

Skin: A mirror of internal malignancy

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ABSTRACT

Skin manifestations are a reflection of many of the internal diseases. Sometimes, skin disease may be the only manifestation of the internal disease. Internal malignancies may give rise to a number of cutaneous manifestations through their immunological, metabolic, and metastatic consequences. Curth proposed criteria to establish a causal relationship between a dermatosis and a malignant internal disease. Malignancy can present with a plethora of cutaneous manifestations. Here, we describe in brief about various skin manifestations of internal malignancies.

Key words: *Cutaneous manifestations, internal malignancy, paraneoplastic syndrome*

INTRODUCTION

Skin manifestations are a reflection of many of the internal diseases; sometimes skin disease may be the only presenting complaint of many of the internal disorders. Internal malignancy, whether organ-specific or hematological can present with a plethora of cutaneous manifestations. The skin lesions can occur as secondaries or as paraneoplastic syndromes or as a part of certain genetic syndromes.^[1] Internal malignancy is also one such entity which indicates its existence by various skin manifestations, so a close observation and a suspicious mind are required for detection of internal malignancy through cutaneous findings. Internal malignancies may give rise to a number of cutaneous manifestations through their immunological, metabolic, and metastatic consequences. Skin disease may sometimes provide the first clue for the diagnosis of internal malignancy. Curth proposed criteria by which a causal relationship between a dermatosis and a malignant internal disease might be evaluated.^[2] These requirements include the following: (a) Both conditions start at the same time, (b) both conditions follow a parallel course, (c) the condition is not recognized as a part of a genetic syndrome, (d) a specific tumor occurs with a certain dermatosis, (e) the dermatosis is not common, and (f) a high percentage of the association is noted. In a recent Indian study, skin changes were found in 27% of patients with internal malignancies. Cutaneous metastasis was seen in 6% and other skin lesions in 25%. Secondaries in the skin usually present as papules, plaques, and nodules,

common site being the anterior abdominal wall. The skin is an infrequent site for metastasis and is only the eighteenth most common site. Cutaneous metastases can arise at any age. However, in keeping with the increased incidence of malignant disease in later life, most cutaneous metastases occurred during or after the fifth decade.^[3] The anterior chest wall is reported as the most common site for cutaneous metastatic lesions, and it held good for this study as well wherein 32% of the lesions were in the chest wall.^[4,5] The morphological patterns of cutaneous metastases corresponded with the primary tumors and their evaluation helped localize unknown primary malignancies. In cases with known primaries, cutaneous metastases upstaged the malignancy and affected the prognosis.^[6]

DIRECT TUMOR SPREAD/CUTANEOUS METASTASIS

Direct tumor spread can occasionally arise after diagnostic or therapeutic interventions such as needle aspiration of a tumor, pleural biopsy, drainage of malignant ascites, or placement of other drains in the vicinity of a tumor. "Tumor spillage," direct contamination of wounds with tumor cells during a laparoscopy or surgical procedure, was once a problem in nearly 20% of cases but is now uncommon; laparoscopic port site metastasis rates and laparotomy wound metastasis rates due to direct tumor inoculation are both in the order of 0.8%.^[7] Carcinoma

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erysipeloides resembles erysipelas but without the pyrexia or toxemia; tumor cells lie within dilated lymphatic vessels in the skin. This pattern is again most commonly seen in breast carcinoma but occurs due to melanoma and pelvic cancers (when it affects the lower abdomen or thigh); it can also occur due to carcinomas of the oral cavity or associated glands, as well as with upper abdominal cancers (stomach, pancreas) or lung cancer.

Cutaneous metastasis occurs in 1%–5% of all patients with internal cancers.^[8] Autopsy studies suggest a higher frequency of skin metastasis than may be apparent from clinical studies; in some studies up to 9% of patients with internal cancer have had skin metastases, a large analysis suggesting that 5% is usual,^[9] and in about 0.5%–1% a metastasis is the presenting feature of internal cancer.^[10,11] Of patients with metastatic cancer, 10% have cutaneous metastases.^[12] The most common sources of cutaneous metastases are breast, melanoma, lung, colon, stomach, upper aerodigestive tract, uterus, and kidney; the most common skin metastases from a previously unknown primary tumor originate from the kidney, lung, thyroid, or ovary.^[11,13,14] Seventy-five percent of metastases are found in the 25% of body surface area that comprises the head, neck, and upper trunk.^[11]

They may be the first sign of extranodal disease in up to 8% of those with metastatic cancer, especially carcinoma lung, kidney, and ovaries. Internal malignancies may metastasize to the skin by direct invasion from underlying structures, by extension through lymphatics, or by embolization into lymphatics or blood vessels. The preferential route by which tumor metastasize often determines the location of its metastasis. Carcinoma breast presents as gross lymphedema of ipsilateral limb skin ulcerations, scaly plaques of Paget's disease, or rarely Peaud'orange-like carcinoma of cuirasse. Carcinoma of oral cavity usually presents with squamous cell carcinoma (SCC) which ulcerates on the face. Lymphoma, leukemia, and myeloproliferative disorders can present with cutaneous infiltration. Renal cell carcinoma mostly metastasizes to scalp and face, but urinary tract malignancies commonly metastasize to abdominal skin. Sister Mary Joseph's nodule (an umbilicated subcutaneous nodule) arises due to metastasis from intra-abdominal malignancy chiefly gastric carcinoma. Thyroid and renal cell carcinoma present with a pulsatile tumor mass and a bruit through overlying skin. Fistula may be seen in carcinoma of urinary bladder or larynx.^[15] Carcinoma en cuirasse is seen in carcinoma breast, stomach, kidney, and lungs due to carcinomatous lymphatic permeation. Carcinoma telangiectodes involve carcinoma breast. Extramammary Paget's disease is seen in *in situ* epithelial carcinoma, genitourinary, or gastrointestinal malignancy.

GENETICALLY DETERMINED SYNDROMES WITH RISK OF INTERNAL MALIGNANCY

A number of mechanisms underlie the association of genodermatoses with internal malignancy; these include chromosomal instability, faulty DNA repair mechanisms, abnormal lymphocyte function, and immunosurveillance, and in some cases, a combination of these. More precise genetic diagnosis, understanding of mechanisms, awareness of the benefits, and ability to focus screening of family members for genetic abnormalities or for cancers, is a constantly evolving area within dermatology and pediatric medicine in particular. Internal malignancies are linked to many of genomic instabilities. Gardner's syndrome characterized by multiple epidermoid cysts, fibromas, and pilomatrixomas. Peutz–Jeghers syndrome manifests as mucocutaneous pigmentation in peri- and intra-oral regions with risk of gastrointestinal malignancy.^[16] Howel–Evans syndrome (palmoplantar keratoderma) involves the risk of esophageal carcinoma. Basal cell nevus syndrome (Gorlin's syndrome) manifests as multiple basal cell carcinomas, mandibular keratocysts, dyskeratotic pits of palms, and soles with the risk of medulloblastoma and ovarian tumors.^[17] Familial melanoma syndrome (dysplastic nevus syndrome) has multiple atypical melanocytic nevi with the risk of pancreatic, gastrointestinal, lung, breast, and laryngeal carcinoma.^[18] Xeroderma pigmentosum presents with severe photosensitivity, marked reduction in the threshold for sunburn, myriads of lentigines with the risk of ocular, and cutaneous malignancy [Figures 1 and 2].^[19] Von Hippel–Landau syndrome presents with hemangiomas and cafe-au-lait spots with risks of hemangioblastoma of the central nervous system (CNS), pheochromocytoma, renal and pancreatic adenoma, carcinoma, and cysts.^[20] Neurofibromatosis type 1 and 2 presents with multiple peripheral neurofibromas, cafe-au-lait macules,



Figure 1: Xeroderma pigmentosum with malignant melanoma, lentigines, and hypopigmented macules in a 6-year-old girl

axillary freckles with the risk of CNS tumors. LAMB syndrome (Carney's syndrome) is characterized by lentigines, atrial myxomas, mucocutaneous myxomas, blue nevi with the risk of gonadal hormone secreting tumors, malignant thyroid tumors [Table 1].^[21] Cowden's disease (multiple hamartoma and neoplasia syndrome) shows warty "cobblestone" hyperplasia of the mucosal surfaces, particularly tongue and buccal mucosa, periorificial facial papules, acral warty keratosis, and punctuate keratosis with gastrointestinal polyposis and cysts or polyps of female genitourinary system along with breast adenocarcinoma.^[22] Muir-Torre syndrome presents with sebaceous lesions and keratoacanthoma with the risk of hereditary nonpolyposis colon cancer. Ataxia telangiectasia (Louis-Bar syndrome) shows



Figure 2: She developed squamous cell carcinoma, multiple malignant melanoma, cutaneous horn after 2 years over face, as well as trunk

Table 1: Pigmentary abnormalities associated with internal malignancy

Pigmentary change	Pattern	Examples
Hyperpigmentation	Diffuse, or diffuse with localized accentuation (addisonian pattern of pigmentation)	Melanoma (rarely causes diffuse slate gray pigmentation)
		Pheochromocytoma (addisonian pattern)
		Ectopic ACTH syndrome (addisonian pattern)
		POEMS syndrome (diffuse or semiconfluent speckled pattern)
		Hyperpigmentation with scleromyxedema and gammopathy
		Diffuse mastocytosis
		Lymphomas (uncommon)
		Ependymoma (mild increase in pigmentation)
		Werner's syndrome (localized or diffuse pigmentation)
		Cachexia due to neoplasia
	Patchy or reticulated	Fanconi's anemia (various pigmentary changes)
		Dyskeratosis congenita (reticulate pigmentation)
	Other distributions	Carcinoid syndrome (photo distributed)
		Pancreatic, gastric and renal tumors (erythema ab igne due to local application of heat)
	Lentigines and freckles	Peutz-Jeghers syndrome (lentigines)
		Carney complex (lentiginosis is characteristic, freckles also occur)
		Xeroderma pigmentosum (freckles)
		Neurofibromatosis (flexural freckle-like macules)
		Cowden's disease and Bannayan-Riley-Ruvalcaba syndrome (genital lentigines)
		Gardner's syndrome (freckles)
		Paraneoplastic acral lentiginosis
	Café-au-lait macules	Neurofibromatosis (Bloom's syndrome multiple endocrine neoplasia types 1 and 2B Fanconi's anemia von Hippel-Lindau disease)
	With epidermal hyperplasia	Acanthosis nigricans
	Melanocytic nevi and melanoma	Associated with pancreatic neoplasia, astrocytomas, and other cerebral neoplasms in some families
Mixed hyper- and hypo-pigmentation	Poikiloderma	Blue nevi and ordinary nevi occur in Carney complex
		Dermatomyositis (speckled pigmentation on hypopigmented background)
Hypopigmentation	Generalized	Rothmund-Thomson syndrome (photo distributed poikiloderma)
		Chediak-Higashi syndrome
		Tuberous sclerosis complex (ash leaf macules)
	Localized, multiple	Mycosis fungoides (hypopigmented variant)
		Halo depigmentation around primary tumor or metastases. Distant leukoderma, usually with centrifugal spread starting on the trunk
	Melanoma-associated (other than regression within the primary lesion)	

POEMS - Polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, skin changes; ACTH - Adrenocorticotrophic hormone

oculocutaneous telangiectasia with the risk of leukemic and breast carcinoma.^[23] Bloom syndrome characterized by sun sensitive telangiectasia, cafe-au-lait macules with the risk of lymphoproliferative neoplasia. Rothmund–Thomson syndrome presents with photosensitivity, poikiloderma along with the risk of osteosarcoma and myelodysplasia.

EXPOSURE TO CARCINOGENS

Several carcinogens such as arsenic, vinyl chloride, and radiation can produce various cutaneous manifestations. Chronic arsenic toxicity causes diffuse or spotty rain drop pigmentation, hypopigmented macules, punctuate palmoplantar keratosis, Bowen's disease, etc., vinyl chloride causes scleroderma-like skin changes with Raynaud's phenomenon and osteolysis of distal phalanges. Radiation causes radiation dermatitis of the neck which may indicate developing papillary carcinoma of the thyroid. Radiation dermatitis or multiple basal cell carcinomas over spine may indicate leukemia.

PARANEOPLASTIC SYNDROMES WITH CUTANEOUS MANIFESTATIONS

Paraneoplastic dermatoses are skin conditions that have an association with internal malignancy but are not themselves malignant. They may be classified in a variety of ways; some authors include genodermatoses within the spectrum of paraneoplastic disorders^[24] whereas others view these as a separate group^[25,26] or distinguish between paraneoplastic dermatoses,^[27] hereditary paraneoplastic syndromes,^[28] and hormonally mediated paraneoplastic syndromes. They may be classified according to strength of association with malignancy [Table 2],^[21] association with certain types of malignancy,^[29,30] by the type of eruption that occurs (papulosquamous, vascular, etc.) or by the apparent mechanism (hormone paraneoplastic syndromes have a wide clinical spectrum, and it is due to certain cytokines like transforming growth factor alpha or peptides released by the malignant cells).^[31,32] Curth's criteria are used to identify the association

Table 2: Strength of correlation of some potentially paraneoplastic dermatoses with internal malignancy

Strength of correlation	Type of reaction pattern	Examples
Strong	Papulosquamous and figurate eruptions	Bazex syndrome Erythema gyratum repens Necrolytic migratory erythema
	Deposition disorders	Primary amyloidosis scleromyxedema Necrobiotic xanthogranuloma POEMS syndrome
	Others	Acquired hypertrichosis lanuginosa Paraneoplastic pemphigus Tripe palms Carcinoid syndrome Trousseau's syndrome
Moderate	Papulosquamous and neutrophilic eruptions	Sweet's syndrome Pyoderma gangrenosum Dermatomyositis
	Others	Multicentric reticulohistiocytosis Pityriasis rotunda
Weak	Epidermal conditions	Acanthosis nigricans in isolation Acquired ichthyosis (unless widespread, deeply fissured, truncal pattern) Eruptive seborrheic keratoses (sign of Leser-Trélat)
	Deposition disorders	Scleredema Calcinosis cutis
	Others	Vasculitis, Raynaud's phenomenon, digital ischemia erythromelalgia Relapsing polychondritis Erythroderma/exfoliative dermatitis Digital clubbing (unless with hypertrophic osteoarthropathy) Pruritus Erythema annulare centrifugum Cushing's syndrome

POEMS - Polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, skin changes

between various dermatoses and underlying neoplasia. Disorders that fit Curth's criteria include acanthosis nigricans and possibly a sign of Leser–Trelat, Bazex's syndrome, Carcinoid syndrome, erythema gyratum repens, hypertrichosis lanuginosa, ectopic adrenocorticotrophic hormone (ACTH) syndrome, Glucagonoma syndrome, neutrophilic dermatosis, Paget's disease, and paraneoplastic pemphigus.^[33] Disorders associated statistically with cancer include dermatomyositis, extramammary Paget's disease, exfoliative dermatitis, mycosis fungoides, palmer keratoses, generalized pruritus without primary cutaneous eruption, porphyria cutanea tarda, and pityriasis rotunda.^[34] Dermatoses possibly associated with cancer includes arsenical keratoses, erythema annulare centrifugum, acquired ichthyosis, multicentric reticulohistiocytosis, necrobiotic xanthogranuloma, classic pyoderma gangrenosum, polymyositis, tripe palms, vasculitis, and vitiligo.

LESIONS DUE TO DEPOSITION OF SUBSTANCES IN SKIN

Icterus is due to extrahepatic destruction due to malignancy of gallbladder, pancreas, bile duct, or adjacent bowel. Melanosis is due to melanin which is seen in ACTH-producing tumors, primary pituitary tumor,

metastasis to pituitary gland, and malignant melanoma. Hemochromatosis is diffuse gray pigmentation of skin due to hemosiderin deposition seen in hepatocellular carcinoma [Table 3].^[21] Xanthomas are seen in multiple myeloma, myelocytic leukemia, myelomonocytic leukemia, diffuse histiocytic lymphoma, and cutaneous T-cell lymphoma. Systemic amyloidosis is seen in multiple myeloma.

VASCULAR AND BLOOD ABNORMALITIES

Flushing is seen in carcinoid syndrome; unilateral flushing is seen in contralateral lung cancer with Pancoast syndrome. Palmer erythema occurs in primary or metastatic liver tumor. Telangiectasias are seen in ataxia telangiectasia, Bloom's syndrome, xeroderma pigmentosum. Localized telangiectasia occurs on anterior chest wall in breast carcinoma. Generalized telangiectasia occurs in malignant angioendotheliomatosis. Progressive telangiectasia is seen in carcinoid tumors. Lymphoma is the most common cause of purpura. Acute leukemia leads to disseminated intravascular coagulation which causes purpura. Leukocytoclastic vasculitis is seen in SCC of bronchus, renal cell carcinoma, leukemia, and lymphoma.^[35] Digital ischemia is seen in carcinoma pancreas, stomach, small bowel, ovary, and

Table 3: Some deposition disorders that are linked with internal malignancy

Material deposited	Disorder	Associated internal malignancies	Comments
AL proteins	Primary and myeloma-associated systemic amyloidosis (AL protein deposition)	Paraproteinemia, myeloma	Amyloidosis occurs in about 15% of patients with myelomatosis
	Secondary amyloidosis (AA protein deposition)	Lymphomas, especially Hodgkin's lymphoma Hypernephroma Other solid tumors	
Mucin/proteoglycans and fibromucinoses	Scleromyxedema/lichen myxedematosus	Paraproteinemia, typically a "slow gamma region"	Paraprotein is present in most cases
	Papular mucinosis	Paraproteinemia	Uncommon
	Scleredema	Paraproteinemia	More commonly associated with diabetes or streptococcal infection
	POEMS syndrome	Paraproteinemia	Features are polyneuropathy, organomegaly, endocrinopathy, M-protein, skin changes
Lipids (as foamy macrophages)	Necrobiotic xanthogranuloma	Paraproteinemia, usually monoclonal IgG, present in about 70% of cases	Also associated with cryoglobulinemia, myeloma, marrow dyscrasias and rarely leukemia; some cases apparently occur in isolation
	Normolipemic plane xanthomatosis	Myeloma	Usually IgG paraprotein
	Xanthoma disseminatum	Gammopathy, bone marrow dyscrasias	Usually IgG paraprotein
Calcium	Metastatic calcification	Lung and other squamous carcinomas Due to primary hyperparathyroidism. may be associated with multiple endocrine neoplasia syndromes	Due to ectopic parathyroid-like hormone secretion
	Dystrophic calcification	Pancreatic carcinoma	Calcification of fat

POEMS - Polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, skin changes; AL - Amyloid; AA - Amyloid A

kidney. Migratory superficial thrombophlebitis is seen in tumors of stomach, pancreas, prostate, lung, liver, bowel, gallbladder, and ovary. Type 1 cryoglobulinemia is associated with multiple myeloma, Waldenström's macroglobulinemia, and B-cell malignancies. Deep vein thrombosis is associated with mucinous adenocarcinoma, myeloproliferative disorders, and metastatic cancers.^[36] Erythromelalgia is seen in polycythemia vera and essential thrombocytopenia.^[37]

BULLOUS DISORDERS

Paraneoplastic pemphigus seems to have an association with non-Hodgkins lymphoma, chronic lymphocytic leukemia (CLL), Castleman tumor, thymoma, etc. Pemphigus is associated with thymoma, Hodgkin's disease. Herpes gestationis is associated with hydatidiform mole and germ cell tumor. Epidermolysis bullosa acquisita is associated with carcinoma of bronchus along with amyloidosis and multiple myeloma. Linear IgA dermatosis is associated with lymphoma, CLL, carcinoma bladder and esophagus, and hydatidiform mole. Cicatricial pemphigoid is seen in carcinoma lung, stomach, colon, and endometrium.^[38]

DISORDERS OF KERATINIZATION

Acanthosis nigricans is seen in gastric and intra-abdominal adenocarcinoma.^[33] May be seen in carcinoma lung, uterus, esophagus, pancreas, colon, breast, ovary, or prostate, as well as lymphoma. Acquired ichthyosis is seen in Hodgkin's lymphoma, carcinoma lung, breast, and cervix. Palmer hyperkeratosis is seen in esophageal carcinoma; palmoplantar keratoderma is seen in breast or ovarian carcinoma. Tripe palms occur in gastric and lung carcinoma. Erythroderma is seen in leukemia, lymphoma. Paraneoplastic acrokeratosis of Bazex characterized by symmetric erythematous and violaceous scaly papules on hands, feet, knees, ears, and nose is seen in SCC of oropharynx, larynx, lung, esophagus, and thymus.^[39] Florid cutaneous papillomatosis is characterized by multiple acuminate keratotic papules is seen in carcinoma stomach, breast, lungs, and ovary.^[40] Sign of Leser–Trelat (rapid increase in size of multiple seborrheic keratosis) is seen in adenocarcinoma of stomach or colon. Multiple cherry angiomas are associated with solid tumors.^[41] Multiple skin tags are associated with colonic polyps. Pityriasis rotunda characterized by fixed, annular, scaly, noninflamed, and hyperpigmented lesions on trunk occurs in hepatocellular carcinoma.

COLLAGEN VASCULAR DISEASE

Dermatomyositis is seen in carcinoma ovary, lung, pancreas, stomach, colorectal, and lymphoma. Lupus erythematosus occurs in lymphoma, thymoma. Scleroderma is seen in carcinoma lung, esophagus. Systemic lupus erythematosus is associated with lymphoreticular malignancies, myeloma, and paraproteinemias.

MULTISYSTEM AND HAEMOPOIETIC TUMORS THAT INVOLVE THE SKIN

Skin involvement occurring in these disorders ranges from very nonspecific like purpura, through to highly specific features such as cutaneous deposits of the malignancy as in lesions of leukemia cutis. There may be features that suggest a particular diagnosis like oral leukemic deposits, most typically seen in myelomonocytic leukemia, or other cutaneous disease associations as seen with neurofibromatosis type 1 associated with juvenile xanthogranuloma and juvenile myelomonocytic leukemia.^[42-44] Involvement of the skin as a part of a multisystem tumor differs from metastases from solid tumors in both mechanism, as well as the fact that lesions are often widespread. Specific cutaneous infiltrations of the skin may occur with myeloproliferative disorders, more commonly with lymphoma, but can also occur with leukemia.^[45]

INTERNAL MALIGNANCY PRESENTING AS PRURITIS

Internal carcinoma is an important cause of pruritus though it is rare and nonspecific. Mechanisms that may be involved include secondary metabolic effects like uremia, cholestasis, or due to iron-deficiency anemia, acquired ichthyosis or xerosis. Paul *et al.* in his 6-year study, in patients with generalized pruritus, found no significant increase in malignancy.^[46] Itch may be a severe problem in patients with Hodgkin's disease and may indicate a poorer prognosis.^[47] Other hematological disorders such as Sézary syndrome, mycosis fungoides, myelomatosis and leukemia, may also cause generalized pruritus.^[48,49] In polycythemia rubra vera (PRV), the initiating factor appears to be rapid cooling of the skin as encountered after bathing. This is thought to be due to the release of pruritogens by degranulated mast cells.^[50] However, patients with PRV can also develop intractable itching unrelated to bathing. Many other visceral carcinomas that can cause pruritus include breast and gastrointestinal cancers and carcinoid syndrome.^[51]

Nerve damage by a tumor at any site can cause neuropathic pain or pruritus. The patterns that are most likely to present to a dermatologist are brachioradial pruritus and localized facial or nasal pruritus. Brachioradial pruritus^[52] most commonly affects the lateral upper arm or dorsum of the forearm. Most of these cases are mechanical due to bony abnormalities, but a case due to a spinal tumor has been reported, with rapid resolution of symptoms after treatment.^[53] Brain tumors are an uncommon cause of pruritus localized to the face.^[52,54] Pruritus limited to the nostrils is particularly linked with tumors invading the floor of the fourth ventricle, but tumors elsewhere in the brain and other cerebral lesions (e.g., abscesses), as well as trigeminal neuralgia, can also produce this distribution of pruritus.

OTHER MANIFESTATIONS OF INTERNAL MALIGNANT DISEASES

Erythema gyratum repens characterized by erythematous bands moving in waves over the body occurs in carcinoma breast, lung, bladder, prostate, cervix, stomach, esophagus, and multiple myeloma.^[55] Erythema annulare centrifugum is associated with CLL, malignant histiocytosis, Hodgkin's disease and carcinoma bronchus, nasopharynx, prostate, ovary, or rectum. Subcutaneous fat necrosis is seen in acinar cell carcinoma of the pancreas. Sweet syndrome characterized by generalized, crimson, agminate papules to large red plaques is seen in acute myelocytic leukemia, myelodysplastic syndrome, multiple myeloma, and lymphoma. Less commonly, it is seen with embryonal carcinoma of testis, ovarian carcinoma, gastric carcinoma and adenocarcinoma of breast, prostate, and rectum. Hypertrichosis lanuginosa acquisita which is the growth of villous hairs over face and ears is caused mainly by drugs but associated with tumors of colon, rectum, bladder, lung, pancreas, gallbladder, uterus, and breast.^[56] Necrolytic migratory erythema characterized by erythema, vesicles, pustules, bullae and erosions involving face, intertriginous area, and perigenital region is seen in glucagonoma syndrome. Porphyrria cutanea tarda is associated with liver carcinoma.^[56] Pyoderma gangrenosum is associated with acute myelogenous leukemia, chronic myeloid leukemia, acute lymphoblastic leukemia, multiple myeloma, and polycythemia rubra vera. Paraneoplastic sweating is seen in Hodgkin's lymphoma, liver metastasis due to release of pyrogens from tumor. Herpes Zoster and Herpes Simplex are associated with lymphomas and leukemias. Insect bite hypersensitivity is seen in hematological malignancies like CLL and also in Epstein-Barr virus-associated lymphoproliferative disease. Clubbing is seen in bronchogenic carcinoma and mesotheliomas.^[57] Scleromyxedema is seen in multiple myeloma, Waldenstrom's macroglobulinemia, Hodgkin's or non-Hodgkins lymphoma, or leukemias.

Lichen planus may rarely be induced by neoplasia.^[58]

Urticaria especially cold urticaria and peripheral gangrene as a result of circulating cryoglobulins, though uncommon, is linked with myeloma and lymphoma.^[59]

Erythroderma and exfoliative dermatitis have both been linked with malignancy.^[33,49] In around 10% cases, the causative neoplasm is mycosis fungoides or its leukemic variant, Sézary syndrome. There are additionally reported cases of erythroderma with cancers of liver, lung, colon, stomach, pancreas, thyroid, prostate, and cervix.^[33,49,60] Ofuji papuloerythroderma has also been associated with peripheral T-cell nonepidermotrophic cutaneous lymphoma.^[61] Granuloma annulare has been reported

in association with lymphomas, other hematological malignancies, and uncommonly with solid tumors.^[62]

"Insect bite-like" reactions are reported in hematological malignancy, usually chronic lymphocytic leukemia.^[63] Cutis verticis gyrata may occasionally occur as a paraneoplastic phenomenon.^[64] Mental neuropathy ("numb chin syndrome") may occur as a feature of metastatic disease and is considered an indicator of poor prognosis.^[65] Tumors causing it include breast, thyroid, renal, lung, prostate, lymphomas, and melanoma.

CONCLUSION

Skin acts like a mirror for various underlying diseases, especially malignancies. Skin manifestation may be sometimes the only symptom of underlying disease. Many underlying malignancies present with cutaneous manifestations, few of them being specific. A keen eye is, therefore, required by a dermatologist to treat all the skin conditions keeping associated malignancies in mind.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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There are no conflicts of interest.

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