## **REVIEW ARTICLE**

# Cutaneous manifestations of internal malignancies: A narrative review

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#### ABSTRACT

In hands of an experienced dermatologist, skin is an important gateway to diagnose various ailments involving the internal organs. One such diagnostic avenue is involvement of skin in various internal malignancies. This may be a manifestation of presence of malignant cells of the primary tumor in the skin, or that of paraneoplastic involvement, or it can be because of genodermatoses involving skin, that predispose to the development of various malignancies. The importance stems from the fact that skin lesions are easily accessible for clinical diagnosis, are amenable for diagnostic biopsy and can also be used as a guide to ascertain treatment (chemotherapy/radiotherapy/targeted therapy/immunotherapy) response. A literature search of scientific publications published in English was done using the electronic databases PubMed, Science direct, Cochrane library and Google Scholar. Search included terms "cutaneous manifestations of malignancy," "distant metastases," "paraneoplastic," "locoregional spread of malignancy," and "genodermatoses with malignancies". Ninety articles and references within the articles so obtained were reviewed to identify additional studies available. Data obtained from studies and case reports were compiled and interpreted to prepare this review. Breast cancer was found to be the commonest primary for locoregional and metastatic skin spread.

This article summarizes the various ways in which the corium can be involved secondarily, to aid earlier diagnosis and augment quicker institution of management.

### INTRODUCTION

Skin is a mirror for the internal diseases. Not only does it act as a reflection of well-being of internal organs, its examination can aid in diagnoses of ailments, because of its easy accessibility to look for signs of the same. Cutaneous manifestations of malignancy may involve skin infiltration with malignant cells via either contiguous locoregional spread or local /distant metastatic deposition of tumor cells, or may represent a paraneoplastic phenomenon. The importance of knowing these signs and symptoms lies in the fact that very often, skin involvement is the first pointer towards an internal malignancy, early detection of which, can prompt adequate investigations to detect the underlying malignancy. This review aims to highlight several of such manifestations in brief.

#### **MATERIALS AND METHODS**

A literature search of scientific publications published in English was done using the electronic databases PubMed, Science direct, Cochrane library and Google Scholar. Search included terms "cutaneous manifestations of malignancy," "distant metastases," "paraneoplastic," "locoregional spread of malignancy," and "genodermatoses with malignancies". Hundred and three articles and references within the articles so obtained were reviewed to identify additional studies

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available. Studies and case reports which met the following criteria were included in the current review:

- 1. English language publications
- 2. Those focusing on skin involvement in internal malignancies.

Data obtained from studies and case reports were compiled and interpreted to prepare this review.

#### RESULTS

Cutaneous manifestations may be differentiated into those due to presence of malignant cells of primary tumor in the skin, paraneoplastic manifestations and genodermatoses involving skin that are predisposed to develop various malignancies.

# I. MALIGNANT CELLS ARE PRESENT IN THE SKIN

A Involvement of the skin by direct

extension from an underlying malignancy The most common manifestations include nodular infiltration and ulceration.<sup>1</sup> In a study by Ayyamperumal A et al, females were more commonly found to have contiguous spread of malignancy, compared to males (66.66% vs 33.33%).<sup>2</sup> The most common malignancy associated with direct spread was breast carcinoma, with lung and gastrointestinal malignancies being other culprits.<sup>3</sup> Carcinoma en cuirasse refers to local metastases, which progresses from an erythematous and edematous phase, to sclerodermoid involvement of the skin with tumor cells. It must be distinguished from radiation dermatitis, radiation induced morphea and inflammatory breast carcinoma.<sup>4</sup> Carcinoma erysipeloides, that spreads to skin via dermal lymphatics, presents as ill to well defined erythematous plaque with raised periphery which results from blocked lymphatics. It resembles cellulitis or erysipelas, hence the name. However, the patient is afebrile.<sup>5</sup> While breast cancer is the commonest primary, malignancies of uterus, prostate, lung, stomach, tonsils, thyroid, pancreas and rectum have led to carcinoma erysipeloides. A case was reported by Alvarez MA et al, with laryngeal carcinoma being the source of tumor cells.<sup>6</sup>

Telangiectatic metastatic carcinoma presents as multiple telangiectasias and as pseudovesicular lesions resembling lymphangioma circumscriptum. However, lesions may become more florid and resemble angiosarcoma.<sup>7,8</sup> Atypical manifestation of the same, in the form of purpuric macules was reported by Shiraishi K and Samaya K.<sup>9</sup>

# B Involvement of the skin from a distant malignancy (lymphatic or hematogenous spread)

Cutaneous metastases can occur in about 0.5% to 10.5% cases of internal organ cancers.<sup>10</sup> These may be precocious (before diagnosis of the internal malignancy), synchronous (occurring at the same time as internal malignancy) or metachronous (occurring months or years after the diagnosis of internal malignancy).<sup>11</sup>

One of the cutaneous malignancies, melanoma can give rise to satellite metastases (within 2 cm of the primary), in-transit metastases (beyond 2 cm from the primary) or distant (hematogenous metastases). The morphology of the satellite and in-transit lesions is similar to the primary, with mode of spread being lymphatic drainage.<sup>12</sup>

Hu et al in a study of 124 cases, found that carcinoma of the breast (2.42%) was the commonest primary, followed by lungs (1.78%), oropharyngeal (1.75%) and colon and rectal tumors

#### $(0.81\%).^{10}$

Lung carcinoma, although rarely, may lead to skin metastases. Histologically, metastases to skin are commonest from adenocarcinoma subtype, followed closely by squamous cell carcinoma (SCC) variant.<sup>13</sup> Clinically, they often present as round to ovoid, firm, red, dark red or black nodules, which may ulcerate. Usually, topographically, the lesions are present supradiaphragmatically, i.e involving skin over chest and sometimes abdomen.<sup>14</sup> Lymphovascular invasion is implicated in lesions undergoing ulcerations.<sup>15</sup> When it comes to cutaneous metastases of gastrointestinal origin, the most common primary is colorectal tumor. This clinically can present as single or multiple papules, nodules and plaques, with or without ulceration, especially over the abdominal wall. The lesions involving the umbilicus are called Sister Mary Joseph nodules.<sup>16,17</sup> While erythema annulare centrifugam like and neurofibroma like nodules can be atypical manifestations of gastric carcinomas, hepatobiliary malignancies can resemble vascular tumors like lobular capillary hemangioma.<sup>18-20</sup> Pancreatic carcinoma, especially acinar cell carcinoma, may rarely present as panniculitis.<sup>21</sup>

Genitourinary malignancies, most commonly renal carcinomas, can metastasize to skin. Upto 3% of skin metastases can be attributed to renal cell carcinomas (RCC).<sup>22</sup> Like hepatic metastases, secondaries from RCCs are vascular and may present as Kaposi sarcoma or lobular capillary hemagioma like lesions.<sup>23</sup> Metastases from bladder and prostate may be in the form of nonspecific rubbery papules and nodules, but atypical herpetiform eruptions and Sister Mary Joseph like lesions may rarely be seen.<sup>24,25</sup>

Amongst gynecological tumors, endometrial

malignancies are the commonest, but they rarely metastasize to skin (0.8%).<sup>26</sup> And therefore, Atallah D et al reported their case report on the same, as 'once in a blue moon' finding.<sup>27</sup> Approximately 3-5% of ovarian malignancies lead to skin metastases, of which commonest primary was found to be serous papillary carcinoma, followed by endometroid and mucinous variants.<sup>28,29</sup> Cutaneous metastases can occur in cutaneous incision of laparotomy, laparoscopy, port and catheter, or drainage scars.<sup>30</sup>

Amongst hematological malignancies, acute myeloid leukemia (AML) is the most likely malignancy to infiltrate the skin, with a prevalence of about 2% to 4%. While metastases with AML are more often reported, chronic lymphocytic leukemia (CLL) is more prevalent disease and produces leukemia cutis at almost similar rates, and therefore CLL is likely more frequent overall cause.<sup>31</sup> Clinically they present as skin colored to erythematous papules, nodules and plaques that may or may not ulcerate.<sup>32</sup>

# II. MALIGNANT CELLS ARE NOT FOUND IN SKIN (PARANEOPLASTIC)

Paraneoplastic dermatoses are the cutaneous manifestations that are concurrently present with an internal malignancy and are thus considered important pointers.<sup>33</sup>

These dermatoses may be obligate paraneoplastic dermatoses i.e the ones that are almost 100% associated with underlying malignancy or may be facultative paraneoplastic dermatoses, that are associated with an internal malignancy in about 3-30% cases. The examples of the former include acanthosis nigricans maligna, bazex syndrome, erythema gyratum repens, necrolytic migratory erythema, pityriasis rotunda and paraneoplastic pemphigus. The examples of later include Sweet's syndrome, dermatomyositis, pruritus, bullous pemphigoid and mucous membrane pemphigus.<sup>34</sup>

Curth's criteria, postulated by German-American dermatologist Helen Ollendorff-Curth, is commonly used to diagnose paraneoplastic dermatoses:<sup>35</sup>

- 1. Concurrence of the malignancy and the dermatoses.
- 2. Parallel course of not only the development of the skin disease with the malignancy, but also that of resolution, with recurrence of the dermatoses suggesting progression or recurrence of the internal malignancy.
- Specificity between type of the tumor and eruption. A specific malignancy may consistently be associated with a certain skin disorder.
- 4. A genetic association between the malignancy and the skin eruption has been already proven.
- 5. Based on reliable case-control studies, there is significant statistical association between the malignancy and the skin disorder.

At least one of these criteria must be fulfilled in order to be able to establish the association between the dermatosis and the suspected underlying malignancy.

Similar defining criteria given by McLean et al includes:<sup>36</sup>

- 1. Development of a dermatosis only after the development of a malignant neoplasm.
- 2. The dermatosis and the malignancy follow a parallel clinical course, so that the cutaneous disease disappears when the tumor is treated and may reappear in cases of recurrence or

metastasis.

The paraneoplastic dermatoses can be variously grouped as inflammatory dermatoses, hyperkeratotic and proliferative dermatoses, bullous eruptions, vascular dermatoses, pigmentary changes, connective tissue disorders, disorders of hair and nail and some miscellaneous dermatoses.

# INFLAMMATORY DERMATOSES 1. Sweet's syndrome:

Sweet's syndrome, also known as acute neutrophilic febrile illness, is characterized by acute onset neutrophilic dermatoses and fever (as suggested by the name). It is classified into classical Sweet's syndrome, drug associated Sweet's syndrome and malignancy associated Sweet's syndrome.<sup>37</sup> Clinically, the lesions are well to ill-defined, erythematous to violaceous, brawny papules and plaques that are warm and tender to touch. The surface may develop pustules or pseudovesicles. They are primarily distributed over face, neck and upper limbs, especially over the dorsae of hands. Malignancy associated Sweet's syndrome may also be associated with oral pustulation followed by ulceration and development of aphthous ulcers.<sup>38</sup> Histoid variant of the disease is more commonly malignancy associated.<sup>39</sup> Commonest malignancies associated with the said dermatosis include acute myelogenous leukemia and myelodysplastic syndrome. Plasma cell dyscrasias, lymphomas and solid tumors may also be the underlying cause.<sup>40</sup>

## 2. Erythema gyratum repens:

Erythema gyratum repens is found associated with malignancy in about 82% cases. The male to female ratio is 2:1.<sup>41</sup> It is characterized by presence of parallel, concentric, erythematous bands that are figurate, gyrate or annular and have trailing edge of scale. This pattern is called wood grain pattern.<sup>42</sup> The immunologic pathogenic basis that has been provided implicates the underlying malignancy in production of autoantibodies that are directed against the basement membrane or polypeptides generated by the tumor bind the self-antigens, rendering them more immunogenic.<sup>43</sup> The pattern of the lesions, wood grain, or fractal-like geometrics, maybe due to change in the body chemistry as a result of excretion by tumor cells or immune response or may be attributed to increased levels of glutamine in concentric rings, that help neoplastic cells to thrive on transport of glutamine into mitochondria, as found by Forrester et al.<sup>44,45</sup>

## 3. Necrolytic migratory erythema:

Necrolytic migratory erythema is considered the most specific clinical manifestation of glucagonoma and may be the presenting complaint in about 70% of the patients.<sup>46</sup> It is clinically characterized by involvement of the perineum, intertriginous areas, abdomen, thighs, perioral sites and other trauma prone locations with an erythematous, eczematous eruption with development of flaccid bullae, erosions and superficial epidermal necrosis. Central healing may give rise to annular lesions.<sup>47</sup> The pathogenesis revolves around the glucagon level abnormality. It has been proposed that excess of glucagon results in decreased tryptophan, which is otherwise responsible for regulation of cell turnover and epidermal maturation. Another hypothesis is that increased levels of glucagon lead to decreased amount of albumin, which is carrier protein for zinc and essential fatty acids. These are involved in maintaining skin vitality and their deficiency leads to a weeping eruption in the friction prone sites.<sup>48</sup> Other manifestations of glucagonoma

include diabetes mellitus, anemia, weight loss, glossitis, cheilitis, steatorrhea, diarrhea, venous thrombosis and neuropsychiatric disturbances.<sup>49</sup>

#### 4. Erythroderma:

Erythroderma is defined as erythema and scaling of more than 90% of body surface area. While most common causes of erythroderma are atopic dermatitis, psoriasis and drug rash, few cases have been attributed to underlying malignancies. It is usually difficult to find the underlying malignancy because of rare association. However, patients of idiopathic erythroderma, especially elderly patients, should be kept under long term follow up.<sup>50</sup> In a study by Akhyani M et al, malignancies were underlying cause in 11.3% patients and in a study by Miyashiro D and Sanches JA, paraneoplastic erythroderma was recorded in 19% patients.<sup>51,52</sup> The most common malignancies associated with erythroderma, albeit rarely, include prostate adenocarcinoma, colon adenocarcinoma, lung adenocarcinoma and neuroendocrine lung tumor. Skin lesions in ATLL are heterogeneous, and erythroderma may be present in 4.2% of the patients.<sup>53</sup> Recently, squamous cell carcinoma of lung was reported to manifest as erythroderma.54

# HYPERKERATOTIC AND PROLIFERA-TIVE DERMATOSES

#### 1. Acanthosis nigricans maligna:

Acanthosis nigricans is a common dermatological disorder characterized by presence of velvety, rugose, hyperpigmented plaques, predominantly in intertriginous areas. Majority cases are benign and are associated with obesity and metabolic dysfunction of diabetes mellitus. However, sometimes it may be associated with underlying malignancy. The pointers towards acanthosis nigricans maligna include rapid progression of lesions, presence in older individuals and occurrence in uncommon sites such as mucosae and acral areas. It has been proposed that tumorderived growth factors, act as key cytokines to bring about epidermal cell proliferation through different growth factor receptors like epidermal growth factor receptor.<sup>55</sup> The most common malignancy associated with this include gastric adenocarcinomas, followed by carcinomas of pancreas, ovary, lungs, breast and urogenital system.<sup>56-58</sup> It has been proposed that involvement of the inner eyelid should alarm the physician towards more detailed workup of the patient.<sup>59</sup>

## 2. Tripe palms:

Tripe palms, also called as acanthosis palmaris, are characterized by increased thickness, with pronounced folds of the palms. About 70-80% of these cases are present along with acanthosis nigricans. The most common malignancies associated with this are carcinoma of lung and stomach.<sup>60</sup> Co-existence of tripe palms with acanthosis nigricans may point towards gastric malignancy, while its presence alone or with clubbing may point towards bronchial/lung malignancy.<sup>61</sup> Pathogenesis is similar to that of malignant acanthosis nigricans and these lesions may co-exist with sign of leser-trelat.<sup>62</sup>

## 3. Sign of Leser-Trelat:

It is characterized by sudden appearance and increase in size of the existing seborrheic keratoses. It usually co-presents with acanthosis nigricans maligna. Pathogenesis has been suggested to be similar to the previous two entities, i.e increased production of various growth factors by the tumors, resulting in increased proliferative dermatoses.<sup>63</sup> Most commonly implicated tumors include the gastrointestinal adenocarcinoma especially stomach, but also those of liver, colorectal, or pancreas. However, lymphoid malignancies like cutaneous T cell lymphoma, breast cancer, and lung cancer, can occur in association with the sign of Leser-Trélat.<sup>64,65</sup>

# 4. Acquired Icthyosis and Palmoplantar keratoderma:

Acquired icthyosis may have multiple causes like drug induced icthyosis, extreme senile xerosis and underlying malignancy. While the morphology of presentation is similar to that of icthyosis vulgaris, presence of scales in folds and on palms and soles may be seen.<sup>66</sup> The commonest malignancy involved in causation of this presentation is Hodgkin's lymphoma, with others being Kaposi sarcoma, non-hodgkin's lymphoma, cutaneous T cell lymphoma, multiple myeloma and solid organ tumors like that of breast, lung and genitourinary tract.<sup>67,68</sup>

Acquired palmoplantar keratoderma, especially diffuse variant, has been reported to be associated with internal malignancy in upto 90% cases.<sup>69</sup> While the most common malignancy associated with this presentation is that of esophagus (squamous cell carcinoma), other tumors implicated include carcinomas of stomach, lung, bladder and uterus.<sup>70</sup>

## 5. Pityriasis rotunda:

Pityriasis rotunda is a rare disorder of keratinization, characterized by presence of sharply demarcated, dry, scaling, icthyosiform, round plaques, that can be made more apparent by scratching. The lesions are predominantly distributed centrally, i.e over trunk, buttocks and thighs.<sup>71</sup> The associated malignancies include multiple myeloma, acute and chronic myeloid lymphoma, hepatocellular carcinoma and carcinoma prostate.<sup>72</sup>

# PARANEOPLASTIC BULLOUS DERMA-TOSES

## 1. Paraneoplastic pemphigus:

Paraneoplastic pemphigus is a rare but potentially life threatening mucocutaneous blistering disorder associated with an underlying malignancy. About 80% of adult cases are associated with hematological malignancies like non-Hodgkin Bcell lymphoma, chronic lymphocytic leukemia, Hodgkin lymphoma and T-cell lymphoma, while the commonest tumor association in pediatric age group is Castleman's disease.<sup>73</sup> Clinically, cutaneous lesions of various morphology i.e flaccid as well as tense blisters, lichenoid lesions, erythema multiforme like and graft vs host disease like eruptions accompany painful oral stomatitis. Oral involvement is resistant to treatment and its absence almost negates the above diagnosis.74 This may be associated with presence of bronchiolitis obliterans and thus the disorder was renamed as paraneoplastic autoimmune multiorgan syndrome (PAMS) to be more inclusive of extra cutaneous involvement.75 Camisa and Helm gave the diagnostic criteria:76

## Major criteria:

- Polymorphous skin eruption
- Concurrent internal neoplasia
- Antibodies with an immunoprecipitation specific pattern

## Minor criteria:

- Histological evidence of intraepithelial acantholysis.
- Positive direct immunofluorescence (DIF) with deposits both intercellularly and at the basement membrane zone with IgG and C3 deposition.
- Positive indirect immunofluorescence (IIF) on rat bladder epithelium.

The reason behind varied presentation lies in the pathogenesis. Autoantibodies are generated due to increased cytokines like IL-6, that stimulate B cells into producing self-reactive antibodies to plakins (desmoplakin, envoplakin, periplakin) and bullous pemphigoid antigen 1( BPAg 1).<sup>77</sup>

# 2. Bullous pemphigoid and Mucous membrane pemphigoid:

Association of bullous pemphigoid with malignancy has been difficult to establish. Many systematic reviews and meta-analysis failed to find link between the two.<sup>78,79</sup>

Ballestri R et al reviewed 40 cases of bullous pemphigoid associated with malignancy of which 7 were associated with hematological malignancy and 33 were associated with solid tumors. In their own survey, out of 91 cases of bullous pemphigoid, 10 were paraneoplastic.<sup>80</sup> Mucous membrane pemphigoid is characterized by development of antibodies against various antigens of basement membrane zone. However, when the targeted antigen as found on salt split smear is laminin 332 or laminin 5, then the suspicion of malignancy is high.<sup>81</sup>

# VASCULAR DISORDERS

Various vascular manifestations that may appear in a paraneoplastic manner include purpura, petechie, raynaud's phenomenon, flushing, erythromelalgia, palmar erythema, chilblain like lesions and vasculitis.<sup>82</sup> These presentations can be seen not only with malignancies but may also be associated with their treatment. Geier M et al reported presence of vascular acrosyndromes in a patient of non-small cell lung carcinoma on gemcitabine and pemetrexed.<sup>83</sup> Flushing has been found in association with carcinoid tumor, pheochromocytoma; telangiectasias in association with carcinoid tumor, carcinoma breast and bronchogenic carcinoma; vasculitic lesions and purpura are encountered with hematological malignancies; cutaneous ischemia can be noted in patients of carcinoma of pancreas, small bowel, ovary, stomach and kidney and deep vein thrombosis are most commonly seen with mucin secreting adenocarcinomas.<sup>84</sup>

### **PIGMENTARY CHANGES**

Hyperpigmentation or rarely, hypopigmentation of the skin may be an associated or presenting sign of underlying malignancy. These changes may be idiopathic or maybe due to the pharmacologic activity of substances produced by the tumor.<sup>3</sup> For example, ectopically produced ACTH production can lead to stimulation of cutaneous melanocytes, resulting in diffuse hyperpigmentation.85 Hemochromatosis, a condition that predisposes to liver cancer, may also present with diffuse hyperpigmentation.<sup>3</sup> Widely metastasizing melanoma has been purported to produce diffuse hyperpigmentation by dissemination of melanin and its trapping by dermal melanocytes. Inversely, vitiliginous depigmentation can also be seen in patients with melanoma.86 Cronkhite-Canada syndrome may produce cutaneous as well as mucosal hyperpigmentation.<sup>3</sup>

## **CONNECTIVE TISSUE DISORDERS**

Dermatomyositis, characterized by presence of proximal muscle weakness, confluent macular violaceous erythema around eyes (heliotrope sign), gottron's papules, gottron's sign and shawl sign, may be associated with malignancy in upto 60% of cases, especially when occurring in patients aged more than 45 years.<sup>87</sup> Commonly associated malignancies include those of lung, ovary, stomach, pancreas, colorectal cancers and non-Hodgkin's lymphoma.<sup>88</sup> In many case reports, scleroderma has been reported to be a paraneoplastic phenomenon. It has variously been reported with mycoses fungoides, mediastinal tumor, cholangiogenic carcinoma, endometrial carcinoma, prostatic adenocarcinoma, and adenoma of the suprarenal gland, among others.<sup>89-91</sup> Scleremyxedema, characterized by eruption of multiple, waxy, flat topped papules, usually arranged linearly, has been found to be associated with paraproteinemias in about 80% of cases.<sup>92</sup> Miraflor AP et al reported it with Sezary syndrome, while Oh SJ et al reported it with gastric carcinoma.<sup>93,94</sup>

## HAIR AND NAIL CHANGES

Hair and nail changes are seldom specific for a particular malignancy. However, hypertrichosis lanuginose acquisita and hypertrophic osteoar-thropathy may point towards malignancy. Hypertrichosis lanuginose acquisita is characterized by lanugo hair, predominantly on face, which may spread to involve chest and trunk.<sup>95</sup> It may be found in patients of adenocarcionoma lung, breast, bowel and kidney, hematological malignancies like CLL and has been reported with Ewing's sarcoma.<sup>96-98</sup>

Hypertrophic osteoarthropathy has been associated with lung cancers.<sup>99</sup>

#### MISCELLANEOUS

Various non-specific, miscellaneous cutaneous features may accompany internal malignancies. One of the most common of such presentation is generalized xerosis and pruritus. This generalized xerosis is different from the acquired icthyoses mentioned above. The contributing factors include dehydration, cachexia and malnutrition. Pruritus may be because of xerosis or may be because of histamine and serotonin released from the tumor.<sup>43</sup> Most commonly implicated tumors include leukemia, Hodgkins lymphoma, multiple myeloma and carcinoid tumor. IL-31 has been pointed out as the pathogenic mediator.<sup>100</sup> Plasma cell dyscrasias like multiple myeloma may be associated with acquired cutis laxa, with "hound dog" like facies.<sup>101,102</sup> Insect bite like reactions, cutis verticis gyrata, numb chin syndrome are rare paraneoplastic presentations.<sup>103</sup>

**Table 1** Skin manifestations and common malig-nancies associated with the same are tabulatedbelow in table 1.

Skin manifestations:	Commonly associated malignancies:	
Sister Mary Joseph nodules	Gastrointestinal malignancies, especially gastric	
Vascular lesions like Kaposi sarcoma	Hepatic and renal malignancies	
Sweet's syndrome	Hematological malignancies	
Necrolytic migratory erythema	Glucagonoma	
Erythroderma	Sezary syndrome, solid organ adenocarcinomas	
Acanthosis nigricans maligna	Stomach and lung cancer	
Sign of leser-Trelat	Gastrointestinal malignancies	
Acquired icthyosis	Hodgkin's and non-Hodgkin's lymphoma, multiple myeloma	
Paraneoplastic pemphigus	Hodgkin's and non-Hodgkin's lymphoma, Castleman's tumor	
Flushing and telangiectasias	Carcinoid tumor, bronchogenic carcinoma	
Vasculitis and purpura	Hematological malignancies	
Addisonian pigmentation	ACTH producing pituitary tumors	
Dermatomyositis	Ovarian cancer, lung cancer	

# GENODERMATOSES WITH INCREASED RISK OF MALIGNANCY

Multiple genodermatoses have an increased risk of development of malignancies and thus their early diagnosis may prove helpful in screening for associated malignancies. These are summarized in the table 2 below:<sup>43,104,105</sup> **Table 2** Genodermatoses involving skin and associated malignancies.

Genodermatoses	<b>Clinical Features</b>	Malignancy Association
Neurofibromatosis	Neurofibromas,	Neurofibrosar-
	café-au-lait macules,	coma,
	seizures, lisch nodules,	Pheochromocy-
	axillary and inguinal	toma,
	freckling	
Tuberous sclerosis	Angiofibromas, ash	Astrocytomas,
	leaf macules, shagreen	renal cell
	patch, koenen's tumors	carcinoma
Gardner's	Epidermoid cysts,	Adenocarcinoma
syndrome	fibroma, lipoma,	colon
	neurofibroma,	
Cowden's	Acral keratosis,	Carcinoma breast
syndrome	keratotic facial	and thyroid
	papules, mucosal	
	papules with	
	cobblestoning	
Peutz-Jegher's	Lentigines over lips,	Adenocarcinoma
syndrome	mucosae, face and	colon
	extremities	
Torres syndrome	Sebaceous tumors,	Adenocarcinoma
	keratoacanthomas	colon
Bloom's syndrome	Photosensitivity,	Leukemias,
	telangiectasias over	Lymphomas
	photo-exposed sites,	
	café-au-lait macules	
Ataxia	Oculocutaneous	Breast carcinoma,
telangiectasia	telangiectasias	Leukemia
Rothmund-	Photosensitivity	Osteosarcoma,
thomson syndrome		Myelodysplasia
Howell-Evans syn-	Palmoplantar	Esophageal
drome	keratoderma	carcinoma
Familial	Multiple atypical	Lung, breast,
melanoma	melanocytic nevus	gastrointestinal,
syndrome		laryngeal
		carcinoma
Carney complex	Lentigines, blue naevi,	Gonadal hormone
	mucocutaneous	secreting tumors,
	myxomas	Thyroid
		malignancy
Birt-Hogg-Dube	Fibrofolliculomas,	Renal
syndrome	Trichodiscomas,	malignancies,
	Pulmonary cysts	Colon carcinomas
Leiomyomatosis	Multiple leiomyomas	Renal
		malignancies

#### CONCLUSION

Skin involvement secondary to an internal malignancy is considered poor prognostic factor and points towards decreased five-year survival rate. However, it is an indicator of recurrence/ distant spread and its resolution can act as therapeutic guide for response to treatment. Thus, by knowing in depth, the various presentations of corium involvement, a dermatologist can assist an oncologist in better management.

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