

“Pseudotumors” in Dermatology

Abstract

In dermatology, “pseudo” is often used as a prefix for entities resembling another standard condition, either morphologically or histopathologically. Correspondingly, “pseudotumor” is a term encompassing dermatological conditions which are not true proliferations, but either have a clinical resemblance to a known tumor (e.g., Pseudokaposi's sarcoma is actually a non-neoplastic condition) or a histopathological resemblance to one (e.g., pseudo-myogenic hemangioendothelioma named due to a histopathological resemblance between myocytes and tumor cells). Often such a nomenclature can create confusion and unnecessary alarm for both the physicians and the patients. Through this article we attempt to summarise “pseudotumors” in dermatology and classify them into clinical and histopathological “pseudotumors”, so as to produce a ready reckoner for this confusing nomenclature.

Keywords: *Pseudo-kaposi's sarcoma, pseudolymphoma, pseudomelanoma, pseudosarcoma, pseudotumors*

Introduction

The Greek term “pseudo” means false or disguised, while the word “tumor” means a swelling. In dermatology, “pseudo” is often used as a prefix for entities resembling another standard condition, either morphologically or histopathologically. Correspondingly, “pseudotumor” is a term variously used to refer to a clinical resemblance to a known entity in dermatology, like Pseudokaposi's sarcoma [non-neoplastic condition (acroangiokeratitis of Mali) resembles a neoplastic condition (Kaposi's sarcoma)] or a histopathological resemblance like pseudo-myogenic hemangioendothelioma [histopathological resemblance between myocytes and tumor cells]. Often such a nomenclature can create confusion and unnecessary alarm, hence this article attempts to summarise “pseudotumors” in dermatology and classify them as clinical and histopathological “pseudotumors”, so as to produce a ready reckoner for this confusing nomenclature.

For the purpose of this article, we tried to prepare a comprehensive list of well-known and less well-known conditions in dermatology texts. These are summarised in Table 1. Details regarding

their etiopathogenesis, clinical features, and management were searched and compiled. The salient conditions are summarised below (in an alphabetical order).

Calcifying fibrous pseudotumor

Also known as calcifying fibrous tumor; it is a rare, benign tumor which generally presents in children in the form of large, hard subcutaneous nodules [Figure 1]. The lesion can arise almost anywhere on the body with equal frequency.^[1]

Histologically, it demonstrates haphazardly arranged collagen fibres, interspersed with bland fibroblasts and areas of dystrophic calcification. There is a scant inflammatory infiltrate composed of lymphocytes and plasma cells.^[2] Surgical excision is the treatment of choice.^[1]

Cutaneous mycobacterial spindle cell pseudotumor

This is an abnormal reaction pattern to mycobacterial (rarely other) antigens arising in patients with iatrogenic or HIV associated immunodeficiency. This pattern replaces the normally expected granulomatous response, probably due to an ineffective cell mediated immunity. The lesions present most commonly as nodules over extremities, more so on the upper limbs than lower limbs [Figure 2].

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Table 1: Characteristic features of "Pseudotumors" in dermatology

"Pseudo"-nym	Real/Alternate name	Histopathological characteristics
Clinical "Pseudotumors"		
Eruptive pseudoangiomatosis	None	Upper dermal edema with dilated blood vessels lined by plump endothelial cells.
Molluscoid pseudotumors	None	Herniated fat and mucoid material, encased in fibrous capsule
Pseudoepitheliomatous keratotic and micaceous balanitis	None	Hyperkeratosis, parakeratosis, acanthosis and mild epidermal dysplasia
Pseudofibrokeratoma	Acral fibrokeratoma or acral digital fibrokeratoma	Hyperkeratotic acanthotic epidermis with extensive vertical collagen deposition in dermis
Pseudo-Kaposi's sarcoma	Acroangiokeratitis (of Mali)	Reactive hyperplasia of vessel wall
Pseudo-melanoma	Recurrent melanocytic naevus	Intra-epidermal melanocytes within the epidermis
Pseudosarcoma	Massive localized lymphoedema	Hyperkeratotic acanthotic epidermis, dilated dermal lymphatics and fibrosis
Pseudotumoral cutaneous sarcoidosis	Cutaneous sarcoidosis (a rare form)	Non-caseating epithelioid cell granulomas
Histopathological "Pseudotumors"		
Calcifying fibrous pseudotumor	Calcifying fibrous tumor	Haphazardly arranged collagen fibers, bland fibroblasts and areas of dystrophic calcification
Cutaneous mycobacterial spindle cell pseudotumor	Cutaneous tuberculosis (a rare form)	Dermal spindle cell infiltrate with intracellular AFB positivity
Cutaneous pseudolymphoma	Different names based on detailed classification	Reactive lymphoproliferative infiltrate in the dermis
Fibro-osseous pseudotumor of the digits	None	Reactive myofibroblastic proliferation with bone formation
Masson's pseudoangiosarcoma	Intravascular papillary endothelial hyperplasia	Intravascular papillary fronds, vascular dilation and obliteration of dermal/subcutaneous vasculature
Pseudomyogenic haemangioendothelioma	None	Rhabdomyoblast like tumor cells.
Pseudo-pyogenic granuloma	Epithelioid haemangioma or angiolymphoid hyperplasia with eosinophilia	Vascular channels, lined by endothelial cells and eosinophilic infiltration.
Pseudosarcoma of skin	Atypical fibroxanthoma	Dermal proliferation of spindle shaped cells which are desmin negative
Pseudosarcomatous fasciitis	Nodular fasciitis	Bundles of myofibroblasts and fibroblasts, with myxoid change and mucin deposition

The most common implicated organism is *Mycobacterium avium intracellulare*.^[3]

Histopathology shows a dermal lesion composed of spindle shaped cells with flat nuclei. It may occasionally extend into the subcutaneous fat. The inflammatory infiltrate is predominantly lymphocytic. Intracellular acid-fast bacilli can usually be demonstrated. Based on the features, a diagnosis of mycobacterial infection can be problematic, as characteristic histopathological features like caseating granulomas are absent. Tissue culture and PCR are often useful in species identification.^[4] Once diagnosed, the lesion is treatable with anti-tubercular therapy depending on the organism isolated.^[3]

Cutaneous pseudolymphoma

Cutaneous pseudolymphomas represents a group of conditions characterized by either a clinical or a histopathological resemblance to cutaneous lymphomas. These are reactive lymphoproliferations in response to a range of diverse stimuli including drugs, allergens, infectious agents and insect bites.^[5]

Cutaneous pseudolymphomas can be classified variously, based on their clinical morphology, etiologic agent, growth pattern or immunophenotype. Recently, a new classification proposed by Mitteldorf and Kempf classifies pseudolymphomas into four groups.^[6]

- Classical pseudolymphoma or Nodular pseudolymphoma:** It is the commonest type of cutaneous pseudolymphoma presenting with lesions resembling lymphoma clinically [Figure 3] and histopathologically. It includes Nodular B cell or T cell pseudolymphomas, and *Borrelia* associated lesions.
- Pseudo-Mycosis Fungoides:** This is a clinically and histologically diverse group with lesions mimicking mycosis fungoides or other cutaneous T-cell lymphomas. It includes lymphomatoid contact dermatitis, lymphomatoid drug reaction, and actinic reticuloid.
- Other pseudolymphomas:** This category includes various clinical entities reported in literature as pseudolymphoma, e.g., T-cell rich angiomatoid pseudolymphoma and cutaneous plasmacytosis.



Figure 1: Calcifying fibrous pseudotumour seen as a single hard nodule on the volar aspect of left hand

A special variant in this category is the HIV-associated cutaneous pseudolymphoma which clinically presents as intensely pruritic, scaly cutaneous nodules or plaques. Other presentations include erythroderma, and alopecia universalis. The disorder is seen in HIV positive patients with profound immunosuppression (CD4 count $<50/\text{mm}^3$) and weight loss. Peripheral blood eosinophilia is seen in majority of the patients.^[7] Histologically there is dermal infiltration of CD8+ cytotoxic T-lymphocytes with eosinophils. The



Figure 2: Cutaneous mycobacterial spindle cell pseudotumor presenting as multiple firm nodules present over left upper limb with secondary skin changes in a HIV positive female

lesions tend to improve satisfactorily upon initiation of anti-retroviral therapy (ART). Some recalcitrant lesions may necessitate initiating systemic immunosuppressants including methotrexate, the response to which is good.^[8]

d. **Intravascular pseudolymphomas:** It refers to a reactive infiltration of small lymphatic vessels with atypical lymphocytes which are benign and may be CD30+.

As these lesions are reactive lymphoproliferations, the treatment options include intralesional or topical immunosuppressants and physical destructive modalities.^[6]

Eruptive pseudoangiomatosis

These lesions are seen as a rare reactive response of the body to certain infectious agents, particularly viruses including enteric cytopathic human orphan (ECHO) virus, Epstein-Barr virus (EBV), Cytomegalovirus (CMV) and bites of certain insects. Clinically, the lesions present as acute onset, multiple, cherry-angioma like, completely blanchable papules over extremities, face and trunk, concurrent with the onset of systemic symptoms like fever, clinically resembling bacillary angiomatosis.^[9]

Histologically, there is presence of upper dermal edema with dilatation of blood vessels which are lined by plump endothelial cells. There is perivascular lymphocytic inflammation and few extravasated erythrocytes. No evidence of vascular proliferation is seen. The lesions



Figure 3: Classical or Nodular pseudolymphoma seen as single, erythematous to violaceous nodule present over left side of face in a young female



Figure 4: Fibro-osseous pseudotumour of the digit seen as ill-defined, hard, immobile subcutaneous nodule present over volar aspect of left thumb in a young male

undergo spontaneous resolution over a period of 2-3 months.^[10]

Fibro-osseous pseudotumor of the digits

This is a reactive myofibroblastic proliferation with bone formation arising on the digits. The condition arises in response to trauma. It most commonly presents in young adult males, involving the fingers, though toes can also be involved [Figure 4].^[11]

Histopathology shows the tumor to be composed of collagen fibers with myofibroblasts and fibroblasts. There may be areas of osteoid formation, mature bone formation, as well as focal myxoid changes.^[12] Surgical excision is the treatment of choice.^[13]

Masson's pseudoangiosarcoma

The condition is more appropriately termed intravascular papillary endothelial hyperplasia. It is a benign, non-neoplastic, vascular lesion which presents clinically as asymptomatic solitary nodule, arising over head and neck. It is more commonly seen in females. It probably represents an organizing thrombus.^[14]

Histologically, the tumor is characterised by intravascular papillary fronds resulting in vascular dilation and

obliteration of the lumen of dermal or subcutaneous vasculature. The papillary fronds are lined by bland endothelial cells and have a hyalinized collagenous core. Surgical excision is curative.^[15]

Molluscoid pseudotumors

This nomenclature is used for lesions seen in classical Ehlers Danlos Syndrome (Type I), which present as blue-grey spongy outgrowths over sites of pressure, like elbows and knees. Histologically, the lesions are composed of herniated fat and mucoid material, encased in a fibrous capsule. Older lesions may undergo dystrophic calcification. No treatment is effective, though surgical excision can be done for larger, distressing lesions.^[16]

Pseudoepitheliomatous keratotic and micaceous balanitis (PKMB)

This entity which presents clinically as thick scaly plaques or 'penile horns' involving the glans penis, is now considered to be a variant of lichen sclerosus et atrophicus. It is not associated with the human papilloma virus infection, but may be associated with verrucous carcinoma.^[17]

Histopathology shows an evidence of hyperkeratosis, parakeratosis, acanthosis and mild epidermal dysplasia. The

inflammatory infiltrate is composed of lymphocytes and eosinophils.^[18] Considering the pre-malignant status of the lesion due to risk of development of squamous cell carcinoma, chemical or physical destructive modalities are helpful.^[19]

Pseudofibrokeratoma

This lesion is classically also known as acral fibrokeratoma or acral digital fibrokeratoma. It is a rare, benign, fibrous tumor which presents as a keratotic papule over the digits, though it can also present elsewhere like lips, face and arms [Figure 5]. When present periungually, it can be a marker of underlying squamous cell carcinoma.^[20]

Histopathology demonstrates a hyperkeratotic epidermis with acanthosis. There is extensive collagen deposition in the dermis with fibers being vertically oriented, along the long axis of fibrokeratoma. Surgical excision is the treatment of choice.^[21]

Pseudo-Kaposi's sarcoma

The lesion is more appropriately termed acroangiokeratosis (of Mali). Its nomenclature is based on the clinical resemblance with Kaposi's sarcoma. It presents as red to violaceous, eczematous papules, nodules or plaques, seen over bilateral lower limbs most commonly [Figure 6].^[22] It has been associated with

chronic venous insufficiency, vascular anomalies like Klippel-Trenaunay syndrome, amputation stump and some coagulation disorders.^[23]

Histopathology demonstrates reactive hyperplasia of vessel wall. There is endothelial proliferation and extravasation of erythrocytes. Unlike Kaposi's sarcoma, perivascular cells stain negative for CD34 and HHV-8.^[23] Management of the underlying disease along with the use of topical immunosuppressants like tacrolimus, helps control the disease.^[23]



Figure 5: Pseudofibrokeratoma presenting as a small keratotic papule with collarette of scales present over right little finger in a young male



Figure 6: Pseudo-Kaposi's sarcoma seen as red to violaceous, eczematous papules, nodules and plaques over left lower limb

Pseudomelanoma

This term refers to a recurrent melanocytic naevus occurring after an incomplete surgical excision or trauma. The condition is more commonly seen in young women. It presents as hyper/hypopigmented macules with linear streaks or mottled pigmentation, arising in an area of scarring after a melanocytic naevus has been treated with an incomplete excision.^[24]

Histologically, there is presence of melanocytes within the epidermis overlying the scar tissue. Nests of naevomelanocytes containing abundant melanin and uniform nucleoli may also be seen. The lesion can be worrisome, thus mandating a complete excision with histopathological examination to rule out melanoma.^[25]

Pseudomyogenic haemangioendothelioma

It is a low-grade malignant vascular neoplasm. It is called a pseudo-tumor because the tumor often lacks histological vasoformative features; however, the tumor cells mimic epithelioid sarcoma or a myogenic tumor. Clinically, it presents as painful dermal or subcutaneous nodules, found over lower limbs in adult males.^[26]

Histologically, the tumor is composed of cells resembling rhabdomyoblasts with presence of an abundant pink cytoplasm. There is predominant infiltration by neutrophils. Cytological atypia and mitotic figures are rare. Immunohistochemistry shows positivity for pankeratin marker AE1/AE3 and FLI1 and ERG. The treatment of choice is surgical excision, which is also curative.^[27]

Pseudo-pyogenic granuloma

Also known as angiolymphoid hyperplasia with eosinophilia (ALHE) or epithelioid haemangioma, it is a benign locally proliferating lesion, which presents clinically as pink to red clustered papules or nodules around the ears or scalp margin, in young adults [Figure 7]. Some of the lesions may resemble pyogenic granuloma.^[28]

Histologically, the tumor is composed of vascular channels, lined by endothelial cells with abundant pink cytoplasm and vesicular nuclei. There is infiltration by lymphocytes and eosinophils are also prominent. Older lesions may show fibrosis. Surgical methods are suitable though radiotherapy is also effective.^[29]

Pseudosarcoma

Also known as massive localized lymphoedema, it is a form of localized lymphedema commonly encountered in patients who are morbidly obese.^[30] It can arise due to other causes also, and present as a localized mass. Though most commonly reported on lower limbs, any other site, including genitalia [Figure 8] can be involved depending on the cause of lymphatic obstruction. Lesions may also be seen on the medial aspect of thighs and lower abdomen. It



Figure 7: Pseudo-pyogenic granuloma seen as pink to red clustered papules or nodules around the scalp margin in a young male

occurs due to a combined effect of lymphedema along with gravity acting on the localized out-pouching of the skin.^[31]

Histopathology demonstrates features of lymphedema including hyperkeratosis, epidermal acanthosis, and dilated dermal lymphatics, along with areas of fibrosis. Management involves both physical and surgical lymphedema reduction with meticulous skin care.^[32]

Pseudosarcoma of the skin

More aptly known as atypical fibroxanthoma, it is a rare benign neoplasm seen in elderly Caucasian males, often after 70 years of age. It presents predominantly over the head and neck region as nodules or plaque.^[33] Chronic ultraviolet (UV) light exposure is a risk factor as evidenced by the presence of UV signature mutations, as well as its association with Li-Fraumeni syndrome and xeroderma pigmentosum.^[34]

Histologically, it is a dermal tumor, with the tumor cells showing varying degrees of pleomorphism, mitosis, solar elastosis and multinucleate giant cells. However, infiltration beyond the dermis, tissue necrosis and lymphovascular or perineural invasion are not seen. The tumor cells are spindle shaped, but stain negative for desmin. Unlike true sarcoma it rarely metastasizes, hence named "pseudosarcoma of the skin".^[35] Surgical excision is the treatment of choice.^[34]

Pseudosarcomatous fasciitis

The lesion is more popularly known as nodular fasciitis. It presents as a rapidly growing painful subcutaneous nodule affecting the forearms commonly. However, it can also



Figure 8: Pseudosarcoma or massive localized lymphoedema involving the right labia majora with secondary lymphangiectasia in an obese female

rarely involve the head and neck region as well as the oral mucosa.^[36]

Histopathology demonstrates a tumor composed of bundles of myofibroblasts and fibroblasts. Prominent myxoid change and mucin deposition give it the characteristic 'tissue culture like' appearance. Many histological variants of the lesion have been reported including ossifying fasciitis, periosteal fasciitis, cranial fasciitis, intravascular fasciitis, intradermal nodular fasciitis and intra-articular nodular fasciitis.^[37] Surgical excision is the treatment of choice, though intralesional corticosteroids have been used.^[38]

Pseudotumoral cutaneous sarcoidosis

This is a cutaneous form of sarcoidosis, where lesions present as cutaneous plaques or nodules, predominantly over trunk. Histopathology reveals typical non-caseating epithelioid cell granulomas.^[39] Pseudotumoral sarcoidosis has been reported to be associated with lymphomas especially non-Hodgkin's lymphoma. The cutaneous lesions may not respond well to the management of underlying malignancy.^[40]

Conclusion

To conclude, many lesions in dermatology are named based on their clinical or histopathological resemblance to other entities which may be more sinister. It is important to

understand the derivation of such terminology and have a holistic understanding of the clinical features and prognosis of such 'pseudo' lesions.

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Conflicts of interest

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