Self-Assessment Answers Cases 1 - 15

Chairs:

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Self-Assessment Answers

Part 1 – Friday 29th September 2017

Case 1

Mona R.E. Abdel-Halim, MD, Dip Dermpath (ICDP-UEMS)

DIAGNOSIS
FLOUROSCOPY INDUCED CHRONIC RADIODERMATITIS

Clinical Summary:

A 66-year-old male patient presented with a well defined square shaped indurated/sclerotic focally ulcerated plaque with atrophic areas on the right sub-scapular area of 2 years duration. The patient's medical history included coronary artery disease for which he underwent percutaneous transluminal coronary angioplasty 6 months prior to the onset of the lesion.

Microscopic Features:

Histopathological examination of a large deep surgical biopsy, including part of the ulcer, revealed: necrotic debris covering the ulcerated area of the epidermis. The adjacent epidermis was hyperplastic with vacuolated keratinocytes and fibrin was focally deposited beneath the epidermis. Blood vessels in the superficial and mid dermis showed luminal thrombosis and some showed fibrin deposition and hyaline material in their walls. Mild perivascular non specific infiltrate composed of lymphocytes and histiocytes was detected in addition to many bizarre shaped fibroblasts, some were multi-nucleated. The dermis was densely sclerotic with esinophilic homogenized collagen, absent hair follicles (with preserved arrector pili muscles), and marked reduction in sweat glands with only few degenerated sweat coils. Subcutaneous fat was reduced with sclerosed areas.

Discussion:

The potential of radiodermatitis developing from interventional fluoroscopy is increasing nowadays with the increased therapeutic and diagnostic indications, complexity and length of procedures, and accordingly doses of radiation used [(1)]**.** A typical fluoroscopic procedure exposes the patient approximately to 0.02 to 0.05 Gy/minute, however doses as high as 0.5 Gy/minute have been reported [(2)]. Cardiac catheterization procedures generally expose patients to an average dose of 2.5 Gy. Due to radiation being focused mainly on stenosed vessels, percutaneous transluminal angioplasty procedures are more hazardous as radiation doses can reach 6.4 Gy [(3)]**.**

As in classic radiodermatitis, fluoroscopy induced radiodermatitis can be acute, chronic or subacute. Acute radiation skin injury can occur with a threshold dose of 2-8Gy and this usually develops within 7-14 days after the procedure. Acute reactions present with erythema, vesicles, erosions, pain and tenderness. On the other hand, a cumulative threshold dose of 10-12Gy usually lead to late onset manifestations of chronic radiodermatitis that may take months to years to develop and are known as fluoroscopy induced chronic radiodermatitis (FICRD) [(4, 5)]**.** These are characterized by permanent erythema, sclerosis, atrophy (white areas), permanent reticulated erythema/telangiectasia, desquamation, refractory ulcerations, discoloration and pruritus [(4)] and may be complicated by invasive basal or squamous cell carcinoma [(6)]**.** Subacute cases exhibit overlapping features [(7)]**.**

The following triad is essential in establishing a diagnosis of fluoroscopy induced radiation dermatitis: history of interventional fluoroscopic procedure, skin lesions with appropriate characteristics of radiodermatitis and location of the lesions at the entrance site of ionizing radiation for that particular procedure which gives it a peculiar geometric outline;

square shaped or rectangular [(4)]**.** The most frequently affected sites related to coronary procedures include: scapular and sub-scapular areas, mid back, right mid axillary and right anterolateral chest depending on which vessels are visualized [(4)]**.**

Due to the possible long interval between the development of FICRD and the actual fluoroscopic procedure, patients usually do not relate the skin manifestations to the procedure and this leads to diagnostic difficulties [(5)]**.** Accordingly, awareness of this entity is important for dermatologists/dermatopathologists and the possibility of FICRD should be raised whenever cutaneous lesions mimicking radiodermatitis are seen in any of the above mentioned peculiar anatomical locations.

References:

1. Aerts A, Decraene T, van den Oord JJ, Dens J, Janssens S, Guelinckx P, Flour M, Degreef H, Garmyn M. Chronic radiodermatitis following percutaneous coronary interventions: a report of two cases. *J Eur Acad Dermatol Venereol.* 2003; 17(3):340-3

2. Malkinson FD. Radiation injury to skin following fluoroscopically guided procedures. *Arch Dermatol.* 1996; 132(6):695-6

3. Lichtenstein DA, Klapholz L, Vardy DA, Leichter I, Mosseri M, Klaus SN, Gilead LT. Chronic radiodermatitis following cardiac catheterization. *Arch Dermatol.* 1996; 132(6):663-7

4. Koenig TR, Wolff D, Mettler FA, Wagner LK. Skin injuries from fluoroscopically guided procedures: part 1, characteristics of radiation injury. *Am J Roentgenol* 2001; 1773- 11

5. Lee J, Hoss D, Phillips TJ. Fluoroscopy-induced skin necrosis. Arch Dermatol. 2003;139(2):140-2

6. Davis MM, Hanke CW, Zollinger TW, Montebello JF, Hornback NB, Norins AL**.** Skin cancer in patients with chronic radiation dermatitis. J Am Acad Dermatol. 1989;20(4):608-16

7. Stone MS, Robson KJ, LeBoit PE. Subacute radiation dermatitis from fluoroscopy during coronary artery stenting: evidence for cytotoxic lymphocyte mediated apoptosis. J Am Acad Dermatol. 1998;38(2 Pt 2):333-6.

Case 2
Dr Asha Kubba

DIAGNOSIS:
PAPULO-NECROTIC TUBERCULIDE

Clinical Summary:
37 F Papulo-nodular eruption on erythematous base, some are ulcerated. Located on upper arms, both legs up to buttocks..

Microscopic features:
A central wedge shaped neutrophilic microabcess extends into mid reticular dermis. Epidermis is completely necrotic. The infiltrate is surrounded by a ring of granulomatous infiltrate including epithelioid cells and multinucleated giant cells including Langhan type . Dense infiltrate of lympho-histiocytes , plasma cells, neutrophils and eosinophils are present in deep dermis and subcutaneous fat. Epithelioid granulomas and fat necrosis are noted. Vasculitis is absent. Fite stain is negative for acid fast organisms.
Second biopsy, of the nodule on the leg shows superficial and deep lympho-histiocytic infiltrate ; extensive lobular necrosis and panniculitis with granulomatous inflammation. A medium sized vessel shows fibrinoid necrosis and lymphocytic inflammation of vessel wall surrounded by epithelioid granulomas and granulomatous infiltrate.

Discussion:
Tuberculides are considered to be a hypersensitivity reaction to M. tuberculosis infection somewhere in the body. Such reactions are seen in individuals with high degree of immunity documented by strongly positive Mantoux test.
Cutaneous lesions of tuberculide may present as a) lichen scrofulosorum; b) papular / papulo-necrotic tuberculide and c) Erythema induratum. Papulo-necrotic tuberculide (PNT) presents as papulo-nodular eruption, some lesions may show central necrosis. Lesions are typically seen on the upper and lower limbs and less commonly on ears and genitals. The papulo-necrotic lesions heal with varioliform scar formation. Sometimes, more than one type of lesions is seen in one patient as illustrated by the present case. Acid fast organisms are not detected by special stains and mycobacterial culture are usually negative. Mycobacterial DNA has been detected by PCR in some cases. Tuberculides respond to antiTB treatment.
Clinically and histologically lesions of PNT can be mistaken for Pityriasis lichenoides et varioliformis acuta (PLEVA). Histologically, PNT lesion may involve the hair follicle resulting in necrosis which has to be differentiated from suppurative folliculitis. Presence of palisading granuloma with necrosis can mimick granuloma annulare. Suppurative palisading granulomas due to infectious cause would be in the differential diagnosis.

References:
1. Jordan HF, Niekerk V, Louw M. Papulo-necrotic tuberculide
Am J Dermpath 1994; 16 (5): 474-485

2. Hakllensleben NDL, deVries HJC, Lettinga KA etal Tuberculides: cutaneous indicator diseases of Mycobacterium tuberculousis infection in young patients. JEADV 2016,30, 1590-93

Case 3

Doina Ivan, M.D.

DIAGNOSIS: CRYSTALOGLOBULINEMIA

Clinical Summary:
A 68-year-old man with a history of progressive IgG lambda multiple myeloma and chronic kidney disease presents with acute renal failure requiring hemodialysis and a rash on bilateral soles and palms associated with pain present for 3 weeks.

Based on the patient's history and the histologic findings, what is the most likely diagnosis?

A. Calciphylaxis
B. Septic vasculitis
C. Perniosis
D. Crystaloglobulinemia
E. Cholesterol emboli

Microscopic Features:
Eosinophilic, non-refringent crystals are noted in small dermal blood vessels, forming thrombi. There is no associated perivascular inflammatory infiltrate.

Discussion:
Crystalglobulinemia (also named cryocrystalglobulinemia) was first described in 1972 and is a rare paraneoplastic syndrome associated with multiple myeloma and is due to spontaneous crystallization of a plasma proteins. The patients typically present with kidney damage and often rapidly progressive renal failure. Cutaneous lesions are also reported, mostly as purpuric lesions made worse by exposure to cold. Raynaud's phenomenon is not a common occurrence. It may be considered as a severe type of cryoglobulinemia (type I) where the cryoglobulins initiate thrombi formation in small blood vessels. The thrombi are represented by eosinophilic, non-refringent crystals, composed of monoclonal immunoglobulins (usually IgG). They can be associated with fibrin and fragmented red blood cells. Usually there is no associated perivascular inflammatory infiltrate.

References:

1. Llamas-Velasco M1, Alegría V, Santos-Briz Á, Cerroni L, Kutzner H, Requena L. Occlusive Nonvasculitic Vasculopathy: A Review. Am J Dermatopathol. 2016

Case 4

Francisco Bravo, MD

DIAGNOSIS: GNATHOSMIASIS

Clinical Summary:
30 y.o. female from Lima, Peru . She likes to eat ceviche, sashimi and sushi.
About 4 weeks ago she noticed an area of induration on the left thigh. The lesion disappeared after a week of antibiotics, but then , it resurfaced a few cm beyond the original location. The surface of the skin in this second time looked like peau d'orange

She had a complete blood count showing high eosinophilic count of 18 %

Microscopic Features:
The most important finding is the presence of interstitial infiltrate of eosinophils in the dermis as well as in the fat tissue. It is exceptional to see the larva

Discussion:
Gnathostomiasis is a parasitic infection that occurs a result of the migration of the third larvarial state (L3) of nematodes of the *Gnathostoma* genus trough human tissues. Most commonly, this migration takes place in the skin and subcutaneous tissues. The disease is mainly seen in areas of the world that are considered endemic, such as Southeast Asia, Japan and Latin America, but is also increasingly seen in travelers after returning to non-endemic areas, such as the United States or Europe. The infection is acquired through the consumption of fresh water fish or eel, either raw or marinated in lemon juice, (containing the L3) in the form of various popular traditional delicatessens such as sushi, sashimi or ceviche

One should suspect gnathostomiasis when dealing with a patient that has

1. A clinical picture of a **wandering**, migratory nodular lesion on the skin. Sometimes the clinical picture simulates cutaneous larva migrans, or is a combination of CLM and a nodular lesion. Exceptionally the larva can become very superficial and the lesion may mimic a furuncle
2. A history of consuming raw fish while living or traveling through endemic countries
3. Presence of tissue eosinophilia, either on skin biopsy or in the peripheral smear. The intensity of the eosinophilia in the skin can be mild to severe, superficial or deep. The presentation may consist mostly of an acute eosinophilic panniculitis. Flame figures may be seen on the skin biopsy
4. It is exceptional to see the larva, except if the patient has already been treated. In such a case, the evolution of a large clinical lesion into a more localized tiny papule signal the location of the larva in the superficial dermis, increasing the chances of seen it in histological cuts.

In most cases, especially in endemic areas, the diagnosis is made on the basis of the clinical picture compatible with gnathostomiasis, and proof of eosinophilia in tissue.

In travelers, for further confirmation, a Western Blot assay has been developed in Asia and Europe ; it is directed against a crude preparation of *G. spinigerum.* The detection of a 24kDa L3 antigen band is considered diagnostic of gnathostomiasis. However, the test is only available at research institutions

Treatment is based on the administration of albendazole or ivermectin

Ganthostomiasis is considered an emerging infectious disease in travelers

References:

1. Herman JS, Chiodini PL. Gnathostomiasis, another emerging imported disease. Clin Microbiol Rev. 2009 Jul;22(3):484-92

2. Laga AC, Lezcano C, Ramos C, Costa H, Chian C, Salinas C et al . Cutaneous gnathostomiasis: report of 6 cases with emphasis on histopathological demonstration of the larva. J Am Acad Dermatol. 2013 Feb;68(2):301-5

Case 5
José Carlos Cardoso

DIAGNOSIS:
ACRAL PERSISTENT PAPULAR MUCINOSIS

Clinical Summary:
A 48-year-old male presented with multiple asymptomatic skin-coloured papules that had started several years before and progressed slowly, distributed bilaterally on the dorsum of the hands and wrists. The patient was otherwise well and had no relevant previous medical history. He was not on any chronic medication.
Ancillary investigation did not reveal any underlying disease and all his laboratory tests were unremarkable, including complete blood count, liver and kidney function tests, serum protein electrophoresis, thyroid function tests and serologies for HIV, hepatitis B and C, and syphilis.

Microscopic Features:
The biopsy of one of the papules revealed a relatively well circumscribed area of mucin deposition in the superficial and mid dermis (confirmed with Alcian blue stain). This was not accompanied by any significant inflammatory infiltrate, fibroblast proliferation or collagen deposition.

Discussion:
Acral persistent papular mucinosis (APPM) was first described in 1986 by Rongioletti et al. as a peculiar variant of localized lichen myxoedematosus (LM). In the classification of mucinoses proposed by Rongioletti et al. in 2001, papular mucinosis or lichen myxoedematosus is divided in 5 forms: one generalized sclerodermoid form associated with IgG monoclonal gammopathies (scleromyoedema) and four localized forms, namely: discrete papular LM, nodular LM, papular mucinosis of infancy and APPM. The latter forms, by definition, are not associated with systemic disease, namely monoclonal gammopathy or thyroid disease. Cases that do not fit the criteria for any of the above categories are classified as atypical LM (e.g. otherwise typical scleromyxoedema without gammopathy or localized papular LM with monoclonal gammopathy).
APPM is, thus, a variant of localized LM characterized by the presence of persistent small (2-5 mm) papules distributed exclusively on the dorsal aspect of hands, wrists and distal forearms. Rarely, the distal parts of the lower limbs can be affected. There is female predominance with a proportion of about 3:1. Histologically, mucin deposition is more often well circumscribed and involves the superificial and mid dermis, usually with a spared thin area in the papillary dermis (grenz zone). Typically, there is no accompanying fibroblast proliferation or collagen deposition (features usually seen in scleromyxoedema). Diagnosis of APPM relies on the recognition of the typical clinicopathological presentation and on the exclusion of associated systemic disease, thus a limited panel of ancillary tests is advisable, including thyroid function and serum protein electrophoresis.
Treatment is usually not necessary since the lesions are typically asymptomatic. Furthermore, there is no clearly effective treatment, although topical and intralesional corticosteroids, topical tacrolimus and pimecrolimus, laser and electrofulguration have been reported.

References:

1. Rongioletti F, Rebora A, Crovato F. Acral persistent papular mucinosis: a new entity. Arch Dermatol 1986; 122: 1237–1239.

2. Rongioletti F, Rebora A. Updated classification of papular mucinosis, lichen myxedematosus, and scleromyxedema. J Am Acad Dermatol 2001; 42: 273–281.

3. Luo DQ, Wu LC, Liu JH, Zhang HY. Acral persistent papular mucinosis: a case report and literature review. J Dtsch Dermatol Ges 2011; 9: 354-359.

4. Harris JE, Purcell SM, Griffin TD. Acral persistent papular mucinosis. J Am Acad Dermatol 2004; 51: 982-988.

Case 6

Agnes Carlotti

DIAGNOSIS: ANAPLASTIC KAPOSI SARCOMA

Clinical Summary:

- Man born in 1947 in Congo
- HIV+ since 1992 treated by Norvir, Kivexa, Isentress, Intelence, Viread, Prezista. CD4 470/mm3, CV VIH < 20 copies. Kaposi sarcoma (KS) since 1992 treated by Radiotherapy and bleomycine untill 1995 and in 2014 because of new lesions
- 2016 sudden onset of an infiltrative tumor of the right leg

Microscopic Features: sheets of epithelioid
and spindle cells exhibiting cytologic atypia, numerous mitoses and necrosis. The vascular nature of the tumor is confirmed by positive immunohistochemical staining
for the endothelial cell markers CD31, CD34 and D2-40 (Dako, Denmark) with a high MIB-1 index and immunohistochemical stain for HHV8 (Novocastra, UK) is positive in nearly 100% of tumoral cells.

Discussion: Anaplastic transformation of KS **,**first described in 1959
by Cox and Helwig(1), is a rare event. Few datas are available, the biggest series comprising 8 cases (2). Clinically, patients with anaplastic transformation of KS
have one or more rapidly progressive infiltrating tumors
The histological presentation is that of an undifferenciated tumor. Positivity of immunohistochemical stain for HHV8 is crucial for differential diagnosis from other malignant vascular tumors especially angiosarcoma.The clinical course differs from angiosarcoma, being usually locally aggressive without metastasis and may respond to chemotherapy and/or surgical treatment

References:

1. Cox FH, Helwig EB.Kaposi's sarcoma. Cancer 1959;12: 289-98.

2. Tourlaki A, Recalcati S, Boneschi V, Gaiani F, Colombo A, Mancuso R, Brambilla L. Anaplastic Kaposi's sarcoma: a study of eight patients. Eur J Dermatol. 2013 May-Jun;23(3):382-6.

Case 7

Bénédicte Cavelier-Balloy

DIAGNOSIS: ACANTHOLYTIC EXTRAMAMMARY PAGET DISEASE (EMPD) MOSTLY INTRAEPITHELIAL WITH INVASIVE FOCI ON THE COMPLETE RESECTION SPECIMEN.

Clinical Summary:

- 82 year old woman / ATCD : Thyroidectomy (nodules) , hysterectomy(fibroma), pulmonary Tuberculosis
- Large erosive painful plaque of vulva , perineum, pubis , inguinal folds with some small exophytic pedunculated lesions / Evolution : 10 years without adenopathy .No underlying associated carcinoma was discovered after explorations

Microscopic Features:

- Marked epithelial acanthosis with papillomatosis with intraepithelial atypical clear cell proliferation with important acantholysis without dermal invasion on biopsy
- Tumoral clear cells showed a strong expression of CK7 without expression of p63.

Discussion:

Acantholytic feature in Paget disease is reported rarely but most often in mammary than in extrammary sites of Paget disease but it may be more frequent than reported. Acantholytic EMPD affects more frequently men than women without relation to age of onset or duration of the disease, nor with associated underlying carcinoma.

Acantholytic EMPD that can take appearance of flat or vegetating lesions is sometimes reported as anaplastic Paget disease and seems to be associated with more common adnexal involvement and with dermal invasion but acantholysis in EMPD has no influence on postoperative recurrence.

Differential diagnosis must eliminate Pemphigus vegetans or Hailey-Hailey disease or a variant of syringocystadenocarcinoma papilliferum . It can be more difficult to eliminate morphologically a variant of clear cell (pagetoid) Bowen disease (variant of squamous cell carcinoma in situ/ classic VIN) Immunohistochemistry confirms usually the diagnosis as tumoral cells in Paget disease express Carcinoembryonic antigen (CEA) ,CK7 ,CK8,CAM5,2 while in pagetoid bowen disease, tumoral cells usually are CK7-, CK8- . But some Bowen disease cells can express CK7 or CK8 and p16 can also be express in EMPD.as in Bowen disease.In these cases, discovering of nuclear expression of p63 is very useful as it is observed in Bowen disease and not in Paget disease.

References:

1. Oh YJ et al .Ann Dermatol. 2011 Oct; 23(Suppl 2): S226–S230 Acantholytic Anaplastic Extramammary Paget's Disease: A Case Report and Review of the Literature

2. Zeng YP et al .Zhonghua Yi Xue Za Zhi. 2017 Feb 28;97(8):598-602 Clinicopathologic study of 56 cases of extramammary Paget disease with or without acantholysis.

Case 8
Heung Chong

DIAGNOSIS:
PLAQUE-LIKE MYOFIBROBLASTIC TUMOUR (OF INFANCY)

Clinical Summary:
A 12 month old boy presented with a firm lesion on the right flank which had developed at eight weeks of age. The lesion was a firm raised violaceous plaque, 25 x 8mm, with nodularity within the plaque as well as a few adjacent satellite nodules.

Microscopic Features:
A fairly well demarcated, moderately cellular, proliferation of bland spindle cells loosely distributed haphazardly and in short fascicles between collagen fibres in the dermis. The overlying epidermis is mildly acanthotic. There is slight involvement of the superficial subcutis with a "pushing" interface between the dermis and the subcutis. The spindle cells show strong, diffuse and uniformly positive staining for smooth muscle actin (SMA). Calponin was also variably positive. CD34 was negative.

Discussion:
Plaque-like myofibroblastic tumor (PLMT) is a rare dermal tumor with onset in the first four years of life. There are only ten cases in the literature to date. Although originally described as "PLMT of infancy" (1), recent publications have shortened the designation to PLMT in recognition that onset can also occur in early childhood (2,4). Most of the cases have occurred on the lower back, with one on the hip and another on the thigh. The lesions presented as firm pink, red or brown plaques which were often pruritic. Nodularity within the plaque was noted in some cases as well as satellite nodules outside the main plaque.

The histological appearances closely resemble a dermatofibroma (DF). However, it would be extremely rare for a DF to present as a plaque on the trunk of an infant. Unlike a DF, there is strong and diffuse staining for SMA in a PLMT. Multiple clustered dermatofibroma (MCDF), a rare variant of DF, shares some clinical and histological similarities to PLMT, although published cases of MCDF show no or minimal staining with SMA.

References:
1. Clarke JT et al. Plaque-like myofibroblastic tumor of infancy. *Pediatr Dermatol.* 2007; 24: E83-E87.

2. Marqueling AL et al. Plaque-like myofibroblastic tumor: report of three cases. *Pediatr Dermatol*. 2013; 30:600-607.

3. Alesini F et al. Plaque-like myofibroblastic tumor of infancy: a new care report and literature review. *Pediatr Dermatol*. 2017; 34(2):176-179.

4. Moulouguet I et al. Plaque-like myofibroblastic tumor: report of 4 Cases. *Am J Dermatopathol.* 2017; electronic publication ahead of print.

Case 9

David S. Cassarino, MD., Ph.D.

DIAGNOSIS
MYCOPLASMA INDUCED RASH & MUCOSITIS SYNDROME (EM-LIKE)

Clinical Summary:
A 14 year old male patient presented with a new onset diffuse vesiculobullous rash with cutaneous and oral, urethral, and conjunctival mucosal involvement, which was felt to be clinically highly suspicious for erythema multiforme (EM)/Stevens Johnson syndrome (SJS).

Microscopic Features:
Histologic examination showed a punch biopsy of skin with prominent subepidermal bullae associated with interface inflammation and numerous dyskeratotic keratinocytes. The dermal infiltrate was composed mostly of small, bland-appearing lymphocytes, with a few scattered histiocytes, neutrophils, and eosinophils. These findings were thought to be most consistent with EM/SJS, especially given the clinical history and diagnosis.

Discussion:
This case was initially diagnosed as EM/SJS, but subsequent clinical and laboratory investigations showed pulmonary mycoplasma infection and elevated serum anti-mycoplasma antibodies, consistent with "Mycoplasma-induced rash and mucositis (MIRM) syndrome". MIRM is a recently described and very rare syndrome, which clinically and histologically closely mimics EM/SJS, but usually has a more favorable clinical course and is typically treated with steroids and antibiotics. Therefore, Pathologists and Dermatologists should be aware of this diagnosis.

References:

1. Canavan TN, Mathes EF, Frieden I, Shinkai K. Mycoplasma pneumoniae-induced rash and mucositis as a syndrome distinct from Stevens-Johnson syndrome and erythema multiforme: a systematic review. J Am Acad Dermatol. 2015;72:239-45

2. Martínez-Pérez M, Imbernón-Moya A, Lobato-Berezo A, Churruca-Grijelmo M. Mycoplasma pneumoniae-Induced Mucocutaneous Rash: A New Syndrome Distinct from Erythema Multiforme? Report of a New Case and Review of the Literature. Actas Dermosifiliogr. 2016;107:e47-51.

Case 10

Reem El Bahtimi, MD

DIAGNOSIS: CUTANEOUS LYMPHADENOMA (ADAMANTINOID TRICHOBLASTOMA)

Clinical Summary:
26 year old man, Right cheek excision, Rule out BCC versus Cyst.

Microscopic Features:
The lesion is a well-circumscribed, un-encapsulated, intradermal nodule of variably-sized, round-to-irregularly shaped epithelial lobules embedded in a fibrous stoma. There is no connection to the epidermis. The lobules are rimmed by small, bland, flat-to-cuboidal basaloid cells with no peripheral palisading or retraction artifact. The lobules are composed of large cells admixed with small mature lymphocytes without plasma cells. The large cells exhibit vesicular nuclei, prominent nucleoli, and abundant clear-to-faintly eosinophilic cytoplasm. Mitoses are rare with, no atypical mitotic figures seen.

Discussion:
Cutaneous lymphadenoma is a benign adnexal neoplasm of folicular differentiation. It is considered to be a variante of nodular trichoblastoma with adamantinoid features. It is rare, 56 cases have been reported in the English literatura with a wide age range. Males are affected more often than females (about 1.5:1).
Most cases occur on the head, especially the cheek**.** The tumor frequently presents as a solitary, small flesh-colored, non-ulcerated, asymptomatic nodule.
The clinical impression is usually that of BCC, nevus or cyst.
This is a triphasic tumor composed of

1- Tumour lobules with an outer rim of non-palisading basaloid cells surrounding a central zone of large cells with clear cytoplasm and large vesicular nuclei.
2- Dense infiltrate of small, mature lymphocytes within the islands.
3- A loose-to-dense fibrous stroma, with no mucin retraction.

The main diffential diagnosis is with Basal cell carcinoma (BCC), Clear cell Syringoma, Ameloblastoma and lymphoepithelial-like carcinoma of the skin. Basal cell carcinoma usually shows the peripheral palisading with mucin retraction and is devoid of the lymphocytes. Syringoma, may have the clear cells, but shows the duct like structures simulating tadpoles and is also devoid of lymphocytes. Ameloblastoma, is a tumor of the mandible usually associated with an impacted tooth, but may occur in the buccal mucosa. It resembles a BCC with epithelial islands lined by basal cell nuclei showing reverse polarization. Lymphoepithelial-like carcinoma of the skin represents a poorly differentiated tumor with a very heavy admixture of lymphocytes, reminiscent of nasopharyngeal lymphoepithelioma.

References:

1. Betti R, Alessi E. Nodular trichoblstoma with adamantinoid features. *Am J Dermatopathol.* 1996;18:192-195.

2. Murphy M, Brierley T, Pennoyer J, et al. Lymphotropic adamantinoid trichoblastoma. *Pediatr Dermatolo*. 2007;24:157-161.

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4. Santa Cruz DJ, Barr RJ, Headington JT. Cutaneous lymphadenoma. *Am J Surg Pathol.* 1991;15;101-110.

5. Soyer HP, Kutzner H, Jacobson E, et al. Cutaneous lymohadenoma is adamantoid trichoblastoma. *Dermpatopathol: Pract & Conc*. 1996;2:32-38.

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Case 11

Lydia R. Essary, MD

DIAGNOSIS:
PRIMARY CUTANEOUS COCCIDIODOMYCOSIS

Clinical Summary:
A 30 year-old immunocompetent Hispanic female presented to clinic with a moderately itchy lesion on the right elbow that had been present for several months. The patient attributed the lesion to an insect bite which had preceded the lesion.

Microscopic Features:
A shave biopsy of the lesion showed a pseudoepitheliomatous hyperplasia and granulomatous infiltrate in the dermis with giant cells and small endospore-containing spherules recognizable as coccidioidomycosis. PAS was also positive for the organism. Of interest, there were also hyphal elements and the characteristic "barrel shaped" arthrospores of coccidioidomycosis.

Discussion: Coccidioidmycosis is a fungal disease endemic to the southwest USA, northern Mexico and parts of Central and South America.[1] While most cutaneous manifestations usually occur secondary to hematogenous dissemination from primary pulmonary disease, skin lesions are sometimes the only sign of clinical infection.[1-2] The areas most commonly affected are head, face (especially the nasolabial fold),extremities, shoulders, back, and chest.1 Therefore, clinical suspicion should be on high in patients presenting with such lesions especially if they are from or have traveled to an endemic region. Microscopically, the lesions are just as variable and difficult to recognize in the absence of abundant fungal organisms which results in multiple tissue sections and fungal stains needing to be obtained in order to identify the diagnostic spherules. A recent case series evaluating 118 biopsies from 104 patients noted that, "organisms that range from 5 to 75 μm in diameter and are usually found in the superficial dermis, but are frequently found in the reticular dermis. Epidermal ulceration with transepidermal elimination of spherules is a common finding, particularly in lesions with a prominent acute inflammatory component." [1] Rarely, the spherules can germinate into hyphae in the skin. In this case, there was evidence that this had occurred as there were hyphal elements and arthrospores visible in the cornified layer.

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Case 12

Maxwell A. Fung, MD

DIAGNOSIS: SCLERODERMOID GRAFT VERSUS HOST DISEASE WITH CUTANEOUS AMYLOID

Clinical Summary:
71, female, arm, history of acute myelogenous leukemia, status post allogeneic stem cell transplant with history of acute graft versus host disease, now presenting with thickened taut skin on the lower extremities, left arm, abdomen, rule out GVHD, scleroderma, amyloidosis, lymphedema.

Microscopic Features:
The punch biopsy shows:

- Pauci-inflammatory atrophic interface dermatitis. The absence of eosinophils is characteristic but not entirely specific.
- Cutaneous amyloid: pale eosinophilic globular deposits in the subepidermal/perijunctional zone associated with melanophages.
- Sclerosis of the deep reticular dermis. The sclerosis creates a somewhat prominent, straight interface between dermis and fat known as a positive "line sign"

Discussion:
This case represents an apparently rare but possibly under recognized subclinical phenomenon. Cutaneous amyloid derived from keratinocyte intermediate filaments typify primary macular amyloidosis, lichen amyloidosus, and nodular amyloid but may also be seen in a diversity of settings as a secondary phenomenon: basal cell carcinoma, trichoblastoma, pilomatrixoma, cylindroma, syringocystadenoma papilliferum, squamous cell carcinoma, carcinoma *in situ*, actinic keratosis, porokeratosis, seborrheic keratosis, melanocytic nevus, sarcoid, mycosis fungoides, Kimura's disease, angiolymphoid hyperplasia with eosinophilia, ichthyosis vulgaris, ILVEN, chronic cutaneous lupus erythematosus, keratosis lichenoides chronica, and GVHD.

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Case 13

Anjela Galan

DIAGNOSIS: GRANULOMA ANNULARE-LIKE METASTATIC BREAST CARINOMA

Clinical Summary:
A seventy-year-old female with lesions on the abdomen. Clinical differential diagnosis was not provided.

Microscopic Features:
Dermal cellular infiltrate of histiocytoid cells arranged between collagen bundles and in palisades. There is cellular atypia, focal pleomorphism, and some cells show intracytoplasmic lumina, and conspicuous nucleoli. Linear files of cells are focally noted. The collagen bundles are thickened. Staining with CK7 was positive in the dermal histiocytoid infiltrate.

Discussion:
Cutaneous metastases occur in <10% of patients with metastatic disease to any organ. Metastases from breast carcinoma comprise 23% of all cutaneous metastases and in women they are the most common (70%). Predilection sites include chest wall (39%), face (22.2%), neck (9%), scalp (13.5%), abdominal wall and other localizations (30.5%). The clinical presentation is variable and can mimic a range of inflammatory skin disorders, as well as benign or malignant primary cutaneous neoplasms.
The common histologic patterns include interstitial, intralymphatic, epidermotropic, and duct-forming. The infiltrate ranges from undifferentiated small cells with hyperchromatic nuclei and minimal cytoplasm, to large pleomorphic cells with abundant cytoplasm and intracytoplasmic lumina. Occasionally, histiocytoid features that mimic a histiocytic process, such as in present case, are seen. The histiocytoid pattern may be confused with granuloma annulare (GA), dermatofibroma or interstitial granulomatous dermatitis. Clues to differentiating breast carcinoma include increased dermal cellularity, cytologic atypia and pleomorphism, intracytoplasmic lumina, and single-file lining. Positive staining with CK7, ER/PR, mammoglobulin, GCDFP-15 confirms the diagnosis (NB: these stains are also positive in cutaneous adnexal tumors). History of breast carcinoma is helpful and was confirmed in our patient.
Rare reports of malignancies (lymphomas, leukemias, sarcomas, and breast carcinoma) mimicking GA clinically and histopathologically have been described.
The correct diagnosis is imperative for prognostic and treatment implications.

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Case 14

Joerg Schaller

DIAGNOSIS:
LIGHT CHAIN DEPOSITION DISEASE (LCDD)
(RANDALLS DISEASE)

Clinical Summary:
A 33-year-old healthy man presented himself with a discrete but recurring punctate purpura due to minor trauma.

Microscopic Features:
Histopathology showed deposits of globular, amorphous, eosinophilic, strongly PAS positive material around the vessels of the upper dermis. The material was lacking green-yellow birefringence in polarized light after Congo red staining and was negative in thioflavin stain. The deposits were immunoreactive with two of the three antibodies directed against lambda light chains and one of the two antibodies directed against kappa light chain. In electron microscopical analysis the material disclosed a fine granular pattern lacking the typical fibrillar structure of amyloid.

Discussion:
Light chain deposition disease (LCDD) was firstly described by Randall et al. in 1976 (1). It is the most common form of non-amyloid immunoglobulin deposition disease and differs from amyloidosis by the lack of typical birefringence in Congo red stain and a granular pattern in electron microscopy in contrast to the fibrillar structure of amyloid. The deposits are composed of kappa light chains in about 80% of the cases (2). About 50 % of LCDD cases are associated with multiple myeloma (MM). In an additional 30 to 40 % of cases a plasma cell dyscrasia/monoclonal gammopathy of uncertain significance is diagnosed (2-6). In up to 10% of patients with LCDD no monoclonal proteins are detectable in serum or urine (4-6).

More than 90 % of patients show a renal manifestation with light chain deposits at the basal membrane of the glomerula leading to renal failure within a few years without therapy (3-6). The second most affected organs are the heart and the liver with symptomatic manifestations (cardiomyopathy, hepatomegaly) in up to 30 % of patients (3-6).

There are only a few reports of skin manifestations in LCDD (7-11). The described clinical symptoms are basically skin nodules, erythematous plaques and purpura.

Histopathologically, there seem to be two major patterns. One is characterized by a more widespread but moderate deposition of small globular material restricted mainly to the upper dermis, clinically presenting as erythematous lesions and/or purpura. The other form shows a more localized deposition with an extensive deposition of globular material also involving the deep dermis and even the subcutaneous tissue presenting itself clinically as confluenting nodules and plaques.

Whether isolated cutaneous LCDD represent a localized form of the disease or are the first

signs of a not yet detectable systemic disease remains unclear. In any case, LCDD should be included in the spectrum of diseases with non-amyloid eosinophilic amorphous cutaneous deposition (11).

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Case 15

Katrin Kerl, Zürich

DIAGNOSIS: LEVAMISOL-INDUCED OCCLUSIVE VASCULITIS

Clinical Summary:
9-year old boy, with nephrotic syndrome. Purpuric papules on the dorsum of the hands, resolving spontaneously. 2-3 days later hemorrhagic lesions on both earlobes.

Microscopic Features:
Thrombotic occlusion of small cutaneous vessels with moderate inflammatory reaction

Discussion:
Vasculitis with purpura and necrosis of the earlobes is a well known side effect of levamisole adulterated cocaine abusus. It may also occur in children under long term treatment with levamisole for nephrotic syndrome. The typical manifestation is a thombotic and leucocytoclastic vaskulitis with circulating ANCA.

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