Methodic elaboration for practical lesson in

Dermatovenerology

for students of Medicine Faculty nr.2

Topic N5

Psoriasis. Lichen planus. Pityriasis rosea

PSORIASIS

Definition: it is a chronic relapsing inflammatory disease of the skin, characterized by sharply demarcated erythematous and scaly plaques, with a strong genetic basis.

Clinical features

1. Psoriasis vulgaris: the lesions are well defined, erythematous and scaly plaques are involving commonly the extensor surfaces of the knees and elbows, the scalp, the sacral area.
2. The colour is ,,salmon pink" to bright red or maroon , the scale is grayish white or silvery white and varies in thickness. The circular-to-oval plaques usually exhibit scaling as a result of epidermal hyperproliferation and dermal inflammation. When scaling is not evident, it may be induced by gently scratching.
3. The removal of scales reveals punctate bleeding points (the Auspitz sing). Blanching of the skin surrounding the lesion with a white ring is the Woronov ring. Central resolution gives the annular or arcuate aspect.

Mortality/Morbidity:

Mortality is exceedingly rare in psoriasis and the primary cause of mortality are due to systemic treatmens (ex:hepatic fibrose due to metotrexate) and phototherapy (skin cancer with metastases may be induced by PUVA)

Morbidity is related to pruritus, dry peeling skin, fissuring and the side effect of therapy.

Sex:

Psoriasis affects adult males and females , but among children girls are more affected.

Age:

Psoriasis can appear during 2 peak age ranges:

1st - between 16 and 22 years of age,

2nd –between 57 and 60 years of age.

Erythrodermic psoriasis

Extensive erythema of all, or almost all body surface and fine scaling. Pruritus, shaking cills, fever, electrolyte imbalance and hypoproteinemia are associated.

Two form exist:

- an extensive plaque psoriasis;
- a generalized erythema and exfoliation, fever and prolonged course.

Psoriatic arthritis: it is present an association of psoriasis of the skin or nails with seronegative spondiloarthropathy in about **7%** of psoriatics. Any joint may be affected, most commonly there are the distal interphalangeal, the sacroiliac and spinal involvements.

There are 5 types:

1. asymmetric oligoarthropathy: proximal interphalangeal and distal interphalangeal involvement;
2. distal interphalangeal involvement;
3. rheumatoid pattern: symmetrical distal arthrophaty;
4. arthritis mutilans;
5. spondilitis or sacroileitis.

Pustular psoriasis

1. **palmo-plantar pustular psoriasis:** one or more well-defined plaques, dusky red, with numerous pustules, 2 to 5 mm in diametr are present, itching is variable. On the hands, the thenar eminence is the most common site. Other localizations are: the hypothenar eminence, the central palm and the distal palm. On the feet, the instep, the,medial or lateral border of the foot at the level of the instep, the sides or the back of the heel are commonly involved, the digital lesions are uncommon. The pustules change to brown crusts or scales.

2. ***Generalized pustular psoriasis:*** There are plaques of erythema, circinate lesions or generalized erythroderma and episodes of pustulation, with sterile pustules; subsiding into exfoliation of the dried pustules. Fever, arthralgias, diarrhea, malaise and other constitutional symptoms are present. Leukocytosis, occasionally hypocalcemia are seen. More frequently a preexisting psoriasis is exacerbated by iatrogenic factors.

Other manifestations:

- **Kobner phenomen**: the tendency for the psoriatic lesions to develop to the skin trauma.
- **Nail involvement**: may be seen nail plate pitting, ridges, grooves, subungueal hyperkeratosis and separation of the nail from the bed, leukonychia, sprinter hemorrhages circular areas of yellow appearance of the nail bed and hyponichium.

Differential diagnosis

Eczema, Tinea corporis, Pityriasis rosea, Secondary syphilis, Lichen planus,Bowen Disease, Nummular Dermatitis,Erythema Annulare Centrifugum, Seborrheic dermatitis, Lupus erythematosus etc.

Histology: the findings consist of parakeratosis microabscesses Monro under stratum corneum, absence of granular layer, spongiform pustules in the malpighian layer, irregular thickening of the epidermis, hyperplasia with elongation of the dermal papillae, large dilated capillary loops in the dermal papillae, T lymphocyte infiltrate in upper dermis.

ETIOLOGY AND PATHOPHYSIOLOGY

1. Genetic predisposition

a. one third of the patients have a positive family history;

b. the pattern of inheritance is multifactorial;

c. studies on HLA system have shown an association with HLA-CW6 and HLA-DR7, B-27 in pustulbr psoriasis;

d. one the genes coding for increased susceptibility to psoriasis may be located on the long arm of chromosome 17.

2. Environmental factors:

a. Stress ,

b. smoking and alcohol;

c. streptococcal infection;

d. systemic drugs; UV

e. Radiation, trauma, hormonal factors etc.

Pathogenic mechanisms:

- epidermal cell kinetics: the epidermal turnover time is going to short from 3 to 4 days, the epidermal maturation is altered, with a persistence above the basal cell layer of keratins 5 and 14 (in addition keratins 6 and 16 are seen), as a result of the rapid cell division.
- Arachidonic acid metabolism: levels of arachidonic acid and of its metabolites: PGE2, LTB4, 12FIETE , 15HETE may inhibit adenylate cyclase and lover intracellular camp;
- Cyclic nucleotides metabolism: cGMP levels are increased in the lesions (proliferations timulus);
- Phosphatidyl inositol cycle: the activity of the epidermal phospholipase C Increases and is leading to increased cell proliferation;
- Immunological mechanisms: keratinocytes are influenced by various stimulus to release IL-l and IL-8. IL-l up regulates the expression of intercellular adhesion molecule-1 (ICAM-1) and E-selectin on vascular endothelium in the dermal papillae and ICAM-l on keratinocyte T helper lymphocytes are accumulating in the papillary vessels. IL-8 from keratinocytes attracts T lymphocytes and neutrophils to migrate into the epidermis. T cells which were accumulated in the epidermis are activated as a result of their interactions with CL cells and keratinocytes and release IFN-gamma, TNF-alfa and IL-2. IFN-gamma and TNF-alfa induce keratinocytes to expess HLA-DR, to up regulate their ICAM-I expression and produce further IL-6,IL-8 and TGF-alfa. IL-2 ensures proliferation of the local T cells. TGF-alfa induces the keratinocyte prolifetation. IL -6 and TNF-alfa elso have keratinocyte mitogenic properties. Bacterial exotoxins promout marked T cell proliferation.
- Psoriatic keratinocytes have an abnormal surface antigen, which, when exposed to the immune system, triggers off the immune response.Antibodiesagainst abnormal keratin are, produced and, when immune complexes are formed, results an inflammatory reaction.

Treatment and prevention

1. **Topical therapy**
   a. emollients: l-2% salicylic acid;
   b. anthralin (Dithranol)-from 0,1% to 10% to 20%;
   c. vitamin D3 (Calcipotriol/calcipotriene and tacalcitol);
   d. corticosteroids;
   e. retinoids: Tazarotene-0,1% gel in monotherapy;
   f. topical immunomodulators and immunosuppressive drugs: *Cyclosporine A* topically; *Tacrolimus oinment*, *5-fluorouracil* cream/ solution;
   g. UVB - 3 10-3 12 nm;
   h. UVA- 320-400 nm;
   i. lasers;
   j. hypertermia.
2. **Systemic therapy:**
   a. cytotoxic drugs (methotrexate);
   b. retinoids *Etretinate* and *Acitretin*; macrolide immunosuppressants: Tacrolomus, Pimecrolimus, Alephacept, Etanercept;
   c. PUVA therapy;
   d. Climatotherapy.

LICHEN PLANUS

Definition: Lichen planus is a papulo-squamous disease that occurs at all ages with equal frequency in both sexes.

The precise cause of lichen planus is unknown, but the disease seems to be immunologically mediated. It is not contagious.

Clinical features

Lichen planus can affect: the skin only, both the skin and mucous membranes or the mucous membranes only.

Skin lesions are small, polygonal, violaceous, flat-topped papules that may coalesce to form patches. A fine whitish network covers the surface of the papules (Wickham striae). The surface is glistening in the light. Adherent scales are frequently seen. Vesicles and bullae are uncommon.

After trauma, scratching, physical trauma results a linear distribution of papules also in scars (Koebner phenomenon or isomorphic response).

The preferred sites are: the flexor surface of the wrists, ankles, inner thighs, lumbo-sacral region, shins and dorsal hands.

Pruritus is variable and may precede the appearance of the skin lesions.

Mucous-membrane lesions are common, occurring in 30 to 70% of cases. Oral lesions may be reticulate, atrophic or erosive.

The usual reticulate lesions are reticulate, whitish, net-like striae located on the sides of the cheeks, but also on the tongue, on the labial mucosa, on the gum margins, on the palate. On the tongue there usually are white, slightly depressed plaques. The erosive or ulcerative forms occur in under half of patients with buccal lichen planus, in which the pain is present. Although the skin plaques are usually itchy, patients rub rather than scratch, so that excoriations are uncommon.

Involvement of the genitalia is common in lichen planus.

Other involvements in lichen planus

- The hair involvement produces small areas of atrophic cicatricial alopecia on the scalp.
- The nails are involved in 10% of patients with longitudinal ridging, irregular pitting, nail plate splitting, pterygium formation and the destruction of the entire nail fold and bed.

Clinical variants in lichen planus:

1. Hypertrophic lichen planus
2. Follicular lichen planus
3. Linear lichen planus
4. Annular lichen planus
5. Bullous lichen planus
6. Lichen planus pemphigoides
7. Ulcerative or erosive lichen planus
8. Atrophic lichen planus
9. Lichen planus actinicus.

Course of the disease: Individual lesions may last for many months and the eruption as a whole tends to last for about 1 year. But the hypertrophic variant of the disease, with thick warty lesions usually around the ankles, often lasts for many years. As lesions resolve, they become darker, flatter and leave discrete brown or gray macules. About one in six patients will have a recurrence.

Complications: Nail and hair loss can be permanent. The ulcerative form of lichen planus in the mouth may lead to squamous cell carcinoma. Ulceration, usually over bony prominences, may be disabling, especially if it is on the soles.

Pathophysiology

Lichen planus is produced by an immunological mechanism with injury to the basal cell of the epidermis.

A liquefaction-degeneration of basal cell with apparition of amorphous colloid bodies and separation of the epidermis from the dermis in bullous forms are seen.

Immunoreactants such as IgA, IgG, IgM, complement and fibrin are present in the basal layer or beneath it. The damaged basal cells have decreased ability to divide and the prolonged retention of cell in the epidermis determines acanthosis, granulosis and hyperkeratosis.

The injury of the basal cell is produced by activated T- helper cells from the dermal infiltrate. Gamma interferon derived from these cells induces HLA-DR expression on keratinocytes. Keratinocytes also produce cytokines that may attract lymphocytes within the epidermis.

Histology of lichen planus

Histological examination shows hyperkeratosis without parakeratosis, hypergranulosis, acanthosis and the vacuolar alteration of the basal layer of the epidermis.

The dermal-epidermal junction is obscured by a band-like infiltrate from the superficial dermis, composed of lymphocytes, histiocytes and melanophages.

The ,,Civatte bodies" present apoptotic keratinocytes in the dermis.

IFD evidentiates immune deposits in the region of the dermal-epidermal junction.

Differential diagnosis

1. Lichenoid eruption induced by drugs or chemicals used to develop colour photographic film
2. Neurodermatitis
3. Eczema with lichenification
4. Lichen nitidus
5. Lichen striatus
6. Lichen amyloidosus
7. Lichenoid syphilides
8. Psoriasis
9. Pytiriasis rosea
10. etc.

Mucous membrane lesions must be differentiated from leucoplakia, candidiasis, mucous syphilis patches, oral lesions in pemphigus, bullous pemphigoid, carcinoma.

Hypertrophic and atrophic lesions – psoriasis, lupus erythematosus, morphea, pseudopelade of Brocq.

Treatment

If some drugs are suspected as the cause of the disease, they should be stopped and substituted with unrelated ones.

- *General treatment*
  - Systemic corticosteroids – prednisolone 30-40 mg, for 5-6 weeks - recommended only in special situations, like unusually extensive involvement, nail destruction or painful and erosive oral lichen planus
  - Aromatic retinoids – etretinate 1 mg/kg/day, for 2 months, isotretinoin and acitretin;
  - Cyclosporine A – helpful in stubborn lichen planus;
  - Antihistamines – diphenhydramine 25-50 mg, 3 times a day, loratadine 10 mg per day, for about one month - to blunt the itch;
  - Synthetic antimalarial drugs: Hydroxychloroquine 200-400 mg daily, for 4-6 weeks;
  - Tranquilizers – diazepam 2 ml i/m, N5, alprazolam 1 mg, 3 times a day, for 10-20 days.
- *Topical treatment*

- Topical corticosteroids – methylprednisolone aceponate 0,1% ointment, clobetasole propionate 0,05% ointment - used to help relieve the symptoms and flatten the plaques;
- Keratolytic agents – salicylic acid 1-2% ointment, urea cream 2-5%;
- Calming creams – menthol 1-2%, anesthesine 2-10%.
- Topical cyclosporine.

- *Radiophysiotherapy*
  - PUVA – starting from 1-4 j/cml up to 8-10 j/cml, 3 sessions a week - photochemotherapy with psoralen and ultraviolet A may reduce pruritus and help to clear up the skin lesions;
  - Ultraviolet B phototherapy.

PITYRIASIS ROSEA GIBERT

Definition -Pityriasis rosea is a papulosquamous disease of the skin, with a self-limited evolution of about 3-8 weeks, characterized by the appearance of round, red and scaly plaques on the trunk and extremities.

Epidemiology -The disease is common, particularly during the winter. It mainly affects children and young adults 10-35 years old, it occurs very rare in children under 10 years of age and in the old. The disease is considered not contagious.

Etiology -The cause of the disease has not yet been certainly established, but there are some theories:

- Infectious theory: according to this theory the disease may be caused by reactivation of either human herpes virus 7 or human herpes virus 6, ECHO virus, parainfluenza viruses, mycoplasma. This theory is also based on the general symptoms of the disease and on the life-long immunity reported in most cases after the disease.
- Immuno-allergic theory: it is suggested by the appearance of pityriasis rosea-like lesions after certain drugs like captopril, metronidazole, izotretinoin, penicillamine, barbiturates, ketotifen, clonidine or after TB vaccination.

Clinical features

- General signs: sometimes there is a short prodromal phase with a slight alteration in general state, headache, fatigue, arthralgia, light fever, pharyngeal catarrhal signs.
- Cutaneous signs: most patients first develop one plaque called the 'herald' or 'mother' plaque before the others. It appears on the trunk, it is larger than later lesions, it has 4-6 cm in diameter, and is rounder, redder and more scaly. After several days many smaller plaques appear, mainly on the trunk, but some also on the neck and extremities. These secondary plaques have 1-3 cm in diameter. An individual plaque is oval, pink-yellow and shows a delicate scaling, adhering peripherally as a collarette. Characteristic features are paleness of central part of the lesion, poor defined scaling margins and light pruritus. Their longitudinal axes run down and out from the spine in a 'fir tree' pattern, along the lines of the ribs. Purpuric lesions are rare.
- Subjective signs: about half of patients complain of itching in the area of the plaques.
- *Atypical clinical forms* of the disease include: the Vidal circinate and marginal form, urticarial form, vesicular form, inverted form, pustular form, hemorrhagic form.
- *Other lesions:* In 16-20% of cases the oral mucosa is affected and is characterized by small hemorrhages, ulcerations, erythematous patches or plaques, vesicles, bullas. The hair is not

affected. On the nails may appear small transverse grooves that lead to nail dystrophy.

Evolution

The herald plaque precedes the generalized eruption by several days. Subsequent lesions enlarge over the first two weeks. The eruption lasts 3-8 weeks and then resolves spontaneously, sometimes leaving hyper-pigmented patches that fade more slowly. Relapses are extremely rare.

Differential diagnosis

- guttate psoriasis
- secondary syphilis
- tinea corporis
- pityriasis versicolor
- acute lichen planus
- parapsoriasis
- eruptions after certain drugs.

Treatment

General treatment:

- it is recommended to wait for spontaneous healing;
- in intense pruritus – antihistamine and desensitizing medicines;
- in nervous and excited patients – sedatives and tranquilizers;
- acyclovir, 800 mg, 5 times a day for 5 days in the incipient stage of the disease;
- in severe forms of the disease – general corticosteroid therapy;
- dapsone, 100 mg, twice a day – in vesicular or pustular forms;
- sunlight or artificial UVB-therapy often relieves pruritus and may hasten resolution;

Local treatment: medium or low-potency corticosteroid creams – metilprednisolone, fluticasone, prednisolone, hidrocortisone.

Prevention

- Avoiding mechanical, thermal, and chemical excitation of the plaques.