac disease, Sjogren syndrome, rheumatoid arthritis, myastenia gravis and erythroblastic anemia, among others. Histologic changes range form neutrophilic folliculitis to spongiform subcorneal pustules with slight epidermal acanthosis. The dermis shows exuberant dermal infiltrate of lymphocytes, neutrophils, and histiocytes. The clinical differential diagnosis includes IgA pemphigus/intraepidermal neutrophilic IgA dermatosis, Sneddon-Wilkinson disease, infection, acrodermatitis enteropathica, and pustular psoriasis. Marzano et al have proposed major and minor criteria to render the diagnosis of amicrobial pustulosis based on anatomic location of the lesions, histopathologic features, and immunologic findings (see table below) (2).
Diagnostic criteria for amicrobial pustulosis of the folds (APF)

<table>
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<tr>
<th><strong>Obligate criteria</strong></th>
<th><strong>Minor criteria</strong></th>
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<tr>
<td>Pustulosis involving 1 or more major folds, 1 or minor folds</td>
<td>Association with 1 or more autoimmune</td>
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<td>and the anogenital area</td>
<td>disorders</td>
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<td>Histological pattern consisting of intraepidermal spongiform</td>
<td>Positive ANA at a titer of 1/160 or higher</td>
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<td>pustules and a mainly neutrophilic dermal infiltrate</td>
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<td>Negative cultures from unopened pustules</td>
<td>Presence of 1 or more serum autoantibodies</td>
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<td>(notably anti-ENA, anti-dsDNA, anti-smooth-muscle, antimito</td>
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<td>mitochondrial, anti-gastric-parietal-cell, antiendomysial)</td>
<td>muscle, antimitochondrial, anti-gastric-pari-</td>
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<td>The diagnosis of APF can be ascertained if obligate criteria</td>
<td>etal-cell, antiendomysial)</td>
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<td>and 1 minor criteria are present.</td>
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<td>ANA= Antinuclear antibodies, ENA= extractable nuclear antigens.</td>
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References:
**Diagnosis:** Fibro-ossifying granulomatous reaction to anabolic steroid injection.

**Clinical History:** A 30-year-old male complaining of several subcutaneous tumours, located on the chest, trunk, arms and thighs (the largest was 12 cm in diameter).

The patient used to practice several sports including weightlifting. Ten years ago, his trainers had given him intramuscular injections of anabolic steroids including Dimetabol ©, Testogan ©, Winstrol ©, Sustanon ©, and Ganabol ©.

**Histology:** There was an ossified fibrous granulomatous reaction with many vacuolated macrophages. In some areas the response mimicked what is normally seen in aluminium granuloma. There were also lobulated microvacuolated foreign bodies with peripheral giant-cell reaction, similar to the ones described after the injection of triamcinolone.

**Differential Diagnosis:** *Granulomatous reaction to corticosteroid injection: clinical information must be necessary. We have not found the lobulated, brain-shaped foreign body in reports on corticosteroids.*

Granulomas to other types of foreign bodies (aluminium, silicone, Artecoll, Bioplastique, Dermalive, …): the morphology of the foreign bodies is different. The vacuolated foreign body is not evidenced in these types.

**References**

Diagnosis: Intralymphatic histiocytosis

Clinical History: A 67-year-old man had an erythematous plaque with poorly defined margins on the left side of the chest. Six weeks evolution

Clinical findings: Our patient, a 67-year-old man, presented with an erythematous plaque with poorly defined margins on the left side of the chest of six weeks evolution. Four weeks later the lesions had considerably spread reaching the right side of the chest. Within this interval a colonic carcinoma was diagnosed. A CT scan disclosed intra and retroperitoneal lymph node involvement. Surgical removal of the tumour and nodes was followed by slow but complete disappearance of skin lesions.

Intralymphatic histiocytosis is a rare condition characterized by the presence of aggregates of mononuclear histiocytes within the lumen of dilated lymphatic vessels. Thirty-five cases have been reported in the English literature, nineteen of them in patients diagnosed of rheumatoid arthritis.

Clinically, all of them had asymptomatic, discrete erythematous to livedoid plaques, with irregular and poorly demarcated margins. Histologically, intralymphatic histiocytosis is characterized by the presence of dilated vascular spaces in the reticular dermis. Whereas some of these vessels were empty, others contained a variable number of epithelioid histiocytes that in some cases could obliterate their lumen. The dilated vessels had irregular shapes with thin walls constituted by flat endothelial cells. Immunohistochemical staining confirmed the lymphatic nature of the endothelial cells (podoplanin, D2-40, Lyve-1 and Prox-1,), as well as the histiocytic origin of the intravascular cells (CD68).

The two main differential diagnoses are intravascular reactive angioendotheliomatosis and intravascular lymphoma. Intravascular reactive angioendotheliomatosis is a benign proliferation of endothelial cells that can obliterate the involved blood vessels. Although it has been proposed that intralymphatic histiocytosis and intravascular reactive angioendotheliomatosis represent two different stages of a single inflammatory process, the advent of new immunohistochemical markers with the ability of exclusively labelling lymphatic vessels, such as podoplanin, D2-40, Lyve-1 and Prox-1, support that they are 2 different disorders, because intravascular reactive angioendotheliomatosis affects only blood vessels whereas intralymphatic histiocytosis is characterized by the exclusive involvement of lymphatic vessels. Intravascular lymphoma is a neoplastic condition with aggressive course that usually involves vessels of the skin and central nervous system. Histology and immunohistochemistry have demonstrated that the vessels involved are blood vessels and the cells inside them are B lymphocytes.

The pathogenesis of intralymphatic histiocytosis has not been clarified, but some authors point to the influence of lymphatic stasis in its development. Joint replacement or the mere presence of chronic inflammation could explain the presence of local stasis, poor clearance of antigens and a persistent immune reaction with accumulation of histiocytes.
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Diagnosis: Porokeratosis ptychotropica

Clinical History: 2-year-old man, since 1 year development of pruritic, hyperpigmented small macules that show confluence to 1-3 cm large, scaly plaques in the natal cleft extending bilaterally onto the buttocks. Lingua geographica, mucosal membranes and integument otherwise normal. No other diseases, no drugs. Family history not conclusive. Topic steroids ineffective. Syphilis serology and mycotic cultures negative.

Histology: Psoriasiform hyperplasia of the epidermis with several foci of parakeratosis with underlying hypogranulosis, large, moderately pleomorphic, vacuolated keratinocytes and scattered dyskeratotic keratinocytes. PAS staining of parakeratotic cells. Involvement of hair follicles and acrosyringia. Superficial perivascular lymphocytic infiltrate.

Differential Diagnosis: Lichen planus, Psoriasis, Contact dermatitis, Candidiasis, Keratosis lichenoides chronica

Comments: Porokeratosis represents a group of keratinisation disorders characterized by a lateral growth of a mutant clone of keratinocytes resulting in a cornoid lamella at the lateral margin and central regression and atrophy. Clinical variants include Porokeratosis Mibelli, giant porokeratosis, linear porokeratosis, disseminated superficial actinic porokeratosis, palmoplantar porokeratosis, and others. Porokeratosis ptychotropica (ptyche, Greek for fold) is another rare variant lacking a family history confined to the perianal area that presents with pruritic keratotic plaques. Histologic hallmark are multiple foci of cornoid lamellae associated with psoriasiform hyperplasia of the epidermis.

References:
Diagnosis: Onychomatrixoma

Clinical History: A 31-year-old woman consulted the dermatologist with a 3 year history of nail dystrophy involving her left middle finger. She did not remember any trauma before the onset of the nail abnormality. Her nail showed a longitudinal heterochromic yellowish dystrophic band. Under the nail plate a 4 mm tufted tumor composed of multiple filamentous digitations was present in the matrix.

Histologically, there was a polypoid fibroepithelial lesion with a papillomatous surface. The papillae were covered by a mature malpighian epithelium lacking a stratum granulosum and without apparent keratinization. The tumor stroma was highly cellular and composed of delicate collagen bundles. Scattered mast cells were observed among the stroma.

Differential diagnosis includes subungual and periungual warts, ungual Bowen disease, fibrokeratoma of the nail bed, subungual keratoacanthoma, subungual squamous cell carcinoma, and subungual exostosis.

References:
Diagnosis: Progressive Mucinous Histiocytosis

Clinical History: A 49 year-old female presents with multiple small firm, shiny, skin-colored papules on trunk, extremities, scalp and face. The first lesions appeared more than 20 years ago and their number increased gradually. The lesions are asymptomatic, except mild, intermittent itching and did not spontaneously regressed. The patient’s daughter and granddaughter (now 3 years old) have similar lesions, but she does not recall anybody else in the family having them.

Histology: Histologically, there is a superficial and mid dermal relatively well-circumscribed, non-encapsulated proliferation of epithelioid and spindle histiocytes with admixed mucin dissecting through the collagen bundles and separated from epidermis by a Grenz zone. Telangiectatic vessels are seen in the background, scattered mast cells are present and no significant inflammatory infiltrate is associated. It has been reported that in old-standing lesions the cellularity is reduced while the mucinous material becomes abundant. Immunohistochemical studies reveal that the histiocytes label for CD68, factor XIIIa, CD31 and are negative for S100 protein and CD1a. By electron microscopy, electron-dense intracytoplasmic inclusions appearing as zebra bodies and resembling lysosomal storage disease are seen and no Birbeck granules are identified.

Differential diagnosis: The differential diagnosis is broad and includes other non-Langerhans cells histiocytosis, mucinosis or fibrohistiocytic lesions, such as: acral papular mucinosis (has usually more mucin and a scant histiocytic infiltrate), scleromyxedema (not well circumscribed, more diffuse process), eruptive histiocytomas (self-resolving, usually no mucin), mucinous dermatofibroma, papular granuloma annulare (necrobiosis is usually seen), multicentric reticulohistiocytosis (characteristic histiocytes with ground-glass cytoplasm), etc. A combination of clinical information, histologic features, immunoprofile and electron microscopy findings is necessary to distinguish between these lesions.

References:

CASE 15

Pablo Umbert
University Hospital Sagrat Cor, Barcelona. Spain

Pau Umbert Millet1, Joaquin Sola Ortigosa1, RM Pujol Vallverdú2
1 Hospital Universitario Sagrat Cor, Barcelona. 2 Hospital del Mar, Barcelona.

Histological slides: S-1645-09, S-1781-09, S-1782-09.
Clinical information: Woman 38 years old with erythematous scaly and crusty nodules on limbs for 1 month, without response to topical and oral antibiotics.
Diagnosis: Lymphomatoid papulosis with pseudocarcinomatous changes

Clinical: Woman 38 years old with erythematous scaly and crusty nodules on limbs for 1 month and other erythematous nodules on arms and chest.
- Laboratory test: normal
- Biopsy culture and PAS: negative
- PCR HPV: + HPV 33 y 58
- FISH study for EGFR and c-myc: normal
- T-cell receptor and immunoglobulin heavy chain gene rearrangements by polymerase chain reaction: negative


Differential diagnosis: Fergusson-Smith syndrome, PLEVA, Cromomycosis, Milker’s nodules

References:

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Elizabeth Ball  
University Hospital of Caracas. Central University of Venezuela

PHAEOHYPHOMYCOSIS IN AND RENAL TRANSPLANT PATIENT

A 50- year old, venezuelan male patient presented with a verrucous tumor on the dorsal aspect of his 4th left finger, which appeared 1 month before as a small papule which grew rapidly to its actual size. The patient is a recipient of a renal transplant in March 2009 for nephroangiosclerosis and receives treatment with prednisone, mycophenolate mofetil, tacrolimus, losartán and amloidine. On physical examination a 2.5 x 2 cm ulcerated verrucous tumor was observed on the dorsal aspect of the proximal interphalangeal joint of the 4th left finger.

Clinical diagnosis:
1. Squamous cell carcinoma.
2. Cutaneous localized leishmaniasis, verrucous form.
3. Chromomycosis
4. Tuberculosis verrucosa

Histopathology: a shave biopsy specimen showed a thick purulent scale-crust with bacterial colonies. An epidermis with pseudoepitheliomatous hyperplasia, multiple neutrophilic abscesses both in the epidermis and in the papillary dermis and large areas of hemorrhage and necrotic debris. Small light brown spores and yeasts-like structures disposed singly or forming short chains were observed inside or adjacent to the suppurative areas. Gromori-Grocott and PAS stains highlighted the fungal structures.

Differential diagnosis:
1. Chromomycosis
2. Squamous cell carcinoma
3. Paracoccidiodomycosis
4. Phaeohyphomycosis: this is the correct answer
5. Protothecosis

References:


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Diagnosis: Superficial cutaneous sarcoma
Clinical History: ulcerated tumor on the scalp, 4 x 3 cm, with 7 months of evolution
Histology: ulcerated malignant dermal tumour of undifferentiated spindle cells with hyperchromatic and pleomorphic nuclei and atypical mitoses

Differential diagnosis: immunohistochemistry is mandatory to exclude other variants of malignant spindle-cell tumours like as malignant melanoma (S100), squamous cell carcinoma (keratin), leiomyosarcoma (SMA), Dermatofibrosarcoma protuberans (CD34) and angiosarcoma (CD34/CD31)

References:

Notes:
Diagnosis: Sjögren-Larsson syndrome

Clinical: A 12-month old girl is brought to pediatric dermatology by her mother with discolored, scaly skin since birth. Emollients and keratolytics have been ineffective. The mother had an uneventful pregnancy and delivery. On exam, the baby is normal height and weight for her age. She has moderate developmental delay of motor and language skills. There is diffuse, yellow, thin, plate-like scale over trunk and extremities, sparing the face. The biopsy and subsequent electron microscopy revealed abnormal intra and extracellular accumulations of granular material. The patient was referred for genetic evaluation for a suspected metabolic defect or storage disorder. See was referred for genetics evaluation. Chromosomal microarray revealed a deletion in ALDH3A2 gene, consistent with Sjögren-Larsson syndrome. The child is being followed by neurology, ophthalmology and medical genetics.

Histology: A biopsy showed papillomatosis, acanthosis and hyperkeratosis, consistent with epidermal nevus. Due to the discordant clinical and histologic pictures, the specimen was reviewed. Abnormal vacuolation of the pilar muscle was noted. Electron microscopy revealed free and intracytoplasmic granular accumulations in muscle and keratinocytes.

Differential diagnosis: The histologic changes in the epidermis are identical to those seen in epidermal nevus and acanthosis nigricans. Clearly, those don’t correlate with the clinical impression. Clinically, ichthyosis vulgaris, the most common type of ichthyosis, might be considered. Histologically, this would show compact orthokeratosis with diminuition of the granular cell layer and would not be associated with developmental delay. X-linked recessive ichthyosis is associated with mental delay. Heterozygous females may have scaling. Histologically, there would be mild acanthosis, normal to increased granular cell layer and hyperkeratosis. The diagnosis would rely on finding increased plasma cholesterol sulfate. Lamellar ichthyosis (ichthyosis congenital, type II) would have a more severe clinical presentation including ectropion, ecbalium and alopecia with a thick scale and often involves palms and soles. Congenital ichthyosiform erythroderma (ichthyosis congenital, types I, III and IV) has a much finer scale than LI, but histologically the two are very similar with mild acanthosis, hyperkeratosis, focal parakeratosis and a normal to slightly thickened granular cell layer. Keratotic plugging of the follicular orifices may be seen along with a mid superficial perivascular lymphocytic infiltrate.
References:


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Diagnosis: Eosinophilic annular erythema

Clinical History: A 52-year-old woman with a six year history of a persistent non pruritic cutaneous eruption forming polycyclic and arcuat e plaques that commenced as erythematous papules and nodules. New lesions often occurred in areas of fading erythema indicating no significant refractory period in previously affected skin. Cellulitic plaques, indurated morphoeiform lesions and bullae were never observed. Extensive investigations showed no abnormalities and in particular no peripheral blood eosinophilia on repeated testing and no evidence of associated parasitic infestation, allergy, autoimmune conditions or malignancy.

Histopathology: Similar histopathologic findings were observed in skin biopsies obtained at the initial consultation and two years later. There was a superficial and deep dermal inflammatory infiltrate consisting of lymphocytes, numerous eosinophils, some histiocytes and a few neutrophils but no plasma cells. Eosinophils were present interstitially and perivascularly. No leukocytoclasia or vessel wall necrosis was observed. The majority of eosinophils were intact with no loose granules and no flamed figures or granulomatous areas were observed. There was focal vacuolar degeneration of the junction and exocytosis of isolated lymphocytes with spongiosis.

Differential Diagnosis:

Histopathology
1. Eosinophilic cellulitis
2. Urticaria
3. Prebullous pemphigoid
4. Eosinophilic annular erythema
5. Drug reaction

References:

Diagnosis: Epithelial remnants of pilomatricoma

Clinical information:
- 13-year-old female
- Right shoulder
- Clinical impression: epidermal cyst

Histopathologic findings: Cystic dermal proliferation of epithelial cells that is discontinuous in foci surrounded by fibroplasia and telangiectases. Outermost epithelial cells are basaloid, arranged in a palisade, have scant cytoplasm, and some contain visible nucleoli. Inner epithelial cells are oval and associated with pink cytoplasm.

Differential diagnosis:
- Epithelial remnants of isthmus-catagen cyst
- Apocrine papillary cystadenoma
- Edge of cystic basal-cell carcinoma

References:

Note: Epithelial remnants of pilomatricoma has not been previously reported, however, the phenomenon of epithelial separation leading to epithelial remnants has been previously documented in cysts (see reference) and may also occur in various adnexal neoplasms, including pilomatricoma.
Diagnosis: Microcystic adnexal carcinoma

Clinical History: A 86 year-old female presented with ill-defined and firm plaque near the left medial canthus for the past 6 months.

Histology: Histologic features are characterized by superficial portion composed of small keratocysts (containing lamellar keratin) with alternating islands and strands of basaloid and epithelioid cells showing variable ductal differentiation. The mid portion of the tumor is characterized by strands rather than islands and the deep portion, extending into the subcutaneous tissue and muscle by even smaller nests and strands of cells in a densely eosinophilic, hyalinized stroma. Perineural invasion is identified. A cytokeratin (CK) 15 immunostain highlights the majority of the neoplastic cells.

Differential Diagnosis: First reported in 1982 by Goldstein et al1, microcystic adnexal carcinoma (MAC) has been referred by a variety of names including sweat gland carcinoma with syringomatous features, malignant syringoma, sclerosing sweat duct carcinoma and syringomatous carcinoma. Although the histology of MAC is fairly distinctive, often only a superficial biopsy is received which precludes the appreciation of the characteristic stratified appearance and perineural invasion. The differential diagnosis of a superficial biopsy usually includes infiltrative/morpheaform basal cell carcinoma (iBCC), desmoplastic trichoepithelioma (dTE), and squamous cell carcinoma (SCC). However, immunostains that have been shown to be useful are few and restricted to carcinoembryonic antigen (CEA) and cytokeratin 7.2-4 CK15, a marker of follicular stem cells, has been shown to be helpful in the distinction of MAC versus mimics.5 In the study we compared the expression of CK15, CK7, CK20, CK903, CEA, CD10, CD15, and BerEP4 in 13 MAC, 8 dTE, 10 iBCC, and 8 SCC of which five exhibited ductal differentiation. We found that the majority of MAC (92%) and dTE (100%) expressed CK15 while the iBCC and SCC cases were negative.5

References:
CASE 22

Denisa Kacerovska
Charles University Medical Faculty Hospital, Pilsen. Czech Republic

**Diagnosis:** Hybrid tumor (neurofibroma/perineurinoma) in a patient with neurofibromatosis type I

**Clinical history:** A 60-year-old woman with a remarkably visible scoliosis, multiple, sharply demarcated, uniformly pigmented macules randomly distributed on the body, freckling in the axillary and inguinal area, multiple skin-colored, polypoid or pedunculated, soft nodules located on the trunk, scalp, and upper extremities. Few of the later were less well circumscribed, more firm and located in the subcutis. One enlarging lesion, sized 1.5 x 2.0 cm on the back, were surgically removed. Additionally, ophtalmologic examination revealed multiple iris pigmented macules affected both eyes and correspondent with Lisch nodules.

**Histology:** The biopsy at first glance resembles a plexiform neurofibroma involving cutis and subcutis and formed by interlacing bundles of elongated cells with wavy nuclei surrounded by collagen. Focally the stroma is myxoid and mast cells are occasionally found. On close inspection, a second population of the cells can be recognized to compose spindled cells with bipolar or stellate nuclei arranged in short fascicles or whorls. The biphasic pattern may be better found on immunohistochemical slides: the spindled cells with wavy nuclei express S-100 protein and are negative for EMA, whereas the cells with bipolar or stellate nuclei demonstrate the reverse staining pattern, being EMA positive and S-100 protein negative.

**Differential diagnosis:** Pure plexiform neurofibroma

**References:**

Diagnosis: Lymphocytic thrombophilic arteritis

Clinical History: A 30-year old Chinese male presented with asymptomatic hyperpigmented ill-defined plaques and nodules on the lower limbs for 6 months. There were neither ulcerations nor purpura clinically. He was otherwise well with no systemic symptoms. Extensive laboratory investigations yielded unremarkable results.

Histopathological Findings: There is a medium-vessel vasculitis affecting small arteries within the dermo-subcutaneous junction or superficial subcutis. An infiltrate of predominantly lymphocytes and histiocytes are seen around and within the muscular vessel wall. Neutrophils are absent or scarce in comparison to the dense lymphohistiocytic infiltrate. The presence of a subendothelial concentric fibrin ring is characteristic. Nuclear dust is commonly seen.

Discussion: First described by Fein et al as “macular arteritis” in 2003, this unique lymphocytic medium vessel vasculitis presents clinically with hyperpigmented macules and ill-defined nodules mainly on the lower limbs.¹ The characteristic subendothelial concentric fibrin ring likened to a strawberry doughnut, presence of severe disease in a patient with factor V leiden mutation, and the predominantly lymphocytic infiltrate around a cutaneous small artery led to the term “lymphocytic thrombophilic arteritis” (LTA) by Lee et al in 2008.² Unlike its neutrophilic counterpart, polyarteritis nodosa (PAN), LTA does not have purpura and ulceration clinically nor systemic involvement. The presence of subendothelial fibrin, nuclear dust and active infiltration of an arterial muscular wall with lymphocytes fulfills criteria for an active lymphocytic medium-vessel vasculitis.³ These features, coupled with the sparsity of neutrophils, help differentiate LTA from the subacute phase of PAN. Other causes of a lymphocytic medium-vessel vasculitis include Sneddon syndrome, Degos disease, Buerger disease, Kawasaki disease, and connective tissue diseases such as lupus erythematosus and behcet’s disease. These diagnoses are excluded clinically and histopathologically.

References:
Diagnosis: Primary extramammary Paget disease

Clinical features: A 74-year-old female with a lesion in the perianal area

Histology: There are intraepithelial cells characterized by vesicular nuclei, prominent nucleoli and abundant pale, clear, basophilic or amphophilic cytoplasm. Focally epidermal acantholysis secondary to infiltration by neoplastic cells and show acanthosis are present and appear as proliferations of the epidermis encasing stromal papillae filled with a dense plasma cell-rich infiltrate. The keratinocytes in the epidermis are almost completely substituted by Paget cells with only the basal layer being preserved, thus occasioning a resemblance to syringocystadenocarcinoma papilliferum in situ. Epidermal acantholysis has been found to be a risk factor for disease recurrence in one study. ¹

Differential diagnosis: Syringocystadenocarcinoma papilliferum in situ. A rare neoplasm which occurs almost exclusively in the head and neck area and associated with nevus sebaceous. ²

References:
Diagnosis: Primary Mucinous Carcinoma of the Skin

Clinical: A 68-year-old African-American male presented to the otolaryngology clinic for evaluation of a persistent, nontender nodule on his left cheek. On physical examination, there was a 2 cm, linear scar, located in the left zygomatic area over the malar prominence, with a palpable, firm, mobile, subcutaneous nodule inferior to the scar. A fine needle aspiration (FNA) from the nodule was performed. Cytopathologic examination revealed groups of atypical epithelial cells suspicious for malignancy. The patient's past medical history was significant for prostatic adenocarcinoma, diagnosed nine years previously, and treated by external radiation, with remission. Positron emission tomography (PET) scan and colonoscopy were negative for a primary neoplasm at other sites. A wide local excision of the left cheek tumor was performed. A 2.5 x 1.0 x 0.8 cm, tan-gray, lobulated, firm-to-gelatinous nodule involving the dermis and subcutaneous fat was identified. The patient was referred to plastic surgery for Mohs surgery and reconstruction. He is alive without residual tumor three months later. He is being closely followed.

Histology: The tumor consists of dermal nests of tumor cells lying within lakes of pale-staining, eosinophilic-to-light blue-tinged, amorphous mucin, separated by thin, fibrous septa, with scanty vasculature. Tumor cells are relatively uniform in size, contained rounded-to-cuboidal nuclei, a prominent nucleolus, and abundant eosinophilic, sometimes vacuolated cytoplasm, forming variably-sized clusters, with duct-like structures. Mitoses are rare, 0-1 per 10 HPF's. Two cell populations are identified, i.e., smaller, dark cells and larger, pale cells. Histochemistry: lakes of mucin are stained 4+ by mucicarmine, PAS with and without diastase digestion, and alcian blue at pH 2.5, but are negative at pH 0.4 with sialidase digestion (sialomucin). Immunostains: pancytokeratin +, CK 7 +, CK5/6 -, CAM 5.2 -, EMA focally weak +, CEA focally weak +, S-100 protein -, and Ki67+ for less than 5% of tumor cells. Additionally, CDX-2, p63, and TTF-1 are stained negatively in the tumor cells.

Differential Diagnoses: Metastatic mucinous carcinoma from (female) breast, gastrointestinal or respiratory tract, salivary gland and lacrimal gland, urinary tract, prostate, or paranasal sinuses.

References:
**Case Summary:** A 35 year-old man presented with a history of oral and genital erosions for several months. There were also papules and pustules over the scalp, trunk, limbs, and body folds that had developed a vegetating aspect.

**Diagnosis:** PYODERMATITIS-PYOSTOMATITIS VEGETANS

**Clinical Features:** Pyodermatitis-Pyostomatitis Vegetans is considered a marker for inflammatory bowel disease, and it usually precedes ulcerative colitis (70% of the cases), or Cohn's disease (15%), although rarely there is no associated disease. Oral lesions (pyostomatitis vegetans) usually precede cutaneous lesions. They are characterized by multiple erythematous small pustules, that evolve to ulcers and erosions that have classically been described as "snail tracks". Cutaneous lesions (pyodermatitis vegetans) are seen in 60% of the patients. They start as erythematous papules and pustules coalescing into vesiculopustular, exudative, vegetating and annular plaques involving the face, scalp, axillae, groins, and genital regions. Biochemical and hematological workup is typically normal, except for an elevated sedimentation rate and blood eosinophilia that can be found in two thirds of cases.

**Histology:** There is an epithelial acanthosis or even pseudoepitheliomatous hyperplasia (vegetative lesions) with eosinophilic and neutrophilic spongiosis. There are usually intraepithelial and subepithelial microabscesses with large numbers of eosinophils and neutrophils. Acantholysis and suprabasilar clefts can also be seen. A dense mixed inflammatory cell infiltrate with numerous eosinophils and neutrophils is seen in the dermis. Both direct and indirect immunofluorescence is usually negative, but in some cases intercellular spaces or basement membrane zone can show weak reactivity for IgA, IgG, or C3.

**Differential diagnosis:** Pemphigus vulgaris, Pemphigus vegetans, IgA pemphigus, Subcorneal pustular dermatosis, Bullous pemphigoid, Dermatitis herpetiformis, Mucous membrane pemphigoid, Epidermolysis bullosa acquisita, Erythema multiforme, Halogenoderma, Behçet's disease, Infectious diseases (herpes simplex, late stages of syphilis, tuberculosis cutis verrucosa, oral candidiasis).

**References:**


Case 2102/04: Female patient, 75 years-old
History: Since one year, presence of an asymptomatic nodule of 5 mm
Localization of the excision: Left thumb
Clinical diagnosis: Eccrine poroma or verruca vulgaris
Histology: Well-demarcated nonencapsulated tumor; proliferation of epithelioid, plasmacytoid, histiocytoid and spindle cells with a hyalin and eosinophilic cytoplasm and monomorphic ovoid nuclei in a myxoid stroma
Histological differential diagnosis:
- Epithelioid dermatofibroma
- Spitz’s nevus / spitzoid melanoma
- Cellular neurothekeoma
- Eccrine poroma
- Epithelioid sarcoma
Histological diagnosis: Cutaneous myoepithelioma
2- Hornick JL, Fletcher CD. Cutaneous myoepithelioma : a clinicopathologic and immunohistochemical study of 14 cases. Hum Pathol 35 : 14-24, 2004
A 73 year-old woman presented with a groin. At physical examination the lesion seemed to be unattached to deeper soft tissues or bone structures. It was completely resected and consisted of a whitish, flashy, 2.5x 2.5 x 2.1 cm mass. Eight months later the lesion recurred locally.

**Diagnosis:** Non-acral myxoinflammatory fibroblastic sarcoma.

**Clinical:** A 73 year-old woman presented with a groin. At physical examination the lesion seemed to be unattached to deeper soft tissues or bone structures. It was completely resected and consisted of a whitish, flashy, 2.5x 2.5 x 2.1 cm mass. Eight months later the lesion recurred locally.

**Histology:** The lesion was restricted to the cellular subcutaneous tissue. It was well-delimited, non-encapsulated, and presented no infiltration of the adjacent adipose tissue. It consisted of variable sized pleomorphic cells, containing prominent nucleoli, some of them reminiscent of Reed-Sternberg cells. Such cells were intermixed with intense mixed inflammatory infiltrate constituted of plasma cells, eosinophils, lymphocytes, and numerous neutrophils. In some areas the inflammatory infiltrate was so intense that the neoplastic cells were barely identifiable, while in other areas the neoplastic cells were easily visible in solid and sheet-like arrangement. The stroma was predominantly collagenous, but in areas mucin pools and nodules containing atypical neoplastic cells and scarce inflammatory cells were noticed. The innermost portion of the tumor harbored vascular thrombi, necrosis, and intense neutrophilic infiltrate. No connection to synovial tissue was observed. Immunohistochemically, the lesion expressed CD68 and smooth muscle actin, but showed negative results for CD15, CD30, CD45, CD245, LMP-1, Melan-A, S-100 protein, EMA, cytokeratins, CD34, and desmin. Myxoinflammatory fibroblastic sarcoma (MIFS) was first reported in 1998. Although initially believed to be restricted to acral parts, later on MIFS was reported in non-acral sites, including in the neck, groin, upper arm, arm, and thigh. Thus far about 8 such cases have been recorded in English literature, all of them were subcutaneous lesions, and harbored similar histological features as compared to acral examples. Non-acral MIFS seems to have a high risk of local recurrence, but no distant metastases or deaths have been documented.

**Differential diagnosis:** The differential diagnoses for the present case include myxofibrosarcoma, melanoma, anaplastic large cell lymphoma, and Hodgkin lymphoma. Except for myxofibrosarcoma, all the other entities can be easily discarded with an adequate immunohistochemical panel. In contrast to MIFS, myxofibrosarcoma tends to be uniformly myxoid, it lacks the pleomorphic Reed-Sternberg-like cells, presents no prominent inflammatory infiltrate, and it harbors a typical curvilinear arrangement of its vessels. The distinction between MIFS and myxofibrosarcoma seems to be important since the later may evolve to higher histological grades and may carry a more adverse prognosis.
References:

**CASE 29**

**Christopher Shea**  
*University of Chicago, Chicago, Illinois. USA*

**Diagnosis:** CUTANEOUS CYTOMEGALOVIRUS VASCULITIS  
“A 49-year-old African American woman rapidly developed purpuric, slightly elevated and scaly plaques over the trunk, arms, and upper legs, and superficial erosions on the buttocks.”

**Clinical:** A 49-year-old African American woman developed shortness of breath, was diagnosed with disseminated tuberculosis, and was started on a four drug anti-TB regimen. A rash on the right leg was initially diagnosed as cellulitis and she received vancomycin and piperacillin/tazobactam. The rash rapidly generalized to purpuric, slightly elevated, scaly plaques over the trunk, arms, and upper legs, and superficial erosions on the buttocks. Dermatology was consulted for a possible drug hypersensitivity reaction.

**Histology:** The dermis had extravasated RBCs and a perivascular and intramural infiltrate of neutrophils and lymphocytes, with abundant intramural nuclear dust. Some endothelial cells had amphophilic cytoplasm and basophilic nuclear inclusions. Anti-CMV antibody highlighted numerous dermal endothelial cells with both a nuclear and cytoplasmic staining pattern.

**Differential diagnosis:**
- Immune complex leukocytoclastic vasculitis
- Septic vasculitis
- Cellulitis with secondary extravasation of RBCs

**References:**
José Luis Mate

Hospital Universitari Germans Trias i Pujol, Badalona. Autonomous University of Barcelona. Spän
Luis Requena  
*Department of Dermatology. Fundación Jiménez Díaz, Universidad Autónoma, Madrid, Spain*

**Clinical History:** A 53-year-old woman was seen with whitish papular lesions involving the dorsum of the hands. She had also similar lesions, although less evident, on the skin of the abdomen. Her mother and her older sister have similar lesions. These lesions appeared when the patient was around 30 years old.

**Diagnosis:** Late-onset focal dermal elastosis.

**Clinical Features:** Focal dermal elastosis is a distinctive entity of late onset characterized by a pseudoxanthoma elasticum-like eruption. The lesions consist of small whitish or yellow papules involving the lateral aspects of the neck, shoulder and arms. The peculiar features of the presented patient were the familiar incidence and the acral location of the lesions.

**Histopathology:** There is an increase of elastic fibers in the mid and deep dermis. Although most authors described that the elastic fibers are normal –appearing, in our opinion they are larger and thicker than normal elastic fibers of the reticular dermis. There are no changes of pseudoxanthoma elasticum and solar elastosis is absent. Thus, it seems to be that chronic exposure to ultraviolet radiation has no influence in the histogenesis of the process.

**Differential Diagnosis:** Focal dermal elastosis of late onset should be differentiated:

1) From clinical point of view:
   a. From pseudoxanthoma elasticum: The histopathology shows fragmented and calcified elastic fibers in mid dermis.  
   b. From pseudoxanthoma –elasticum like papillary dermal elastolysis: Histopathology shows loss of elastic tissue in papillary dermis.

2) From histopathologic point of view:
   a. From elastoma: The lesions consist of solitary or multiple papules associated with osteopoikiloisis.  
   b. Linear focal elastosis: The lesions are palpable stria-like yellow lines on lumbosacral region.  
   c. Elastoderma: Localized wax, wrinkled skin.

**References:**
Diagnosis: Small lymphocytic lymphoma / B-cell chronic lymphocytic leukaemia.

Clinical history: 65-year old man with several erythematous plaques, 2-6 cm in diameter, developing in the arms and the sacral region over a 14-month period. The patient was initially treated with Peitel ® (Prednicarbate 0,25 %) without clinical improvement. Dermatological diagnosis was Sarcoidosis Vs Mycosis Fungoides.

Histology: The biopsy showed a nodular and diffuse, dense, dermal lymphocytic infiltrate. The lymphocytes were small, with round nucleus and fine chromatin, without nucleoli. Immunohistochemical stains showed positivity for CD20, CD5, CD23 and CD43 in the neoplastic cells, admixed with scattered reactive CD3 positive lymphocytes. A clonal heavy chain immunoglobulin rearrangement was demonstrated using the BIOMED-2 protocol. Additionally, a bone marrow biopsy was performed. The trephine showed a nodular and interstitial infiltrate of small CD20 / CD23 /CD43 positive lymphocytes. Cytogenetic and FISH analysis showed a trisomy 12.

Differential diagnosis: The differential diagnosis include other small B-cell lymphomas of the skin, such as cutaneous marginal zone B-cell lymphoma, follicular lymphoma and mantle cell lymphoma, as well as pseudolymphomas.

References:
Norberto López, MD; Enrique Herrera, MD.

Department of Dermatology. University Hospital. School of Medicine, Malaga. Spain

**Diagnosis:** Aggressive CD30+ nasal-type natural killer/T-cell lymphoma

**Clinical:** A 62-year-old woman presented with a midline acute facial ulcer

**Histology:** A skin biopsy revealed an atypical angiocentric mononuclear cell infiltrate. Immunoperoxidase stains showed that the cells were of natural killer type. Further studies revealed Epstein-Barr virus sequences. Moreover a prominent CD30 staining was detected.

**Differential diagnosis:** Anaplastic large cell lymphoma, lymphomatoid granulomatosis, Wegener granulomatosis

**References:**

**Notes:**
Jose Luis Rodriguez-Peralto  
Department of Pathological Anatomy, Hospital Universitario 12 de Octubre, Madrid. Spain

Clinical History: A 50-year-old female was admitted at “12 de Octubre Hospital” because of several subcutaneous nodules on legs, back and forehands of 1 year follow-up. One of the forehead lesion was excised with the clinical diagnose of erythema nodosum.

Diagnosis: HISTIOD LEPROSY

Clinical: Histioid leprosy, a well-recognized entity described by Wade in 1963, is a clinical variant of multi-bacillary lepromatous or unstable borderline and indeterminate leprosy. This condition usually occurs in patients on long-term diamino-diphenyl-sulfone treatment, with initial improvement followed by relapse. Irregular and inadequate therapies, as well as resistance to dapsone and/or mutant organisms, may further compound its occurrence. Histioid leprosy is clinically recognized by firm to palpation, reddish, or skin-colored, dome-shape or oval papules or nodules, regular in contour with translucent shiny and starched overlying skin. Sometimes, plaques with similar appearance may be apparent. The lesions may be few or numerous usually located over the lower back, buttocks, face, extremities and bony prominence.

Histology: Microscopically, the lesions are better recognized if an entire surgical resection of an initial lesion is performed, before the administration of the multidrug therapy. The panoramic view demonstrates an expansile and well circumscribed lesion, usually located in the dermis, subcutis or both, composed by a proliferation of numerous spindle-shape hisiocytes organized in interlacing fascicles, whorls, spoke-wheel-like arrangement and at times, thigh curlicues, resembling a fibrohistiocytic tumor or dermatofibroma. Atrophy of the overlying epidermis is the rule but hyperplasia or pseudocarcinomatous appearance can be observed. At higher magnification, the cells reveal slight vacuolation of the cytoplasm, less prominent than cytoplasmic vacuolation of typical lepra cells in the full stage of development. Stain for acid-fast bacilli reveals numerous organisms and fragmented mycobacterium leprae. The acid-fast bacilli are longer than ordinary lepra bacilli and they are arranged in groups or parallel bundles aligned along the axis of the cells or isolated scattered throughout the lesion. They are considered as mutant bacilli resulting from the development of drug resistance against sulfones. Cystic spaces full of acid-fast bacilli can also be observed.

Differential diagnosis: When histioid leprosy occurs in the appropriate clinical setting, that is, in a patient previously diagnosed of lepromatous leprosy on antileprosy therapy, the diagnosis is really easy to perform. The problems start when patients, usually travelers, develop the lesions in nonendemic countries, where the level of suspicion and familiarity with leprosy is low, or when the preceding lepromatous leprosy is missed or is not evident. The main differential diagnosis must be performed with dermatofibroma, malignant fibrohistiocytic tumor, atypical post-Kala-azar dermal leishmaniasis, cutaneous sarcoidosis, cutaneous infection with Mycobacterium avium intracellulare in a HIV patient and secondary syphilis.
References:


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CASE 35

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**Diagnosis:** Clear cell mesenchymal neoplasm.

**Clinical history:** 8-year old boy with a pink soft pre-auricular papule, 6mm in diameter, of 3 months’ evolution. Clinical diagnosis was Spitz nevus vs Xantogranuloma

**Histology:** The biopsy showed a proliferation of clear cells that tended to form compact lobules with smooth broad borders. The lesion involved almost the whole dermis infiltrating the arrector pilaris smooth muscle but sparing a subepidermal band (Grenz zone). The clear cells had medium sized oval bland vesicular nuclei with one or two small nucleoli. There were occasional pleomorphic elements and mitotic rate was low (less than 1x25 HPF). Cytoplasms were round or polygonal, optically clear but with a multivacuolated, reticular or slightly granular texture. Some intermixed coarse collagen fibers as well as some thin walled dilated vessels, mostly superficial, were present.

Tumor cells were widely positive for vimentin and focally for CD68 whereas wide spectrum keratin, factor XIIIa, CD34, s-100 protein, smooth muscle actin, desmin, EMA and HMB-45 were negative.

**Differential diagnosis:** The differential diagnosis includes most clear cell dermal tumors such as pecoma, clear cell dermatofibroma, xanthomas and xanthogranuloma, clear cell hidradenoma and neurothekoma that share many microscopical and immunohistochemical features with this entity.

**References:**


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Clinical Summary: 56 years old female patient with multiple infiltrate violaceous nodules in both cheeks. The lesions have been present for 10 years. The rest of the exams are normal.

Microscopic Features: Dense a polymorphous infiltrate in the dermis with some lymphoid folicules. The infiltrate is compose of lymphocytes, a variable number of large lymphoid cells with hypercromatic, convoluted nuclei, plasma cells and eosinophils. There are dilated blood vessels and the epidermis shows sparse exocytosis.

Discussion: Actinic reticuloid has been separated from the other chronic photodermatoses on the basis of its histopathological picture, which shows a variable resemblance to a T cell lymphoma. Actinic reticuloid has clinical features that overlap with those of photosensitivite eczema and persistent light reaction. Differences include episodes of an erythroderma like picture involving also non exposed areas of the body and extreme sensitivity to ultraviolet B and ultraviolet A radiation and often to visible light as well. A positive photopatch test is present in less than 10% of affected individuals, although contact allergic sensitivity without the involvement is sometimes present. Offending agents in this category include oleoresins of various plants in the compositae family and certain fragrances. Persistent light reaction sometimes evolves into actinic reticuloid indicating that the chronic photodermatosis are part of spectrum. Avoidance of ultraviolet/visible light often leads to sustained improvement.

The few reports of lymphoma developing in patients with actinic reticuloid appear to represent a chance occurrence, particularly as the patients with actinic reticuloid are usually elderly. Furthermore, DNA aneuploidy has not been demonstrated using DNA flow cytometry. More importantly, clonal T cells have not been identified. Although the pathogenesis of actinic reticuloid is unknown, theories similar to those advanced for persistent light eruption have been proposed. Of interest is the finding that cultured fibroblast from the skin of individuals with actinic reticuloid show cytopathic changes and inhibition of RNA, synthesis after exposure to ultraviolet A radiation.

Differential diagnosis: The main differential diagnosis is cutaneous T cell lymphoma.

References: