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TOPIC HIGHLIGHT

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Paraneoplastic dermatological manifestation of gastrointestinal malignancies

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Abstract

Numerous dermatological disorders have been associated with underlining malignancies of the gastrointestinal (GI) tract. Such cutaneous manifestations might have an important diagnostic value if they are the sole expressions of otherwise asymptomatic carcinomas. The recognition of some typical paraneoplastic dermatologic disorders can lead to the prompt diagnosis of the underlying malignancy, timely administration of therapy, and ultimately, better prognosis. In this review we discuss the most common paraneoplastic dermatological syndromes from the perspective of the practicing gastroenterologist. We also outline a comprehensive practical approach for the evaluation for occult malignancy in patients presenting with cutaneous findings potentially associated with GI cancers.

Key words: Paraneoplastic; Dermatological; Gastrointestinal; Cancer; Malignancy

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INTRODUCTION

Numerous cutaneous disorders have been associated with underlining malignancies of the gastrointestinal (GI) tract. In some cases the skin can be directly infiltrated by cancer cells that represent metastatic spread from a GI malignancy (e.g. a Sister Mary Joseph nodule). In other cases, the skin lesions are related to the underlying presence of malignancy, but they do not contain malignant cells and are referred to as paraneoplastic dermatological syndromes[1]. Some of them, such as Muir-Torre, Peutz-Jeghers, and Cronkhite-Canada syndromes, are inherited and are caused by genetic factors, others however, have unknown etiologies and unpredictable expression and prognosis.

Dermatologists have the advantage of recognizing certain cutaneous signs, which hint at underlying visceral malignancies. From a practical perspective, such cutaneous manifestations might have an important diagnostic value if they are the sole expressions of otherwise asymptomatic carcinomas. The recognition of some typical paraneoplastic dermatologic disorders can lead to prompt diagnosis of the underlying GI malignancy, timely administration of therapy, and ultimately, better prognosis. In this review we will discuss the most common paraneoplastic dermatologic syndromes from the perspective of the practicing gastroenterologist (Table 1).

ACANTHOSIS NIGRICANS

Acanthosis nigricans (AN) is a classic example of a paraneoplastic dermatosis, and its frequent relation with GI tract malignancies was emphasized by Darier at the end of the 19th century[2]. The disease initiates with symmetric skin hyperpigmentation in the axillary and inguinal folds, submammary region, around the mammilla, umbilical, and ano-genital regions. Later, the skin lesions can infiltrate and become slightly hyperkeratotic pigmented velvety plaques surrounded by acrochordons (Figure 1). The neck region is frequently

Table 1 Relationships between morphologic features of cutaneous paraneoplastic disorders and gastrointestinal malignancy

Dermatologic disorder	Cutaneous manifestations	Localization	Associated gastrointestinal malignancy
Acanthosis nigricans	Pigmented papillomatous plaques	Axillar and inguinal folds, submammary and mammilla region, ano-genital regions	Gastric carcinoma; Colorectal carcinoma
Palmo-plantar keratoderma	Diffuse epidermal thickening with rugose appearance	Palms, fingers and soles	Gastric carcinoma; Hepatic metastases
Acrokeratosis paraneoplastica (Bazex syndrome)	Erythematous psoriasiform plaques	Hands, feet, ears, nose, elbows and knees	Squamous cell carcinoma of oropharynx/ esophagus; Adenocarcinoma
Leser-Trélat syndrome	Multiple seborrheic keratoses	Trunk and extremities	Gastric carcinoma; Colorectal carcinoma; Esophageal carcinoma; Pancreatic carcinoma
Muir-Torre syndrome	Sebaceous adenomas; Sebaceous carcinomas; Keratoacanthomas	Head, trunk and extremities	Colorectal carcinoma; Colorectal adenomatous polyps
Paraneoplastic dermatomyositis	Periorbital heliotrope erythema and edema; Gottron papules; Gottron sign	Eyelids, upper cheeks, forehead; Phalangeal joints; Elbows, knees	Colorectal carcinoma; Gastic carcinoma; Hepatocellular carcinoma
Paraneoplastic pemphigus	Erosions; Vesicles and blisters, Erythematous to violaceous patches papules, plaques	Oral cavity; Head, trunk and extremities	Castleman's disease; Sarcoma; Adenocarcinoma; Squamous cell carcinoma
Peutz-Jeghers syndrome	Hyperpigmented macules	Buccal mucosa, gums; Tips of the fingers and toes	Multiple intestinal polyps; Colorectal carcinoma; Pancreatic carcinoma; Gastic carcinoma; Small bowel carcinoma
Cronkhite-Canada syndrome	Hyperpigmented macules; Nail plate separation, discoloration and atrophy; Alopecia	Hands, palms, arms, neck and face; Fingernails and toenails; Scalp	Hamartomatous polyps; Colon carcinoma; Gastic carcinoma
Paraneoplastic hypertrichosis lanuginosa acquisita	Lanugo hairs	Head, trunk and extremities	Colorectal carcinoma; Pancreatic carcinoma

affected in childhood. Similar pigmented papillomatous lesions can be observed on the mucous membranes of the oral cavity, nasal, and laryngeal mucosa, and vulva. The areola of the nipple can also be affected. Nails are brittle and hyperkeratotic, and leukonychia have been reported. Noncicatricial alopecia in the axilla and pubic regions is also possible.

AN can be idiopathic when related to endocrine disorders (obesity, insulin resistance, or overt diabetes mellitus), and only in some cases is it associated with malignancy[3]. Only 20 cases of oral malignant AN were reported in the English language literature from 1968 to 2002[4]. In malignancy-associated acanthosis nigricans the lesions are often more extensive and severe than when the cause is benign, and skin irritation can be a prominent and distressing symptom. Moreover, the skin lesions usually appear before the onset of any other GI symptoms[5]. Malignancy-associated acanthosis nigricans is frequently seen with GI cancers[6-8].

Anderson *et al*[8] presented a 66-year-old male patient with poorly differentiated, metastatic gastric adenocarcinoma, who complained of severe pruritus and developed severe AN on the chest and nipples. The patient was treated with 5-fluorouracil, cisplatin and epirubicin chemotherapy resulting in dramatic improvement of the dermatological disorder and quality of life; however, the patient died six months latter due to lymphangitic carcinomatosis. The authors assumed that factors affecting epidermal proliferation are involved because of the reduction in papillomatosis and increase in cutaneous pigmentation after chemotherapy administration[8]. Pentenero *et al*[4] reported a case of a 53-year-old man with gastric adenocarcinoma who suddenly developed hyperkeratotic, verrucous, slightly pigmented, brownish papules in the axillae and thickened mucosa with a velvety and papillomatous surface, without hyperpigmentation on the lips, buccal mucosa and palate. Skin biopsies, performed from the buccal mucosa and the axilla, confirmed the diagnosis of AN with mucosal localization[4].

Palmo-plantar keratoderma or "tripe palms" is a recognized feature of acanthosis nigricans and presents with epidermal thickening with a rugose appearance and broadened rete ridges bounded by deep sulci of the palms and fingers[4,9] (Figure 2). Breathnach and Wells describe five patients with palmo-plantar keratoderma and acanthosis nigricans associated with gastric adenocarcinoma and in two patients they found squamous cell carcinoma[9].

The exact pathophysiological mechanism of the paraneoplastic AN has not been well defined, but it could be related to cancer byproducts. Transforming growth factor alpha, structurally related to epidermal growth factor (EGF), has been considered as possible causative agent[3,4].

The prognosis of the malignancy associated acanthosis nigricans tends to be poor because the underlying malignancy appears to behave aggressively. The average survival time of patients with signs of paraneoplastic AN is two years, although cases in which patients have survived for more than 10 years have been reported. Importantly, older patients with new onset AN usually have associated internal malignancy and therefore targeted investigation should be carried out (see below).

ACROKERATOSIS PARANEOPLASTICA (BAZEX SYNDROME)

The first patient with this entity was described by

Bazex *et al*[10] in 1965, as "paraneoplastic syndrome with hyperkeratosis of the extremities". Clinical manifestations include erythematous or livid squamous plaques resembling psoriasis, which are symmetrically distributed in acral regions and affect mainly the hands, feet, ears, nose, elbows and knees[11]. Skin biopsies usually reveal nonspecific findings, including hyperkeratosis, acanthosis, parakeratosis, vacuolar degeneration, pigment incontinence, and a perivascular infiltrate of lymphocytes and histiocytes and occasionally dyskeratotic keratinocytes[11].

Bazex syndrome predominates in males over 40 years and is most commonly associated with squamous cell carcinoma (SCC) of the upper bronchial and GI tracts[11,12]. Adenocarcinomas of the stomach[13], colon[14], biliary system and hepatocellular carcinoma[11], are also described in the literature. In a retrospective study of the primary location of malignancies in 113 patients with Bazex syndrome, Bolognia *et al*[15] reported the following results: oropharynx and larynx (48.6%), lung (17.7%), unknown location (16%), esophagus (10.6%, one of them with an associated pyriform sinus carcinoma), and isolated cases in the prostate, liver, stomach, uterus, vulva, and bone marrow.

LESER-TRÉLAT SYNDROME

Ulysse Trélat (1884) and Edmund Leser (1901)[16], both surgeons, were the first to propose that multiple seborrheic keratoses could be associated with internal malignancy. Denucé, who was a resident of Trélat, wrote in 1899 that the professor had often stressed the symptom of "Trélat's nevi" associated with deep tumors of the abdomen and pelvis in his lectures[17]. The indication of Leser-Trélat or Leser-Trélat syndrome (LTS) is an eruptive appearance of, or at least a sudden increase in, the number or size of multiple seborrheic keratoses in association with an internal malignancy[18,19]. No evidence of dermatitis or erythroderma precedes the seborrheic keratoses appearance on the skin and pruritus is a leading symptom in about half of the cases[20]. Seborrheic keratoses associated with malignancy show no clinical or histological differences compared to patients without neoplasia[21]. The majority of patients with LTS have adenocarcinomas, most commonly of the stomach[22,23], colon or rectum[19,21,24-28], and less frequently carcinomas of esophagus[29], duodenum[30], pancreas[31], gallbladder[32] or hepatocellular carcinoma[33].

We observed a 66-year-old man who presented with multiple flat, sharply demarcated, yellowish to brown lesions with a verrucous surface located mainly on the trunk arms and thighs, which were clinically very suggestive of seborrheic keratoses (Figure 3). The patient developed fever and night sweats. A barium enema detected a tumor in the rectum. Computed tomography (CT) showed no evidence of distant metastasis. The rectal lesion was removed surgically, and histology showed moderately differentiated rectal adenocarcinoma involving muscularis propria with no evidence of perirectal lymph node involvement. However, three months after the operation, seven lung metastases were visualized by CT. During courses of 5-fluorouracil, oxaliplatin and capecitabine chemotherapy, the cutaneous lesions markedly diminished but did not completely disappear[19]. We found 14 other published cases of Leser-Trélat syndrome associated with colorectal adenocarcinoma in the literature from 1972 to 2004[19].

About two-thirds of patients with LTS can have other paraneoplastic disorders, the most frequent of which is acanthosis nigricans, which accounts for one third of these cases[34]. Moreover, Andreev *et al*[35] considered that Leser-Trélat syndrome represents a particular clinical variant of acanthosis nigricans. The pathogenesis of LTS remains unclear. As in malignant acanthosis nigricans, an increased epidermal staining for the transforming growth factor alpha receptor has been observed[36].

MUIR-TORRE SYNDROME

In 1967 Muir *et al*[37], and later Torre[38], reported patients with multiple sebaceous neoplasms and visceral malignancies. Muir-Torre syndrome (MTS) is defined by the development of internal malignancy, most commonly colon cancer, in association with sebaceous adenomas and epitheliomas, sebaceous carcinomas and multiple or early-onset keratoacanthomas[39]. The syndrome has autosomal dominant inheritance, and is considered as a subtype of hereditary nonpolyposis colorectal cancer syndrome (HNPCCS). Sixty percent of patients with MTS have a strong family history of visceral malignancy and show clinicopathological overlap with HNPCCS[40]. The pathogenesis includes mutations in the DNA mismatch repair genes (MLH-1 or MSH-2)[39]. HNPCC and MTS usually result from an inherited defect in one allele of either MLH1 or MSH2[41]; however, Muir-Torre syndrome more commonly involves a mutation of MSH2, while HNPCC shows a roughly equal prevalence of MLH1 and MSH2[42].

Sebaceous gland tumors in MTS include sebaceous adenoma, sebaceous carcinoma and keratoacanthoma with sebaceous differentiation[40]. Sebaceous hyperplasia and ectopic sebaceous glands do not appear to be significant markers of the syndrome. Sebaceous adenoma is believed to be the most specific lesion of Muir-Torre syndrome and these can sometimes show cystic change or keratoacanthoma-like architecture[42]. Between 24%-30% of patients with MTS have sebaceous carcinomas[39,43].

Cancers of the GI tract comprise more than 60% of the visceral malignancies in MTS, and colorectal cancer is the predominant neoplasm[39,44]. Tumors are located predominantly in the proximal colon (cecum to splenic flexure), in contrast to the general populace, whose colorectal tumors are usually distal to the splenic flexure[44,45]. An association with colorectal adenomatous polyps was observed in 26% of patients with MTS[45].

Recently, a 54-year-old Japanese man with MTS who developed a sebaceous carcinoma and concurrently adenocarcinoma of the colon was reported[46]. A novel germline mutation of the *MSH2* gene with duplication of the genomic region involving exon 7 was identified[46].

Multiple sebaceous tumors or sebaceous tumors

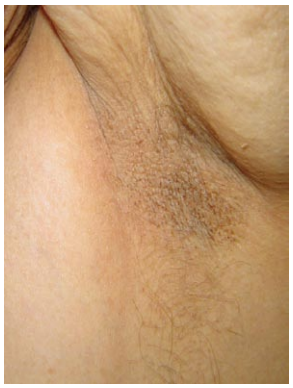

Figure 1 Hyperpigmented papillomatous plaques in left axial of a male patient with acanthosis nigricans.

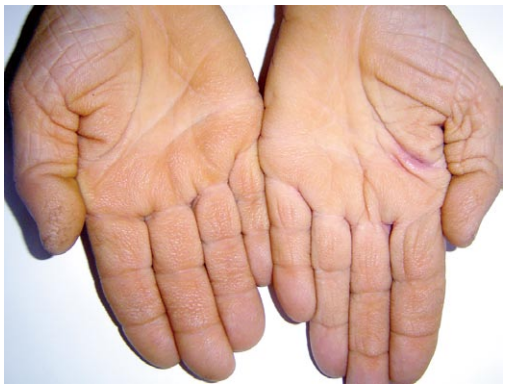

Figure 2 "Tripe palms" keratoderma on the palms of the same patient.

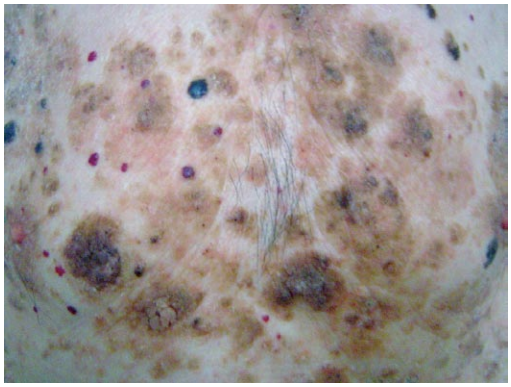

Figure 3 Multiple eruptive seborrheic keratoses on the trunk of a 66-year-old patient with rectal adenocarcinoma.

occurring before the age of 50 years are strong indicators of Muir-Torre syndrome. Moreover, MTS should be suspected in all cases when sebaceous gland tumors or multiple keratoacanthomas have been diagnosed. Some authors suggest that all patients with sebaceous-gland neoplasms should be screened for MTS in contrast to those with keratoacanthomas because they are less likely to be markers of MTS[47]. All patients with MTS should undergo a colonoscopy to detect colorectal neoplasms.

PARANEOPLASTIC DERMATOMYOSITIS

The first report of paraneoplastic dermatomyositis (PDM) was by Stertz[48], who in 1916 observed a patient with proximal muscle weakness, eyelid changes, muscle

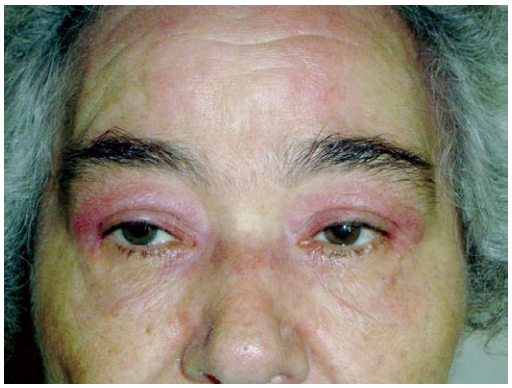

Figure 4 Periorbital heliotrope erythema and edema in a patient with paraneoplastic dermatomyositis.

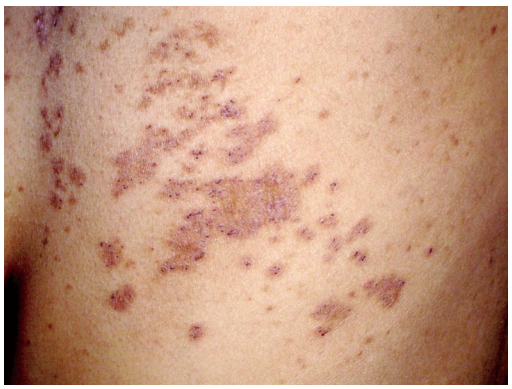

Figure 5 Violaceous plaques with erosions on the trunk of a patient with paraneoplastic pemphigus.

biopsy evidence of myositis, associated with gastric cancer. Dermatomyositis (DM) is a rare idiopathic inflammatory myopathy that presents clinically with proximal muscle weakness and characteristic cutaneous manifestations[49]. Skin lesions can be classified as pathognomonic, characteristic, and compatible with DM[50]. The more specific or pathognomic manifestations of DM are the periorbital heliotrope rash, and erythematous maculopapular lesions covering bony prominences, described by Gottron in 1931 and named after him as Gottron papules and Gottron sign[49,50]. The "Heliotrope" rash presents as a red to purple-colored confluent, macular erythema involving symmetrically the eyelids, upper cheeks, forehead, and the temples and is often associated with edema of the eyelids and periorbital tissues (Figure 4). Other characteristic skin lesions include: shawl sign (a violaceous erythema disposed in a "shawl" distribution over the neck, upper back, and shoulders), photosensitive poikiloderma, diffuse redness and shininess of the nail folds, "mechanic's hands" hyperkeratosis, cutaneous calcinosis, and scalp erythema[49,51]. Other contemporary criteria for diagnosis of DM include the appearance of symmetric proximal muscle weakness, an elevation of serum skeletal-muscle enzymes levels, abnormal electromyography, features of inflammatory infiltration in muscle biopsy, autoantibodies against RNA syththetase antigens (Jo-1, PL-7, PL-12, and OJ) or against Mi2 or SRP antigens in patients' sera[52].

The increased risk for developing cancer in DM patients has been convincingly demonstrated in several studies from Sweden[53], Australia[54], and Scotland[55]. The malignancy can precede, occur concurrently with, or follow the diagnosis of dermatomyositis. In patients with dermatomyositis several predictive factors for the presence of underlying malignancy have been described including: age over 50 years, male gender, the presence of cutaneous necroses and ulcers, increased erythrocyte sedimentation rate and C-reactive protein, and highly elevated or normal serum creatinine kinase[56-58].

Different types of tumors are observed in dermatomyositis patients. Adenocarcinomas are the most common and, in general, the frequency of each cancer type corresponds to those in the general population. In a study of 750 patients with polymyositis or dermatomyositis in Sweden, Sigurgeirsson *et al*[53] reported that the colon (including the rectum) and the lungs were the most frequent cancer sites. Hatada *et al*[59] mentioned that in Japan, gastric cancer was the most frequent malignant disease (25.4%) among patients with dermatomyositis. In South-Eastern Asia, the incidence of nasopharyngeal carcinoma is elevated in the male population with or without dermatomyositis[60]. In another retrospective study, 12 patients with internal malignancy were described among group of 64 patients with polymyositis and 28 patients with dermatomyositis[61]. Of those 12 patients, four had GI tract malignancies (two male patients, 74- and 75-year-old respectively had gastric carcinoma; another 51-year-old female had pharyngeal carcinoma and one female had pancreatic cancer)[61]. From 1941 to 1988 only one case of paraneoplastic dermatomyositis associated with gastric cancer has been reported in Bulgaria[62]. Since then, twelve additional PDM cases have been documented[63]. Two of these 12 cases in our retrospective study of patients with PDM, had GI malignancy; a 54-year-old female who had rectal adenocarcinoma and a 64-year-old patient with pancreatic cancer[59].

Many authors have stressed the importance of early investigation targeted at detecting malignancy in dermatomyositis. A detailed search for malignancy should be carried out during the first three to five years after the disease onset, however the optimal cancer-screening regimen necessary for patients with a recently diagnosed myositis remains uncertain.

PARANEOPLASTIC PEMPHIGUS

Paraneoplastic pemphigus (PNP) is an autoimmune bullous disease characterized by the production of various autoantibodies against plakin proteins in keratinocytes. The disease was described by Anhalt *et al*[64] in 1990. Patients with paraneoplastic pemphigus have to fulfill at least four of the following five criteria: polymorphic eruption on skin and mucous membranes, histopathological features that include intraepidermal acantholysis and dyskeratosis with vacuolar changes, intraepidermal and/or basal membrane zone deposition of IgG and C3 on direct immunofluorescence (IF), and serum autoantibodies against 250, 230, 210 and 190 kDa antigens (mainly desmoglein 1 and 3, periplakin and envoplakin) in immunoblotting[64,65].

The mucosal involvement includes erosions of the oral cavity, conjunctiva, pharynx, anogenital areas and even the GI mucosa[65,66]. Cutaneous manifestations of PNP are heterogeneous, and include vesicles and blisters, erythematous to violaceous maculae, papules, plaques, and even erythroderma (Figure 5). The morphology of the lesions resembles a variety of dermatological diseases, including pemphigus vulgaris, bullous pemphigoid, erythema multiforme, and lichen planus[64,66,67].

Paraneoplastic pemphigus cases have been reported more often in patients with a history of lymphomas, chronic lymphocytic leukemia, poorly differentiated sarcoma and Castleman's disease. In a retrospective study of 163 cases with paraneoplastic pemphigus reported between 1990 and 2003 carcinomas were diagnosed in 14 cases; consisting of adenocarcinoma in seven, squamous cell carcinoma in two, multiple basal cell carcinomas in one, and bronchogenic carcinoma also in one patient[68]. Ostezan *et al*[69] presented a patient with severe mucocutaneous involvement of PNP associated with hepatocellular carcinoma. However, PNP is not always accompanied by neoplasia[69], suggesting that other factors such as drugs and inflammatory diseases can trigger autoantibody formation related to PNP in the absence of a neoplasm[70].

In 2001, Nguyen *et al*[71] proposed a new term for this disease-"paraneoplastic autoimmune multiorgan syndrome" (PAMS), which, according to them, reflects the presence of target antigens and the pathologic damage frequently occurring in multiple organ systems including lung, kidney, and muscle.

PEUTZ-JEGHERS SYNDROME (HEREDITARY INTESTINAL POLYPOSIS SYNDROME)

Peutz-Jeghers syndrome (PJS) is an autosomal dominant disorder described in 1921 by Peutz, who noted a relationship between the intestinal hamartomatous polyps and mucocutaneous macules in a Dutch family[72]. The syndrome is caused by mutations in *STK11/LKB1*, serine/threonine kinase 11 genes, located on band 19p13.3[73].

Cutaneous lesions consist of 1-5 mm diameter hyperpigmented macules, irregularly distributed over the buccal mucosa, gums, hard palate and lips, mainly on the lower lip. Lentigines usually appear during early childhood, and have a tendency to increase in size[74]. Larger maculae (melanosis) are rarely seen over the back of the hands, the tips of the fingers and toes, and over the palms and soles[75].

GI tract manifestations include numerous intestinal polyps in the jejunum, ileum and less frequently in the colon, rectum, stomach and duodenum that are typical hamartomas[75]. Histology reveals pseudo invasion of the epithelial cells, forming benign glands surrounded by smooth muscle. About half of PJS patients die from cancer before the age of 60. The cumulative risk for

developing GI tract associated cancers in patients with PJS aged 15-64 years varies according to the localization from 0.5% for the esophagus, 29% for the stomach, 13% for the small intestine, 36% for the pancreas to 39% for the colon and rectum[76].

CRONKHITE-CANADA SYNDROME

In 1955 Cronkhite *et al*[77] described two women with acquired generalized GI polyps with features of hamartomatous polyps and epidermal changes.

Cutaneous lesions in patients with Cronkhite-Canada syndrome (CCS) include hyperpigmented macules ranging from a few millimeters to 10 cm in diameter, localized on the dorsal surface of the hands, palms, arms, neck, face and scalp[74]. Fingernails and toenails have discoloration, atrophy, nail plate separation and shedding. Alopecia occurs rapidly and in some cases leads to total hair loss[74,78].

GI lesions in CCS are hamartomatous polyps histologically revealing pseudopolypoid-inflammatory changes. Although considered a benign condition, in 1967, Gomes da Cruz[79] reported an association of this syndrome with a cancer of the cecum and descending colon. Among 387 cases published in literature by the end of 2002, Cronkhite-Canada syndrome associated with colon cancer has been reported in 31 (8%) cases, and other 19 CCS patients (5%) had concomitant gastric cancer[80].

Some authors propose phenotypic overlap between the features of CCS, and Peutz-Jegher syndrome, particular in the morphology of cutaneous and intestinal lesions[81,82]. In contrast to PJS, however, no underlying genetic mechanism has been found so far in Cronkhite-Canada syndrome.

PARANEOPLASTIC HYPERTRICHOSIS LANUGINOSA ACQUISITA

In 1865, Turner reported a woman with breast cancer whose face and body in two or three weeks became covered with a thick crop of short and white downy hair[83]. Lanugo hairs are long, thin and unpigmented, affecting the face and spreading in a caudal direction on the entire integument. Paraneoplastic hypertrichosis lanuginosa acquisita (PHLA) is predominant in women, and colorectal carcinoma is the most frequently associated malignancy, followed by lung and breast cancer[84-86]. Patients usually have metastatic disease at the time of diagnosis and a poor prognosis[86]. PHLA is associated with other paraneoplastic disorders such as acanthosis nigricans (which supports the hypothesis of tumor-produced cytokines stimulation over hair follicles).

EVALUATION OF PATIENTS WITH DERMATOLOGICAL MANIFESTATIONS ASSOCIATED WITH GI MALIGNANCY

The described dermatologic syndromes are not always associated with malignancy, but in many cases can be idiopathic. Therefore the practicing physician is confronted with the great challenge of carrying out a comprehensive search for underlying cancer in a systematic and cost effective manner. There are no universally accepted algorithms for the scope of the evaluation in such a patient, but, in general, the work-up should be guided by the following principles: (1) Initial thorough medical history and physical examination (including rectal exam in both sexes, pelvic exam in women and prostate exam in men) followed by basic laboratory testing (complete blood count, erythrocyte sedimentation rate, serum chemistry panel, and urinalysis). At that point, targeted evaluation of any specific patient symptoms or laboratory abnormalities should be pursued (e.g. iron deficiency anemia should be investigated with colonoscopy and upper endoscopy); (2) If the patient is asymptomatic or has no risk factors for a particular type of cancer, age-appropriate cancer screening tests should be carried out (e.g. colonoscopy in patients older than 50); and (3) Limited additional testing, such as CT scan of the chest, abdomen, and pelvis, are recommended for patients with significantly increased risk of malignancy (e.g. smoking, positive family history for cancer). The role of screening with serum prostate specific antigen (PSA), CA125, and CA19-9 has not been well determined.

CONCLUSION

A wide variety of dermatologic signs have been associated with GI malignancy. Cutaneous manifestations might develop before the GI neoplasm is recognized and their prompt recognition can significantly aid in the diagnosis. Once one of the cutaneous lesions associated with GI cancer is diagnosed, an evaluation for underlying malignancy should be undertaken. The evaluation for cancer should start with thorough medical history, physical examination, and basic laboratory testing. In asymptomatic patients, age-appropriate cancer screening tests should be carried out. Targeted additional testing, such as CT scans of the chest, abdomen, and pelvis, is recommended for patients with significantly increased risk of malignancy.

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