Knuckle lesions in inherited and acquired disorders

Abstract
Skin lesions occurring over the knuckles can be a primary or characteristic manifestation of a disorder. Characteristic knuckle lesions may also be important cutaneous features of various internal disorders when they serve as useful clinical pointers, as well as may speak of the disease severity in certain instances. Furthermore, knuckle lesions also speak of various external factors as the underlying cause of the disease/lesions, such as trauma — occupational or otherwise, and contact dermatitis. Although knuckles essentially imply dorsal aspect of the metacarpophalangeal joints, many of the lesions described as those ‘involving the knuckles’ are seen over the proximal and/or less frequently, the distal interphalangeal joints as well. This review presents a compilation of various inherited and acquired dermatoses and dermatological manifestations of various internal disorders associated with different forms of knuckle lesions.

**Keywords:** Acquired disorders, inherited disorders, knuckles

Involvement of knuckles is seen in a variety of primarily cutaneous and internal disorders. The relevance of knuckle lesions lies in the fact that they may be the predominant, characteristic, or exclusive site of involvement reflecting on to the nature of the diseases that favour exposure, repetitively trauma-prone areas, or areas coming repeatedly in contact with offending agents. Furthermore, certain knuckle lesions form an important component of many genodermatoses and also serve as cutaneous markers of internal diseases. Table 1 lists the different forms of knuckle lesions seen in various disorders.

**Knuckle Thickening (Knuckle Pads)**
Knuckle pads are a form of superficial fibromatoses characterized by thickened skin-colored papulonodules predominantly involving the proximal interphalangeal joints, commonly seen in the Whites. They generally appear between 15 and 30 years of age, slowly enlarge and persist throughout life.[1,2] Knuckle pads can be broadly grouped into idiopathic and those in association with inherited and acquired disorders [Table 2]. These ‘true’ knuckle pads are differentiated from the ‘pseudo-knuckle pads’ by their development being spontaneous and unrelated to trauma, being asymptomatic, and being persistent. The ‘pseudo-knuckle pads’ are essentially callosities, developing due to repetitive trauma or friction. They are seen in certain clinical conditions and as occupational or sports related dermatoses. They typically regress upon removal of the precipitating factors.[2]

**Idiopathic knuckle pads**
Isolated knuckle pads are commonly sporadic cases. Isolated familial form, often inherited as autosomal dominant trait has also been described but is quite rare and most of the familial forms of knuckle pads are associated with other inherited disorders as discussed below and outlined in Table 2.[2,3]

**Knuckle pads associated with inherited disorders**
Most of the familial forms of knuckle pads are associated autosomal dominant palmoplantar keratodermas summarized in Table 3.[4] Other familial disorders in which the knuckle pads can be seen are described below.

**Camptodactyly**
Camptodactyly refers to uni- or bilateral fixed flexion deformity of the proximal
interphalangeal joint of little fingers. Many cases are sporadic but autosomal dominant inheritance has been described as well. Association with knuckle pads has been described and a plausible genetic basis has been proposed as well.\[5\-8\]

**Acrokeratoelastoidosis of Costa**

Acrokeratoelastoidosis of Costa is a rare disorder characterized by discrete and confluent keratotic papular lesions, typically involving the sides of the fingers and hands. The childhood form has an autosomal dominant pattern of inheritance and adult onset forms are usually sporadic.\[9\] Knuckle pads and knuckle pad-like keratosis have been described in association with the disease.\[10,11\]

**Keratosis punctata of palmar creases**

Keratosis punctata of palmar creases is an autosomal dominant or sporadic disorder characterized by multiple, well-defined punctate pits conspicuously involving the palmar creases. This benign entity may be associated with striate keratoderma, Dupuytren contracture, and knuckle pads. It should be differentiated from keratosis punctata palmoplantaris, which is characterized by multiple palmoplantar pits and being associated with atopy, nail dystrophy and colorectal malignancy.\[12,13\]

**Pseudoxanthoma elasticum**

Pseudoxanthoma elasticum is an autosomal recessive disorder of connective tissue characterized by elastorrhexia
with progressive calcification of elastic fibers predominantly of the skin, retina, and cardiovascular systems.\textsuperscript{[14]} Knuckle pads involving the thumb have also been described in association with the disorder.\textsuperscript{[15]}  

**Peeling skin, leukonychia, acral keratoses, cheilitis, and knuckle pads syndrome**

The peeling skin, leukonychia, acral keratoses, cheilitis, and knuckle pads (PLACK) syndrome is an autosomal recessive form of generalized peeling skin syndrome affecting the pediatric age group and characterized by generalized peeling, punctate keratoses on the palms and soles, dorsal aspect of the toes, leukonychia, cheilitis, and knuckle pads. Other abnormalities described in various reports include follicular hyperkeratosis, facial telangiectasia, woolly hair, and sparse eyebrows and eyelashes.\textsuperscript{[16,17]}

**Knuckle pads associated with acquired disorders**

**Fibromatoses**

Knuckle pads are seen in association with superficial fibromatoses, such as Dupuytren contracture, Ledderhose disease, and Peyronie’s disease. Knuckle pads are also seen

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**Table 2: Knuckle pads in various dermatoses**

| Knuckle pads | Associated disorders |
|--------------|----------------------|
| Inherited disorders | *Idiopathic (familial and sporadic)* |
| | *Associated with inherited palmoplantar keratodermas* |
| | Epidermolytic palmoplantar keratodermas |
| | Loricrin keratoderma |
| | Mal de Meleda |
| | Gamborg-Nielsen palmoplantar keratoderma |
| | Vohwinkel syndrome |
| | Bart-Pumphrey syndrome |
| | Palmoplantar keratoderma and deafness syndrome |
| | Striate palmoplantar keratoderma |
| | *Associated with other inherited disorders* |
| | Camptodactyly |
| | Acrokeratolastoidosis |
| | Keratosis punctata of plantar creases |
| | Pseudoxanthoma elasticum |
| | Peeling skin, leukonychia, acral keratoses, cheilitis and knuckle pads (PLACK) syndrome |
| Acquired disorders | *Associated with fibromatosis* |
| | Peyronie’s disease |
| | Ledderhose disease |
| | Dupuytren’s contracture |
| | Polyfibromatosis syndrome |
| | Pachydermodactyly |
| | *Associated with other disorders* |
| | Seborrheic dermatitis |
| | Finger clubbing |
| | Oral leukoplakia |
| | Glossitis |
| | Vitamin A deficiency |
| | Esophageal cancer |
| | *Iatrogenic* |
| | Phenytoin treatment |
| **Traumatic or friction associated (pseudo-knuckle pads)** | Occupational: In carpet layers, tailors, sheep shearers, live chicken hangers, pillar knockers |
| | Athletes: Boxers, surfers, football players, other sports (athletes nodules) |
| | Bulimia nervosa (Russel’s sign) |
| | Obsessive compulsive disorders (chewing pads, habitual knuckle cracking) |
as a component of polyfibromatosis syndrome associated with keloids and fibromatosis involving the penile and palmoplantar tissues.[1,3] Knuckle pads are also described in pachydermodactyly.[18,19]

**Other disorders**

Knuckle pads have also been reported in association with finger clubbing, oral leukoplakia, glossitis, seborrheic dermatitis, vitamin A deficiency [Figure 1b], and phenytoin therapy.[2,3] Knuckle pads have also been reported in esophageal cancer with oral leukoplakia and keratosis pilaris.[20]

**Pseudo-knuckle pads**

Pseudo-knuckle pads are callosities [Figure 2] developing as a result of repeated trauma, disappearing gradually on removal of the precipitating factors. They are typically seen in two settings – occupational or sports related, and associated with disorders like obsessive compulsive disorder and bulimia nervosa as outlined in Table 2.[2,3,21]

**Hyperkeratotic lesions**

**Palmoplantar keratoderma**

Disorders like Vöhwinkel syndrome, Greither syndrome, Mal de Meleda, and Papillon-Lefevre syndrome [Figure 3a] exhibit hyperkeratotic knuckle lesions. Such lesions in Vöhwinkel syndrome typically have a stellate aspect (starfish keratosis) and are prone to develop keratinocytic skin cancers.[4]

**Focal acral hyperkeratosis**

Focal acral hyperkeratosis is identical to acrokeratoelastoidosis in terms of inheritance and clinical appearance. The distinguishing feature is the dermal elastorrhexis in acrokeratoelastoidosis, absent in focal acral hyperkeratosis. Lesions on the dorsal aspect of the hand may be seen predominantly involving the knuckles.[22]
Acral acanthosis nigricans

The acral form of acanthosis nigricans is a distinctive entity known as acral acanthotic anomaly. It is characterized by velvety keratotic thickening and hyperpigmentation of the knees, elbows, dorsal aspect of feet, and dorsal aspect of the hands, principally involving the knuckles [Figure 3b]. Although considered as a benign disorder of the darker skin and without any associations, it has been observed in diffuse progressive systemic sclerosis, obesity with increased leptin levels, and in malignancies like dermatofibrosarcoma protuberans, lymphoma, and gastric adenocarcinoma.

Inflammatory dermatoses

Various infectious and noninfectious inflammatory dermatoses can involve the knuckles as keratotic lesions in the form of isolated lesions or as extension from the hand. The examples include hypertrophic lichen planus, palmoplantar psoriasis [Figure 4a], and pityriasis rubra pilaris. Being exposed sites, viral warts and inoculation site cutaneous tuberculosis [Figure 4b] commonly involve the knuckles.

Papulonodular Lesions

Rheumatoid nodules

Rheumatoid nodules are the most common extra-articular feature of rheumatoid arthritis seen in about 30% of the cases, frequently associated with high titers of rheumatoid factor and severe arthritis. They commonly affect periarticular bony prominences especially around the elbows, and dorsa of the hands involving the metacarpophalangeal and interphalangeal joints. Rheumatoid nodules are generally asymptomatic as opposed to ‘accelerated rheumatoid nodulosis’ which is characterized by sudden development of multiple painful nodules, predominantly involving the hands and feet following methotrexate therapy. Presence of rheumatoid nodules is a predictor of increased risk of cardiovascular disease and vasculitis. Rheumatoid nodules may also be seen in rheumatic fever, systemic lupus erythematosus, ankylosing spondylitis, granuloma annulare, chronic active hepatitis, and Felty syndrome. They may occasionally occur in healthy individuals.

Huntley papules (in diabetes mellitus)

Huntley papules (diabetic finger pebbles) represent one of the manifestations of diabetic cheiroarthropathy due to irreversible cross-linking of dermal collagen along with accumulation of advanced glycation end products. They are characterized by minute skin-colored grouped papules on the knuckles and extensor aspects of the fingers. Diabetic cheiroarthropathy is of significance as the affected patients have an increased risk of renal and retinal vascular disease, and increased incidence of frozen shoulder and Dupuytren contracture.

Bouchard and Herbenden nodes (in osteoarthritis)

Bouchard and Herbenden nodes are seen as localized skin colored nodules that essentially are osteophytes.
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involving the proximal and distal interphalangeal joints, respectively. They have a strong familial predilection and their presence indicates a more severe form of osteoarthritis. Although these nodes are strong indicators of interphalangeal joint osteoarthritis, Herbenden nodes were found in more than 60% of osteoarthritis of the knee and were indicators of disease progression as well.[38-40]

**Dupuytren nodules (in Dupuytren contracture)**

In contrast to the knuckle pads in Dupuytren contracture (see above), the Dupuytren nodules (dorsal Dupuytren nodules) are specific to the disease. Unlike the knuckle pads which are thickenings of the skin over the knuckles, Dupuytren nodules are freely mobile subcutaneous nodules and are associated with a strong diathesis.[41] Some authors however believe it is unnecessary to differentiate between these nodules and the knuckle pads observed in the disease.[42]

**Calcinosis cutis**

Calcinosis cutis involving the knuckles is usually seen in scleroderma (the CREST syndrome – calcinosis, Raynaud phenomenon, esophageal dysmotility, sclerodactyly, and telangiectasia) and dermatomyositis as a form of dystrophic calcification [Figure 5].[43] Cutaneous calcinosis in systemic sclerosis develops many years after the disease onset. In childhood dermatomyositis, it is a much earlier and an important diagnostic feature of the disease.[44]

**Gouty tophi**

Gouty tophi are the pathognomonic cutaneous manifestations of chronic tophaceous gout characterized by firm yellow-white colored papules and nodules located in the deep dermis or subcutaneous tissue. Most common sites are the bony prominences (especially the knuckles

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**Figure 3: Hyperkeratotic knuckle lesions in inherited (a), Papillon-Lefevre syndrome) and acquired (b), acanthosis nigricans) disorders**

**Figure 4: Hyperkeratotic knuckle lesions of psoriasis (a) and tuberculosis verrucosa cutis (b)**
and interphalangeal joints) and auricular pinna. Differential diagnoses for gouty tophi include rheumatoid nodules, Herbenden and Bouchard nodes, calcinosis cutis and granuloma annulare.[45,46]

Xanthomata

The tuberous, tendinous, and eruptive xanthomata can involve the knuckles, when they have to be differentiated from gouty tophi, rheumatoid nodules, Bouchard and Herbenden nodes, and calcinosis cutis. Tuberous and tendinous xanthoma are firm, well-defined subcutaneous papules, and nodules with a yellowish hue. The former commonly involves the knees, elbows, and knuckles, and the latter involves the Achilles tendon and tendons on the dorsal hands. Eruptive xanthomata are generalized yellow-orange papular lesions. Tuberous xanthoma is commonly associated with type III hyperlipoproteinemia, tendinous forms are commonly seen in familial hypercholesterolemia but may also be seen in cerebrotendinous xanthomatosis, sitosterolemia as well as in acquired causes of hyperlipidemia, such as diabetes, obstructive liver diseases, and myxedema. Eruptive xanthomata is associated with hypertriglyceridemia due to uncontrolled type II diabetes, chronic renal failure and associated with systemic retinoid, oral contraceptives and steroids therapy.[45,47-51]

Granuloma annulare

The localized forms of granuloma annulare, such as the classical annular, subcutaneous, and perforating types favor distal extremities especially the dorsal hands and fingers (especially knuckles). The classical lesions are smooth erythematous or skin-colored papular and annular lesions [Figure 6], the subcutaneous forms are deep seated skin-colored nodules and the perforating ones appear as papules or nodules with central umbilication or ulceration. The subcutaneous forms resemble rheumatoid nodules, both of which exhibit palisading granulomatous reaction pattern on histology. The granulomas in rheumatoid nodules are deep seated as opposed to the much superficial location in granuloma annulare. The essential differentiating feature, however, is the presence of prominent mucin in granuloma annulare which is minimal to absent in rheumatoid nodule.[52,53]

Scleromyxedema

Scleromyxedema is a rare multisystem progressive fibrosing dermopathy associated with monoclonal gammopathy which induces increased fibroblast proliferation leading to excessive mucin deposition in various tissues including the skin. The chief cutaneous manifestation is the generalized induration of the skin with overlying waxy papules. Induration of the skin over the proximal interphalangeal joints with central depression (donut sign) is a characteristic feature. Extracutaneous disease (e.g., mucinous cardiomyopathy, dermato-neuro syndrome) may be fatal at times.[54,55]

Palisaded neutrophilic and granulomatous dermatitis

Palisaded neutrophilic and granulomatous dermatitis is a form of reactive neutrophilic granulomatous dermatitis usually associated with rheumatoid arthritis or systemic lupus erythematosus. It is clinically characterized by erythematous or skin colored papules or nodules with central umbilication or ulceration with crusting, principally
involving the extensor aspects of the upper extremities, predominantly the dorsal aspects of the hands and knuckles.\cite{56,57}

**Erythema elevatum diutinum**

Erythema elevatum diutinum is an uncommon chronic cutaneous small vessel vasculitis characterized by erythematous to violaceous papules, plaques, or nodules. The lesions typically involve the acral skin over the joints, such as elbows, knees, knuckles, and ankles and are distributed symmetrically and is associated with infections, autoimmune disorders and malignancies, or may be idiopathic.\cite{58-60}

**Frictional lichenoid dermatitis**

Frictional lichenoid dermatitis is a chronic recurrent disorder of childhood associated with outdoor activities commonly seen in summer and spring. The lesions are characterized by monomorphic discrete and coalescent lichenoid papules predominantly over the elbows, knees, and dorsal aspect of hands and fingers [Figure 7]. There is frequent association with atopic diathesis. A similar disorder in adults is designated as dermatosis papulosa adultorum.\cite{61,62}

**Others**

As the lepra bacilli favour cooler areas, nodular lesions in lepromatous leprosy can predominantly involve the acral areas such as the dorsum of hand and knuckles [Figure 8].\cite{63} Hemispherical pitted papules are described over the knuckles following frostbite or in acrocyanosis.\cite{64-66} Papular thickening of the skin characterized by a leathery or pebbly appearance, most prominently over the knuckles and nose is seen as a chronic cutaneous manifestation in erythropoietic protoporphyria.\cite{67}

**Erythematous Papulosquamous Lesions**

**Gottron papules and sign (in dermatomyositis)**

The Gottron papules are one of the pathognomonic features of dermatomyositis. They are characterized by erythematous or violaceous umbilicated scaly papules over the metacarpophalangeal and interphalangeal joints [Figure 9]. The ‘Gottron sign’ corresponds to macular pink to violaceous erythema over the interphalangeal joints.\cite{68} They can also occur over the elbows, knees, ankles, and rarely over the toes.\cite{69} ‘Inverse’ Gottron papules refer to erythematous scaly or keratotic papules seen over the palmar aspect of the interphalangeal joints and are associated with anti-melanoma differentiation associated gene 5 (MDA5) antibodies and interstitial lung disease.\cite{70,71} Lesions resembling Gottron papules without any features of dermatomyositis have been described in systemic lupus erythematosus as Gottron-like papules.\cite{72}

**Hydroxyurea dermopathy**

Hydroxyurea dermopathy (hydroxyurea associated dermatomyositis-like eruption) is associated with long-term hydroxyurea therapy, characterized by typical dermatomyositis-like cutaneous lesions without any systemic manifestations that resolve on cessation of the drug. The manifestations include diffuse xerosis, Gottron papules, and heliotrope rash. It is suggested that the disorder may represent a premalignant precursor for nonmelanoma skin cancers associated with hydroxyurea as focal confluent expression of p53 has been observed in the basal layer attributable to the antimetabolite effect of hydroxyurea together with ultraviolet exposure.\cite{73,74}
Hand eczema

Eczematous lesions due to various causes affecting the hands may extend on to or involve the knuckles prominently. Examples include adult atopic eczema which is characterized by symmetrically distributed lichenified inflamed lesions, localized to the back of the hands and fingers (especially knuckles) [Figure 10a], and on the flexor aspects of the wrists.[73] Occupational hand dermatitis is often characterized by involvement of the dorsal hands as well [Figure 10b].[76]

Scabies

Owing to the roughness and wrinkling of the skin over the knuckles, this site is also a favored area for scabetic lesions [Figure 11].[77,78] Erythematous scaly papular lesions on the knuckles resembling Gottron papules along with periungual erythema have been described due to prolonged topical steroid use in a case of scabies.[79]

Ulcerative lesions

Chrome ulcers

Chrome ulcers or chrome holes are cutaneous ulcers occurring in industrial workers due to heavy exposure to chromium, typically involving the base of fingernails and knuckles. The ulcers are circular and appear punched-out with raised indurated edges and the floor covered with exudates. Chrome ulcers also affect nasal septum and may cause perforation as well.[80,81]

Vasculopathic ulcers in dermatomyositis

Vasculopathic ulcers are common in dermatomyositis associated with anti-MDA5 antibodies. The anti-MDA5-antibody associated dermatomyositis is distinctive form wherein majority of the cases are clinically amyopathic, exhibit rapidly progressive therapy resistant interstitial lung disease, and certain characteristic cutaneous manifestations. The latter include vasculopathic ulcers and palmar papules. The ulcers are deep punched-out surrounded by dusky violaceous border and are principally located over the finger pulps, knuckles, elbows, and knees. The palmar papules are painful and characteristically located on the palmar aspects of the metacarpophalangeal and interphalangeal joints which histologically exhibit occlusive vasculopathy.[82,83] Papulosquamous lesions on the palmar aspects of the interphalangeal joints (inverse Gottron papules) are also reported as described above.

Trophic ulcers

Trophic ulcers over the knuckles are not uncommon as these are bony prominences and exposed areas. Apart from the digital tips, trophic ulcers also develop over the knuckles in systemic sclerosis which may be accompanied by gangrene and autoamputation of the digits [Figure 12]. The digital ulcers in systemic sclerosis are indicative of sever disease course as well as systemic complications even in early phase of the disease.[84,85] Although the feet are the frequent areas for anesthetic deformities.
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in leprosy, trophic ulcers over the knuckles may also be seen as a result of continued use of the anesthetic hand [Figure 13a].

**Others**

As described above, the rheumatoid nodules, gouty tophi, calcinosis cutis, Gottron papules, granuloma annulare, and palisaded neutrophilic and granulomatous dermatitis occurring over the knuckles may be ulcerated as well. Nontrophic ulcers over the knuckles due to small fibre and microvascular involvement by lepra bacilli have also been described in leprosy [Figure 13b].

**Vesiculobullous Lesions**

**Epidermolysis bullosa**

Knuckle involvement is described frequently in inherited epidermolysis bullosa and lesions typically heal with scarring and milia formation, commonly in the dystrophic type [Figure 14a and 14b]. Epidermolysis bullosa aquisita preferentially involves the acral areas and lesions over the knuckles are very common.[88,89]

**Herpes gladiatorum**

Herpes gladiatorum refers to herpes simplex infection involving face, arms, neck, and upper trunk in athletes engaged in contact sports like wrestling and rugby. Herpes simplex typically distributed over the knuckles has described in boxers due to sharing of contaminated boxing gloves (boxing glove herpes).[91,92]

**Others**

Vesicular hand eczema, vesiculobullous irritant contact dermatitis, and friction blisters can involve knuckles as well.

**Pigmentary lesions**

**Due to excess adrenocorticotropic hormone**

Excess adrenocorticotropic hormone (ACTH) levels are seen in three situations – Addison disease, Cushing disease and syndrome, and Nelson syndrome, all of which are characterized by cutaneous hyperpigmentation due to stimulation of melanogenesis by increased ACTH.[93] Hyperpigmentation of the skin is a hallmark and the earliest feature of Addison disease. The ‘Addisonian’ hyperpigmentation has certain characteristics such as a) involvement of sun-exposed areas; b) involvement of bony prominences and pressure points like knuckles [Figure 15a], knees, elbows, waist line and underneath the brassier straps; c) darkening of the normally pigmented areas such as areola, nipples, axillae, groins, and perineum; d) darkening of the pigmented lesions such as café au lait macules and melanocytic nevi; e) pigmentation of the nails (longitudinal melanonychia) and palmar creases; and f) pigmentation of the scars developing after the disease onset.[94,95] Cushing disease and syndrome, and Nelson syndrome also exhibit Addisonian pattern of hyperpigmentation.[96,97]

**Vitamin B12 deficiency**

The predominant cutaneous manifestations of megaloblastic anemia due to vitamin B12 deficiency include recurrent stomatitis, angular cheilitis and reversible oral, and knuckle hyperpigmentation [Figure 15b and 15c]. The latter occurs due to decreased levels of reduced glutathione that normally exerts an inhibitory
effect on tyrosinase activity. Knuckle hyperpigmentation is a prominent feature in majority of the cases and can be the sole manifestation. Knuckle pigmentation was observed to be associated with a greater degree of vitamin B12 deficiency. The cutaneous hyperpigmentation may paradoxically be associated with hair depigmentation as well.[98,99]

**Alkaptonuria**

Alkaptonuria is a rare autosomal recessive inborn error of metabolism due to deficiency of homogentisic acid oxidase with resultant excess of homogentisic acid being excreted in urine and getting deposited in various tissues, especially the fibrous tissue imparting a dark color. The early manifestation of the disease is darkening of urine on standing. By the third decade of life, pigmentation becomes apparent initially involving the sclera (Osler sign) and ear cartilage. Pigmentation also involves the nasal cartilage and tendons. The latter is visible over knuckles on flexing the joints which themselves become pigmented as well.[100,101]

**Transient cutaneous hyperpigmentation in newborns**

Transient epidermal cutaneous pigmentation in neonates is attributable to maternal hormones (e.g., estrogen and progesterone) in fetal circulation that stimulate the melanocytes and clinically manifests as linea nigra, hyperpigmentation of axillae, perineum and areola. Pigmentation is also conspicuous over the fingers, typically involving the knuckles and periungual areas. It is more common in darker skin phototypes and gradually fades away by the age of 1 year.[102-104]

**Cluston syndrome**

Cluston syndrome is an autosomal dominantly inherited hidrotic ectodermal dysplasia characterized by a triad of
alopecia, nail dystrophy, and palmarplantar hyperkeratosis. Pigmentation over the bony prominences, which may be associated with thickening, is also a frequent feature involving the knuckles, elbows and knees.[105,106]

**Carotinemia**

Carotinemia is characterized by yellowish discoloration of the skin due to elevated beta carotenes in the blood that preferentially accumulates in areas of thicker skin and areas rich in eccrine glands, such as palms, soles, knuckles, nasal tip and nasolabial folds, forehead, chin and retroauricular areas. It is common in children due increased dietary consumption of carotene rich food. It may also be associated with hypothyroidism, diabetes, liver disease, and hypothalamic amenorrhoea. The sclera is conspicuously spared which helps in differentiating from icterus.[107,108]

**Poikilodermatous Lesions**

Poikiloderma, characterized by atrophy and telangiectasia involving the knuckles, may be seen in scleroderma, graft versus host disease, and dermatomyositis.[68,109]

**Knuckle Depressions**

Knuckle depressions or dimpling due to shortening of the fourth and fifth metacarpals (brachymetaphalangism) is a pathognomonic feature of Albright’s hereditary osteodystrophy and is described as ‘knuckle, knuckle, dimple, dimple’ sign. Albright’s hereditary osteodystrophy is an inherited disorder associated with pseudohypoparathyroidism (target tissue level unresponsiveness to parathormone) and characteristic phenotype – short stature, obesity, short neck, round face, and short nasal bridge.[110]

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