

Title

Author

Date of Submission: 09-05-2025

Date of Acceptance: 19-05-2025

I. Introduction

Most dermatoses have their origin within the skin or skin appendages presenting with characteristic clinical features. . Skin may be affected in many systemic conditions too because of alteration in the skin structure and/or physiology resulting from the common aetiopathogenesis. Very occasionally, we encounter a few conditions which present within the skin but the pathology is not indigenous to that site. Such anomalous, non-indigenous presence of any condition within the skin is called ectopic which pose a difficulty in their diagnosis and management. A high index of suspicion and awareness of the ectopic dermatologic conditions are indispensable pre-requisites. After thorough searching through standard dermatology textbooks and databases of pubmed, Scopus, Medline and Index medicus, we have compiled a list of such intriguing ectopic conditions. They have been classified based on their aetiologies (table 1) and their contents (table 2).

1. Cutaneous calcification: Deposition of calcium salts or calcification in skin can occur in various conditions. Broadly, it can be either calcinosis cutis (deposition of calcium phosphate) or osteoma cutis (deposition of calcium hydroxyapatite along with osteoblasts and osteoclasts). Calcinosis cutis has 4 main types: dystrophic, metastatic, idiopathic and iatrogenic.¹ Dystrophic form is commonly seen following trauma, connective tissue diseases such as systemic sclerosis and dermatomyositis and genetic diseases e.g., pseudoxanthoma elasticum and Ehler-Danlos syndrome. Hyperparathyroidism, renal failure and sarcoidosis are few causes of metastatic calcification. Idiopathic scrotal calcinosis also exists [Figure 1]. Osteoma cutis due to membranous ossification in dermis without cartilage which can be primary or idiopathic and secondary usually associated with chronic inflammatory diseases. Morphologically, idiopathic type may have 4 presentations: isolated, plate-like, widespread and multiple miliary osteoma cutis.¹
2. Cutaneous endometriosis: The presence of endometrial tissues in skin accounts for less than 1% of all cases of endometriosis. Cutaneous endometriosis can be primary (without any prior surgical history) or secondary (due to iatrogenic implantation of endometrial cells after surgery. Umbilicus is the most common site of primary cutaneous endometriosis, known as Villar's nodule.² Vascular or lymphatic migration were proposed for primary forms.
3. Cutaneous meningioma: It is characterized by meningotheial elements present in the skin or subcutaneous layer and also known as Meningeal heterotopia, rudimentary meningocele and meningeal hamartoma. It typically presents as a skin-colored nodule on the scalp over the midline, sometimes surrounded by a ring of long, dark, coarse hair (hair collar sign) and along the spine.³
4. Deep apocrine glands in Nevus sebaceous: In this condition, sebaceous glands are large and hyperplastic along with lack of terminal hair follicles and epidermal hyperplasia.⁴ Ectopic apocrine glands with their dilated ducts are often located deep in the dermis.
5. Ectopic breast tissue: Breast develop from two mammary ridges or milk lines which extend from the anterior axillary folds to inguinal folds. Normally, all the mammary ridges involute except in the pectoral region to form breasts. Persistence of any mammary ridge along the milk lines lead to ectopic breast tissue, also known as supernumerary or accessory breast.⁵ It may have both glandular tissue and nipple-areola complex, called as polythelia. Polymastia term is used if there is only glandular tissue. In 2/3rd cases, it is found just below the inframammary crease. Axillary ectopic breast has about 20% incidence. Occasionally, fibroadenoma, carcinoma or phyllodes tumor may develop within ectopic breast.
6. Ectopic desmoglein 3 expression: Paraneoplastic pemphigus (PNP) is an autoimmune bullous disease of the skin and mucous membranes mediated by the IgG autoantibodies which target the desmoglein 3 (Dsg 3) and plakins. Interestingly, ectopic expression of Dsg3 has been reported in respiratory epithelia which may be a reason of significant pulmonary involvement in the form of bronchiolitis obliterans in PNP.⁶ Any preceding lung injury can also lead to such ectopic expression of Dsg3.
7. Ectopic hair: In 'music box spine keratoderma', an idiopathic autosomal dominant keratinization disorder, spiny keratotic papules develop on margin of palms and soles, which represent ectopic hairs due to hair type keratinization.⁷

8. Ectopic hidradenitis suppurativa: Hidradenitis suppurativa (HS) is mainly seen in the flexures rich in apocrine glands. Humidity and friction are local predisposing factors. Rarely, it has been reported in areas devoid of apocrine glands such as thigh, chest, abdomen, amputated limb, dorsal foot, eyelids, knee and scalp.⁸ Knowledge of such presentations of HS is essential to avoid the misdiagnosis.
9. Ectopic nails: It is also called as onychoheterotopia which shows nail growth outside the digit's nail unit. It is mostly seen on the palmar aspect of 5th digit in its congenital form, sometimes being associated with Pierre Robin syndrome.⁹ In acquired form, trauma may result in ectopic nail growth, commonly on the dorsal aspect of the digit **[Figure 2]** **[Figure 3]**.
10. Ectopic teeth: Schinzel syndrome or ulnar-mammary syndrome is a rare inherited disorder characterized by bony abnormalities of upper limb and spine and apocrine glands dysfunction. In some cases, it may have ectopic upper canines.¹⁰ Second example is Treacher Collins syndrome which has many dental anomalies including ectopic maxillary canine and 1st molar.¹¹ Other characteristic facial features are convex facies, prominent nose and retruded chin, downslanting palpebral fissures, upper eyelid coloboma, absence of the lower eyelashes, external ear malformations, macrostomia and cleft palate.
11. Ectopic-extramammary Paget's disease (E-EMPD): It is a very rare ectopic apocrine gland neoplasm affecting areas that usually lack apocrine glands such as the chest, abdomen, thigh, eyelids, face, and external auditory canal. Aberrant transformation of stem cells to abnormal keratinocytes with apocrine markers at those locations may be the reason. Intraepidermal Paget's cells and dermal lymphocytic infiltrates are the typical findings similar to the EMPD.¹²
12. Fibrofolliculoma/trichodiscoma: These are benign, folliculosebaceous neoplasms of perifollicular mesenchymal tissues which mostly present as slightly raised, round or oval, skin colored, dome shaped papules on head and neck. Syndromic form is more common (Birt-Hogg-Dube syndrome) in which multiple lesions are seen. Solitary, non-syndromic forms are rare. The typical histopathology shows central acanthotic, dilated infundibulum containing keratins (with no hair shaft formation) surrounded by fibroepithelial proliferations and multiple radiating, thin, anastomosing bands of basaloid cells embedded in the mucinous stroma. Of note, mature adipocytes are often seen in the epithelial cords **[Figure 4]**.¹³ Folliculosebaceous cystic hamartoma also shows dermal adipocytes.
13. Fordyce spots: These are ectopic sebaceous glands commonly seen as asymptomatic multiple, discrete, barely elevated, yellowish papules around the vermilion border of the lips and within the oral mucosa **[Figure 5]**. Occasionally, it can be extensive requiring treatment. Some authors prefer to make the diagnosis of epidermisation of lip instead of Fordyce spots in some cases. Based on the dermoscopic examination, epidermisation of lip is better to be considered as closely set Fordyce spots.¹⁴
14. Hidradenoma papilliferum: It is a benign tumor of apocrine gland exclusively seen in females. It has also been described as ectopic forms on other sites such as head and neck, chest, and extremities which is attributed to the presence of heterotrophic and specialized version of apocrine glands in those areas.¹⁵
15. Nephrogenic rest: These are considered precursor of Wilms' tumor. It is usually seen as perilobar and intralobar lesions in the kidney. Rarely, it can be present in lumbosacral and sacrococcygeal region (frequently associated with spinal dysraphism), inguinal canal, and testis. In lumbosacral region, it may present as a soft polypoid mass covered by normal skin.¹⁶
16. Lingual thyroid: The ectopic presence of thyroid gland at the base of tongue is the result of failure of the normal descent of thyroid gland along a path from foramen cecum in the tongue to the final position.¹⁷ It usually remains asymptomatic but may enlarge and cause dysphagia or dyspnea. Hypothyroidism is a common problem in this condition.
17. Nasal glioma: Due to abnormal closure of fonticulus nasofrontalis, ectopic rest of neuroglial tissue are left extracranially. It is mostly present on or within the nose as a round, firm papule. Other less common sites are face, scalp, lip, tongue, oropharynx, nasopharynx and orbit.¹⁸ Intracranial connection is rare unlike an encephalocele.
18. Nevus lipomatosus cutaneous superficialis (NLCS): The presence of mature ectopic adipocytes in the dermis is the hallmark of this entity. The onset is at birth or in early childhood. Exact cause is unknown but there are multiple hypotheses such as adipose metaplasia in the course of dermal degenerative changes, developmental displacement of adipose tissues or adipogenesis from perivascular mononuclear cells differentiating into lipoblasts **[Figure 6]**. Clinically, it can be multiple, grouped skin-colored, pedunculated nodules or solitary dome-shaped sessile papule or nodule.¹⁹
19. Parameatal cysts: It is considered as embryological anomaly that is likely thought to develop from ectopic urethral mucosa or ectopic periurethral Littre's glands. It is located ventrally in midline anywhere from the urethral meatus to the perineum **[Figure 7]**. The mechanism is not clearly understood. Following hypotheses have been proposed about its origin: (1) the persistence of cystic spaces, during the process of preputial separation from glans, (2) urethral epithelial remnants left secondary to incomplete fusion of median raphe, (3) outgrowths of urothelium after primary closure of the raphe, (4) ectopic periurethral

glands of Littre and/or (5) from blockage of paraurethral ducts which may occur secondary to infection or trauma in some cases.²⁰

20. Umbilical polyp: It is a congenital ectopic remnant of intestinal mucosa at umbilicus due to incomplete distal closure of the omphalomesenteric duct, characterized by the presence of a firm, reddish, half-moon shaped, discharging polypoid lesion [Figure 8].²¹

References:

- [1] Niebel D, Poortinga S, Wenzel J. Osteoma Cutis And Calcinosis Cutis: "Similar But Different". J Clin Aesthet Dermatol 2020;13(11):28-31.
- [2] Loh SH, Lew BL, Sim WY. Primary Cutaneous Endometriosis Of Umbilicus. Ann Dermatol 2017;29(5):621-625.
- [3] Miedema JR, Zedek D. Cutaneous Meningioma. Arch Pathol Lab Med. 2012;136(2):208-11.
- [4] Simi C M, Rajalakshmi T, Correa M. Clinicopathologic Analysis Of 21 Cases Of Nevus Sebaceus: A Retrospective Study. Indian J Dermatol Venereol Leprol 2008;74:625-627.
- [5] Gajaria PK, Maheshwari UM. Fibroadenoma In Axillary Ectopic Breast Tissue Mimicking Lymphadenopathy. J Clin Diagn Res 2017;11(3):ED01-ED02.
- [6] Takahashi H, Kouno M, Nagao K, Et Al. Desmoglein 3-Specific CD4+ T Cells Induce Pemphigus Vulgaris And Interface Dermatitis In Mice. J Clin Invest 2011;121:3677.
- [7] Mohtashim M, Amin S, Adil M, Tabassum H. Localized Music Box Spiny Keratoderma: A Rare Variant. Indian Dermatol Online J 2020;11:842-3.
- [8] Rondags A, Diercks GF, Werker PMN, Jonkman MF, Horváth B. Ectopic Hidradenitis Suppurativa On The Dorsal Foot Of A Road Maker. JAAD Case Rep 2017;3(5):429-431.
- [9] Khurana A, Sehgal VN. Acquired Ectopic Nail Or Onychoheterotopia. Indian J Dermatol 2015;60(6):621-622.
- [10] Ramirez, R. N., & Kozin, S. H. (2014). Ulnar Mammary Syndrome. J Hand Surg Am 2014;39(4):803-805.
- [11] Ramos Zanchetta LM, Jost P, Peixoto AP, Costa B, Da Silva Dalben G. Dental Anomalies In Individuals With Treacher Collins Syndrome – Tomographic Analysis. JSM Head Face Med 2018;3(2): 1012.
- [12] Ximena E, Del Puerto C, Mario P, Sergio G. Ectopic Extramammary Paget's Disease On The Face. Indian J Dermatol Venereol Leprol 2012;78(6):760-2.
- [13] Kacerovska D, Michal M, Kazakov DV. Trichodiscoma With Lipomatous Metaplasia And Pleomorphic Stromal Cells. J Cutan Pathol 2010;37:1110-1.
- [14] Neema S, Radhakrishnan S, Shelly D. Transmigration Or Epidermization Of Lip: Does An Entity Exist?. Indian Dermatol Online J 2020;11:1001-2.
- [15] Shukla P, Malaviya AK. Ectopic Hidradenoma Papilliferum Of Eyelid: A Rare Entity With Diagnostic Challenge. Indian J Pathol Microbiol 2018;61:287-9.
- [16] Horenstein MG, Mancini EA, Walker AB, Dehner LP. Lumbosacral Ectopic Nephrogenic Rest Unassociated With Spinal Dysraphism. Am J Surg Pathol 2004;28(10):1389-92.
- [17] Kumar SS, Kumar DM, Thirunavukarasu R. Lingual Thyroid-Conservative Management Or Surgery? A Case Report. Indian J Surg 2013;75(Suppl 1):118-119.
- [18] Krishna L G, Uppoor R, Rao K N, Harish K. Heterotopic Central Nervous Tissue - Nasal Glioma : A Case Report. Indian J Radiol Imaging 2005;15:511-6.
- [19] Lima CDS, Issa MCA, Souza MB, Góes HFO, Santos TBPD, Vilar EAG. Nevus Lipomatosus Cutaneous Superficialis. An Bras Dermatol 2017;92(5):711-713.
- [20] Aggarwal P, Aggarwal K, Amrani A, Jain VK. Parameatal Urethral Cyst. Clin Dermatol Rev 2018;2:44-5.
- [21] You Y, Yang X, Hao F, Zhong B. The Umbilical Polyp: A Report Of Two Cases And Literature Review. Int J Dermatol 2009;48(6):630-632.

Legends:

- Figure 1: multiple scrotal calcified nodules
 Figure 2: fully formed ectopic nail on dorsal aspect
 Figure 3: partially formed ectopic nail
 Figure 4: Fibrofolliculoma showing mature adipocytes in dermis
 Figure 5: Fordyce spots on upper lip
 Figure 6: Mature dermal adipocytes in Nevus lipomatosus cutaneous superficialis
 Figure 7: Parameatal cyst
 Figure 8: Umbilical polyp

Table 1: Aetiological classification of ectopic cutaneous conditions

Idiopathic	Developmental origin				Multidermal	Secondary to trauma, inflammatory or neoplastic conditions
	Endodermal	Mesodermal	Ectodermal			
Primary osteoma cutis	Umbilical polyp	Lingual thyroid	Surface ectoderm	Neuro-ectoderm	Both ectodermal and mesodermal	Secondary cutaneous endometriosis
Idiopathic calcinosis cutis	Parameatal urethral cyst	Subcutaneous nephrogenic rest	Ectopic teeth	Cutaneous meningioma	Ectopic breast's tissue	Ectopic Dsg 3 expression in respiratory epithelia
Primary cutaneous endometriosis			Ectopic nail	Nasal glioma	Fibrofolliculoma /trichodiscoma	Post-traumatic ectopic nails on dorsum of hands or feet
Ectopic hair			Deep apocrine glands in Nevus sebaceous			Secondary osteoma cutis
Ectopic hidradenitis suppurativa			Fordyce spots			Dystrophic calcinosis cutis
			Ectopic EMPD			Parameatal urethral cyst (after surgery)
			Ectopic hidradenoma papilliferum			

Table 2: Classification based on the ectopic contents

Deposition or expression of acellular contents	Ectopic glandular tissue	Ectopic adipose tissue
i. Calcification - Osteoma cutis and Calcinosis cutis ii. Keratinization - hair type keratinization in music box spiny keratoderma iii. Ectopic Dsg 3 expression in respiratory epithelia	i. Apocrine glands – a. deep apocrine glands in nevus sebaceous b. Ectopic Hidradenoma papilliferum c. Ectopic Hidradenitis suppurativa d. Ectopic EMPD ii. Sebaceous glands – Fordyce spots iii. Mammary glands – Ectopic breast iv. Thyroid gland v. Endometrial glands vi. Periurethral Littre's glands	i. Nevus lipomatosus cutaneous superficialis ii. Fibrofolliculoma/trichodiscoma iii. Folliculosebaceous cystic hamartoma
		Ectopic neuromeningeal tissue
		i. Nasal glioma
		ii. Cutaneous meningioma
		Ectopic visceral tissue
		i. Subcutaneous nephrogenic rest
		ii. Umbilical polyp
		Other ectodermal appendages
		i. Ectopic teeth (mostly canines) ii. Ectopic nails