

Paraneoplastic disorders

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Definition

- Skin conditions that have an association with internal malignancy but are not themselves malignant

Criteria of paraneoplastic dermatosis

- The malignancy and the cutaneous disorder may occur concurrently
- The two disorders may follow a parallel course
- There can be a specific tumour site or cell type associated with the cutaneous disease
- There may be a statistical association between the two processes
- There may be a genetic association between the two processes

Mechanism

- not clearly understood
- hormone secretion
- autoimmune
- cytokine/growth factor

Strong association with tumors

Examples:

- Malignancy-associated acanthosis nigricans
- Bazex syndrome
- Erythema gyratum repens
- Necrolytic migratory erythema
- Paraneoplastic pemphigus
- Sign of Leser-Trelat

Moderate association with internal malignancy

Examples:

- Sweet's syndrome
- Pyoderma gangrenosum
- Dermatomyositis

Week association with internal malignancy

Examples:

- Isolated acanthosis nigricans
- Acquired ichthyosis
- Erythroderma
- Pruritus

Strong association with tumors

Malignancy-associated acanthosis nigricans

- Symmetrical, hyperpigmented velvety plaques, sometimes with prominent acrochordon-like papillomatosis arising from the plaques
- Site: axillae and other flexures, in one half of the patients mucosal involvement
- May coexist with sign of Leser-Trelat and tripe palms
- Can precede neoplasm

Malignancy-associated acanthosis nigricans

Tumours:

- gastrointestinal tract (70-90%)
- **gastric carcinoma** is the most frequent
- Other locations: intestine, liver, bile duct, lung, breast, endometrium, kidney, bladder, prostate, cervix, thyroid gland, adrenal glands, lymphoma, sarcoma

Tripe palms

- Acanthosis palmaris
- Thickened skin of the palms and occasionally the soles, causing velvety or less commonly honeycombed pattern
- Occurs particularly in men
- Neoplasia in 90% of cases

Tripe palms

Tumours:

- Bronchial cancer
 - Gastric cancer
- } Over 50% of malignancies
- Other: genitourinary tract, breast
 - Tripe palms and nail clubbing → Bronchial cancer
 - Tripe palms and acanthosis nigricans → Gastric cancer

Acrokeratosis paraneoplastica (Bazex syndrome)

- Acraly located papulosquamous lesions, hyperpigmentation, keratoderma, paronychia and nail dystrophy
- Initially violaceous erythema and scaling on the peripheries, especially helices of the ears, tip of the nose, hands and feet
- Subsequently the eruption may become generalized

Acrokeratosis paraneoplastica (Bazex syndrome)

Malignancy:

- Squamous cell carcinoma (especially metastatic):
 - oropharynx,
 - larynx,
 - lung
 - oesophagus
 - prostate
 - bladder

Erythema gyratum repens

- More common in men
- After seventh decade
- Regular waves of erythema spread over the body to produce a series of concentric figurate bands in a pattern resembling the grain of wood
- Day-to-day migration of the edge 1 cm

Erythema gyratum repens

- About 80% of cases is associated with malignancy
- Malignancy:
 - **Lung cancer**
 - Bowel
 - Oesophagus
 - Urogenital tract
 - Breast
 - Pancreas
 - Haematological neoplasia

Necrolytic migratory erythema

- Glucagonoma syndrome
- More common in women, age 45-55
- Weight loss, anemia, glucose intolerance, diarrhoea, weakness, venous thromboses, psychiatric disturbances

Necrolytic migratory erythema

- Rash – initially macular, extends to form superficially eroding areas of erythema that progress to fragile vesicle and bullae formation,
- Irregular centrifugal extension of the annular lesions, polycyclic, geographical pattern
- Angular cheilitis, glossitis

Paraneoplastic pemphigus

- Heterogenous, multiorgan, autoimmune, mucocutaneous syndrome
- Clinical features:
 - pemphigus-like,
 - Pemphigoid-like
 - Erythema multiforme-like
 - Lichen planus-like
 - Graft-versus-host disease-like

Paraneoplastic pemphigus

- Antibodies against:
 - Bullous pemphigoid antigen
 - Desmoglein 1
 - Desmoglein 3
 - Envoplakin
 - Periplakin

Paraneoplastic pemphigus

Malignancy:

- Non-Hodgkin lymphoma
- Chronic lymphocytic leukemia
- Castelman's tumour
- Thymoma
- Spindle cell neoplasms
- Waldenstroem's macroglobulinaemia

The sign of Leser-Trélat

- Sudden development of numerous seborrhoeic keratoses in an eruptive fashion
- With or without pruritus

The sign of Leser-Trélat

Tumours:

- Adenocarcinomas (50%)- most of them arise in **gastrointestinal tract**
- Other: breast, malignant haemangiopericytoma, melanoma, renal carcinoma, transitional cell carcinoma of the bladder, lymphoproliferative diseases

**Moderate association with internal
malignancy**

Pyoderma gangrenosum

- Rare, non-infectious neutrophilic dermatosis commonly associated with underlying systemic disease
- Variety of clinical presentations, classic/ulcerative variant is the most common
- Rapid (usually $>1\text{cm/day}$) progression of painful, necrolytic ulceration with an irregular, undermined, violaceous border, usually with a preceding papule, pustule or bulla

Pyoderma gangrenosum

Malignancy:

- Colon
- Pancreas
- Breast
- Bronchus
- Carcinoid

Sweet syndrome

- Acute onset of painful, erythematous papules, plaques or nodules
- Fever, peripheral neutrophil leukocytosis
- 3 types:
 - classical (idiopathic),
 - malignancy-associated
 - drug-induced

Sweet syndrome

Malignancy:

- acute myelogenous leukaemia
- Myelodysplastic syndrome
- Aplastic anaemia
- Fanconi anaemia
- Monoclonal gammopathy
- lymphomas
- Genitourinary
- Breast
- Gastrointestinal
- Prostate
- Larynx
- others

Dermatomyositis

Clinical features:

- Heliotrope erythema,
- Gottron's papules,
- V-neck sign
- Redness and shininess of the nail folds
- w/o muscle involvement

Dermatomyositis

- Likelihood of the neoplasm – 6-50%
- Malignancy:
 - In men lung cancer, colorectal cancer
 - In women breast cancer, gynaecological cancer

Week association with internal malignancy

Acquired ichthyosis

- Sudden onset of ichthyosis in adults
- Tumours:
 - **Hodgkin disease** (over 70% of cases)
 - Other lymphoreticular tumours: T-cell lymphomas, leukemias, myelodysplastic syndrome, multiple myeloma, polycythemia rubra vera, ovary, kidney, liver, breast tumor, leiomyosarcoma

Pruritus

- Rare manifestation of malignancy
- Can be both generalized and localized
- Many mechanisms can be responsible e.g. uraemia, cholestasis, anemia, xerosis, ichthyosis, nerve damage, other
- Malignancies: **Hodgkin lymphoma**, other lymphoproliferative disorders, brain tumours (uncommon cause of the pruritus localized to face)

Erythroderma

- Any inflammatory skin disease that affects more than 90% of the body surface
- Many causes (eczema, psoriasis, lymphoma and leukaemia, ichthyosis, pityriasis rubra pilaris, pemphigus, drug-induced reactions, others)

Erythroderma

Malignancy:

- Cutaneous T-cell lymphoma
- Hodgkin's lymphoma
- Leukaemia
- Myelodysplasia

Bullous pemphigoid

- Association with malignancies controversial
- Subepidermal blistering disease of elderly people which often starts with pruritus and urticated and erythematous lesions, later large, tense blisters develop both on erythematous and on normal skin
- There may be mucosal involvement with blisters and erosions

Bullous pemphigoid

Malignancy:

- Breast
- Lung
- Thyroid
- Larynx
- Skin
- Soft tissue
- Stomach
- Colon
- Lymphoreticular system
- Prostate
- Cervix
- Bladder
- Kidney
- Uterus

Skin metastases

- 10% of all patients with cancer
- Solitary or multiple dermal or subcutaneous nodule
- Spread: lymphatic, haematogeneous or contiguous
- Usually older patients

Skin metastases

Malignancy:

- Melanoma (blue to gray to black nodules, firm to indurated, may be solitary, few or multiple)
- Breast
- Nasal sinuses
- Larynx
- Endocrine glands
- Oral cavity
- Esophagus
- Kidney
- Stomach

Thank you for your attention