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Evaluation of Psoriasis Patients

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Abstract

Psoriasis represents a chronic inflammatory skin disease with multisystemic involvement. The development of this autoimmune disorder depends on a complex interplay of genetic and environmental factors. Besides presenting the conditions associated with psoriasis, the chapter outlines the role of hormones (sex hormones, prolactin, and thyroid hormones) in psoriasis pathogenesis and evolution. The chapter indicates the clinical approaches recommended in practice: a detailed medical history collection (including prior exposure to treatments and evaluation of co-medication), a thorough physical examination (with the completion of specific severity and QoL scales), laboratory investigations and screening for malignancies (including lymphoma and skin cancer) or infection (Tuberculosis, Crohn's disease). European Guidelines encourage the dermatologist to check for hypersensitivity, metabolic, gastro-intestinal and renal disorders, check for the need of vaccines and contraception. We discuss pre-treatment, during-treatment and post-treatment evaluation options and underline the necessity of clear evaluation steps in the assessment of psoriasis patients.

Keywords: psoriasis, evaluation, genetic factors, comorbidities, sex hormones, prolactin, thyroid hormones, medical history, severity scales, DLQI, SkinDex, malignancies, tuberculosis, Crohn's disease, metabolic syndrome, hepatitis

1. Introduction

Psoriasis is an inflammatory chronic skin disease, affecting over 100 million individuals worldwide [1, 2]. The development of this autoimmune disease depends on a complex interplay of genetic and environmental factors. In the immunological mediated process involved, the epidermal keratinocytes and mononuclear leukocytes lead to the formation of the psoriatic lesion [3, 4]. The peripheral HTA axis of the skin modulates inflammatory mediators in response to stress and stress-related hormones that influence the disease development and the response to treatment. Besides stress, other endogenous factors with impact upon psoriasis are allergies and hormones [5–7]. Sex hormones and prolactin seem to have a major role in psoriasis pathogenicity, while glucocorticoids, epinephrine, thyroid hormones and insulin may influence psoriasis clinical manifestations [7]. Psoriasis has a multisystemic involvement and it is associated with several comorbid conditions: cardiovascular disease (hypertension, prothrombotic state, and atherogenic dyslipidemia), metabolic syndrome (in which the main pathogenic factor is obesity with risk of developing insulin-resistance), nonalcoholic fatty liver disease and diabetes mellitus [5].

This chapter focuses on the clinical approaches to psoriasis patients that are reliable in practice. Besides describing the current status of psoriasis diagnosis, the chapter focuses on psoriasis comorbidities. The chapter also provides an objective

assessment of the main investigation tools: detailed medical history collection (including prior exposure to treatment and evaluation of comedication), the physical examination with a complete check for malignancies before and during psoriasis treatment (including lymphoma and skin cancer, evidence of active and chronic infection: Tuberculosis or Crohn's disease), the dermatologic assessment with the completion of the objective scales (PASI/BSA/PGA; arthritis scales, completion of DLQI and checking for depression or anxiety signs. The major part of the chapter is devoted to the European Guidelines for special populations of psoriasis patients, that encourage the dermatologist to check for hypersensitivity, metabolic, gastro-intestinal and renal disorders, hepatitis or other hepatological dysfunctions, HIV, neurological and psychiatric diseases, to check also for the need of vaccines and contraception (must be pursued 20 weeks after discontinuation of biological therapy) and to pay attention to females with wish for pregnancy in the near future (pregnancy, breast-feeding, fertility).

We discuss three different categories of evaluation options: pre-treatment, during-treatment and post-treatment. The chapter presents the recommended laboratory investigations in pretreatment and when indicated by medical history or physical examination findings (usually every 2–5 months): blood count (Hb, Htc, leucocytes, platelets, differential blood count), CRP, liver enzymes (ALT, AST, AP, γ GT), serum creatinine/eGFR, urine status (including urine pregnancy test in females), as for hepatitis B, C and HIV testing, they are optional only in some cases. Further specific testing may be required according to clinical signs, risk, and exposure.

The chapter also presents the great physical, emotional and social burden generated by psoriasis, (leading to an impaired quality of life that is often similar to that of patients who have heart failure and cancer), suggesting the need of psychological evaluation and support. In this context, we underline the necessity of a complete screening by using precise evaluation tools for the assessment of psoriasis patients.

2. Detailed medical history

The medical history section or case history of a patient starts by noting the patients' **gender** and age. Psoriasis is considered equally prevalent in both sexes, even if some studies indicated that the disease is more common in men [5]. Psoriasis can occur at any **age**, but the average age of onset for psoriasis is 33 years and the two peaks of the disease onset are between 16 and 22 years of age and 57–60, respectively [6, 8]. It is important to determine the date/age of onset in order to classify psoriasis according to the **date of onset** into type I (onset before or at the age of 40, positive family history and frequent association with Human Leukocyte Antigen Cw6, noted HLACw6) or type II (onset after the age of 40, negative family history and normal frequency of the Cw6 allele [9]. Positive **family history** for psoriasis patients is common in 30% up to 90% of cases, as genetic factors have an important role in the disease susceptibility and expression [10–12]. Literature findings present a threefold increased risk of developing psoriasis in monozygotic twins compared to fraternal twins [13]. **Race** of the patient is also important, as psoriasis is more common in Caucasians (3.6%), followed by African Americans (1.9%) and Hispanics (1.6%) [3, 4].

One of the most important things in collecting the information consists of listening to the patient carefully. The dermatologist must identify if other dermatological, autoimmune, endocrinologic diseases, chronic illnesses or psychiatric disorders are present in the past medical history of the patient, and if positive, they should be properly investigated and treated. It is necessary to determine if **associated factors**

are present, such as: smoking, alcohol intake, metabolic syndrome, lymphoma, depression, melanoma, cardiovascular disease, respiratory disease, diabetes, kidney disease or arthritis. It has been reported that there is an association between smoking and the development of psoriasis (also smoking increases the disease severity), as smoking leads to oxidative stress, which may stimulate chronic inflammation. Some literature data confirm that excessive alcohol intake may be a risk factor for psoriasis development [2].

One should document illnesses prior to the onset of psoriasis or other possible **trigger factors** in the previous months, such as stress, injury of skin, certain medication, infections which may determine psoriasis onset (streptococcus infection associated with guttate psoriasis onset) or flare-ups (earache, bronchitis, tonsillitis, respiratory infection) and allergies (with low scientific proof) [14]. The patient can usually tell if the onset of psoriasis was correlated to other medical issue or personal event. A study revealed that a recent life crisis was the trigger for plaque psoriasis in more than 45% of the cases, as **stress** represents the catalyst for the onset and later, the exacerbation of *psoriasis* [15–17]. The **medication** used by the patient should also be taken into consideration, as Lithium, Antimalarial, Inderal, Quinidine, Indometacin may induce psoriasis onset. Co-medication (with CYP3A4 enzyme inducers, warfarin, AINS, etc.) must be assessed in order to prevent drug–drug interactions or drug-triggered psoriasis. In most of the cases, the psoriatic lesions are induced by **trauma** (scratches, insect bites, vaccinations and sunburns) and appear 7 to 14 days after injury, aspect called the Koebner sign or the isomorphic response. Psoriasis lesions can appear at all sites of the skin injury and the lifetime prevalence of the phenomenon ranges between 25 and 75% [18].

Physiological changes, such as childbirth, should be considered, too as psoriasis lesions slowly improve during pregnancy in 60% of the female patients, and if so, the same experience will be found across the next pregnancies. In some cases the stress attributed to **childbirth** will lead to the development of psoriasis. Postpartum, females will usually face a significant disease flare. More than 50% of the patients have genital involvement, raising discomfort in the delivery and postpartum period. During pregnancy and for breastfeeding patients, the treatment options are unfortunately limited [19]. Other physiological changes such as **menopause** may affect psoriasis evolution, since dropping estrogen levels lead to psoriasis flares [7]. Some dermatologists consider that hormone replacement therapy during menopause with contraceptives does not affect psoriasis symptoms, therefore they do not recommend it [7].

The dermatologist should also focus on the chronology of the **symptoms and complaints**, which may include: worsening of a long-term erythematous scaly area, sudden onset of many small areas of scaly redness, pain (long-term rash with recent presentation of joint pain or joint pain with stiffness, pain, throbbing, swelling, tenderness, but without any visible skin findings), pruritus, sometimes fever, a viral infections, dystrophic nails, ocular findings such as redness and tearing due to conjunctivitis or blepharitis [20].

It is also important to assess how much does each of the above bother the patient [6]. The **psychological impact** of this skin disorder is severe in more than 62% of the patients with psoriasis, especially for those with disfiguring symptoms (scaling, redness etc.) on readily visible portions of the body [21, 22]. Patients with a longer disease history, particularly with the onset during childhood and adolescence, seem to be affected to a higher degree [14].

Next, the dermatologist must find out what **type of treatment** (topical, systemic therapy and new oral treatment, phototherapy, biological through injection or perfusion, complementary or alternative treatments, etc.) the patients have used until now and with what outcome from their personal point of view. Finding out

what type of treatment the patient would prefer, in order to achieve a good patient compliance and disease management with the reduction of symptoms is important, too [23].

The patient will be questioned about the **rate of the disease progression** and if it has any season pattern. Fewer symptoms and flares have been reported during summer and more during winter times. Psoriasis is an incurable, but treatable chronic condition, and symptoms may vary in severity and occur in cycles: active disease, flare-up, improvement or remission [24]. Patients should be asked if they can avoid some of the triggers, in order to reduce flare frequency and extend remission periods, which are common in almost half of the psoriasis population. Psoriasis is an unpredictable disease and spontaneous remission (without treatment) has been observed in some individuals [25].

3. Patients assessment

3.1 Dermatological examination

Psoriasis lesions consist of red, inflamed patches of skin with erythematous macules, that progress into maculopapules and well-demarcated, noncoherent, raised plaques with white micaceous scale, overlying a glossy homogeneous erythema [1–5]. The dry flakes of skin scales result from the excessively rapid proliferation of skin cells triggered by inflammatory responses, the rapid overproduction leading to the buildup of skin cells.

Lesions may vary in size (from pinpoint papules to large plaques) and in distribution, but are usually found symmetrical on the scalp, postauricular skin, elbows, back, gluteal cleft, and knees. Clinical findings are variable among patients and can change quickly within the same patient [18]. Even after plaques have cleared, permanent dyschromia may be present. Literature reports state that the most common symptoms of psoriasis include: scaling of the skin in non-scalp areas (92% of cases), itching (72%), erythema (69%), fatigue (27%), swelling (23%), burning and bleeding (20% of the individuals) [26]. Another study found rash (74% of cases), skin pain and scaling of scalp areas (62%), flare-ups (49%), joint pain of swollen, stiff joints (42%), skin cracking (39%), dry skin that may bleed or ooze (34%), physical discomfort (32%) and nail modifications (thick, ridged nails in 22% of patients) [27].

The diagnosis of psoriasis is clinical. Pinpoint bleeding caused by removing the scale is called the Auspitz sign and represents the dilated capillaries below the epidermis and thinned suprapapillary plate. A hypopigmented ring on the periphery of an individual plaque, called Woronoff ring, may occur after treatment with UV radiation or topical steroids and is associated with lesional clearing and good prognosis [18].

Besides examining the patient's skin and scalp for psoriasis lesions, the dermatologist should also check the nails, oral mucosa and tongue for specific signs of psoriasis.

3.2 Common psoriasis forms, classification according to phenotype

Findings on physical examination depend on the type of psoriasis present: Plaque Psoriasis, Pustular Psoriasis, Erythrodermic Psoriasis, Guttate psoriasis, Inverse Psoriasis or others including Scalp psoriasis and Nail psoriasis. The area of the skin involvement varies with the form of psoriasis. Psoriasis has a common etiology underlying diffuse erythroderma, or exfoliative dermatitis.

Classic plaque psoriasis also called chronic stationary psoriasis or psoriasis vulgaris is the most common type of psoriasis, affecting 58–97% of patients [28, 29]. It is characterized by inflammatory red, sharply demarcated, raised, dry, differently sized erythematous plaques covered by thick silver or white scale and variable shape or diameter with a predilection for scalp and retroauricular regions, extensor surfaces (especially elbows and knees), trunk and lumbosacral area.

Pustular psoriasis presents as clearly defined, raised, small, coalescing pustules, filled with non-infectious pus, appearing generalized (diffusely over the body as a single episode, called von Zumbusch variant, accompanied by fever and intense ill feeling) or localized to the distal extremities (palms, fingertips, nails and soles of feet, called Acrodermatitis continua of Hallopeau). Pustular psoriasis affects between 1 and 12% of cases, and patients may cycle through erythema, pustules, then scaling [29, 30].

Erythrodermic psoriasis typically occurs in 0.4–7% of cases, in people with unstable plaque psoriasis and presents as a deep red rash all over the body, with burned look skin and shedding of skin in sheets, instead of small scales with severe pain and itching. It may be accompanied by fluctuating body temperature (fever, chills, hypothermia), dehydration secondary to the large body surface area involvement, fluid retention with ankle swelling. It represents a potentially life-threatening situation, as the patient may experience cardiac instability and hypotension due to massive vascular shunting in the skin, and may pneumonia [29, 30].

Guttate psoriasis is characterized by small red 1–10 mm in diameter drops-like papules and plaques, predominately on the trunk, arms and legs. It classically appears suddenly in 0.6–20% of patients in childhood or adolescence, approximately 2–3 weeks after a streptococcal infection of the upper respiratory tract or other infection [29, 31].

Inverse or intertriginous psoriasis affects 12–26% of patients and it is characterized by smooth, flat, deep-red or white, inflamed lesions wet patches or plaques without scaling, due to the moist nature of the areas affected: flexural skin folds, axillae, antecubital fossae, inframammary creases, umbilicus, groins and genital area, gluteal cleft, popliteal fossae or body folds [30, 32].

Scalp psoriasis affects approximately 50% of patients and is characterized by erythematous raised plaques with silvery white scales on the scalp. Severe forms may induce severe dandruff and itching, even hair loss [33].

Nail psoriasis occurs in 4–69% of psoriasis patients and may cause pits on the nails and oil spots (specific findings, caused by exocytosis of leukocytes beneath the nail plate), also generating a thickened and yellowish nail, that can be confused with nail fungus [34]. Onycholysis can occur due to the parakeratosis of the distal nail bed, and one or more nails can associate with severe nail destruction or loss, restricting manual dexterity [5]. Psoriatic nails develop onychomycosis or bacterial infections in 4–30% of the cases, because of the nail separation and subungual debris [31, 35]. Patients with nail psoriasis have significantly higher psoriasis severity scores, days unfit to work and lower quality of life (QoL) compared to those without nail involvement [36].

Oral psoriasis may present with whitish lesions on the oral mucosa, changing daily in severity and can trigger different symptoms (oral pain, burning or change in taste perception) that resemble other conditions affecting the mouth and lips, such as stomatitis, oral thrush, or chronic eczema. It may also present as severe cheilosis with extension onto the surrounding skin, crossing the vermillion border. Psoriasis patients may be prone to develop the geographic tongue (unpainful red areas of varying size surrounded by a white border, appearing on the top and sides of the tongue), considered to be an oral form of psoriasis [37].

3.3 Psoriasis diagnostic by biopsy

Most cases of psoriasis are diagnosed clinically, but some pustular forms are difficult to recognize. Punch biopsy of the skin may act as a confirmatory workup procedure for atypical cases and exclude other conditions in cases of diagnostic uncertainty: atopic dermatitis (eczema), tinea corporis (ringworm), pityriasis rosea or rubra pilaris, seborrheic dermatitis, etc. Biopsy of acral skin may be less useful for the clinician as chronic eczematous dermatitis may be psoriasiform, while psoriasis of the palms and soles may show spongiosis more often associated with eczema [38].

3.3.1 Procedure

After local disinfection with alcohol, iodine or similar solution, the local anesthesia is usually performed with 1% lidocaine with epinephrine. After a wait time of 10 minutes (for maximum vasoconstriction), the punch tool (a 4 or 6 mm-punch biopsy for vertical sectioning) is placed on top of the skin. The pressure is applied until the sampling goes down to subcutis, then with the help of a needle tip, the excised skin is removed. The skin defect can be closed with classic stitches (removed in 10–14 days) or dissolving stitches (dissolving in 6–8 weeks), still in most of the cases the wound is left open.

Another method that can be used is the shave biopsy. A thin sliver of skin is shaved off using a very sharp blade, causing some bleeding. The dermatologist will apply pressure to the area, apply a dressing and sometimes a topical medicine [39].

3.3.2 Biopsy results

Biopsy of the skin lesion may reveal basal cell hyperplasia, proliferation of subepidermal vasculature, absence of normal cell maturation and keratinization, neutrophils aggregation in the epidermis.

The following histologic dermal findings are present:

- signs of inflammation throughout the dermis
- marked hypervascularity and enlarged dermal papillae
- an activated CD3⁺ lymphocytic infiltrate around blood vessels
- neutrophils aggregation in the dermis that extends up into the epidermis

The histologic epidermal findings include the following:

- Mitotic activity of basal keratinocytes is increased almost 50-fold, with keratinocytes migrating from the basal to the cornified layers in only 3–5 days rather than the normal 28–30 days. Stratum corneum contains flattened nuclei (parakeratosis).
- Abnormal keratinocyte differentiation throughout the psoriatic plaques is manifested by the loss of the granular layer.
- The epidermis becomes thickened or acanthotic and the rete ridges are increased in size. The epidermis can be variably spongiotic.

- Two findings are pathognomonic for psoriasis and can be found in active plaque psoriasis, also in the pustular form:
 - a. Microabscess of Munro –collections of neutrophils are sandwiched between layers of parakeratotic stratum corneum, surrounded by parakeratosis.
 - b. Spongiform pustule of Kogoj—accumulation of neutrophils within a spongiotic pustule [40, 41].

4. Evaluation of psoriasis complications and associated diseases

Besides skin, nails and mucosa assessment in psoriasis patients, an eye and joints checkup should also be performed. Screening is needed for the most common psoriasis comorbidities: cardiovascular disease (hypertension, prothrombotic state, atherogenic dyslipidemia), metabolic syndrome (central obesity, atherogenic dyslipidemia, systemic arterial hypertension, insulin resistance), type 2 diabetes mellitus, nonalcoholic fatty liver disease. Long-term monitoring is indicated and it is specific for the type of psoriasis treatment applied: screening for cancers (skin cancers after phototherapy and lymphomas after systemic treatment with immune-suppressing medications), screening for active and chronic infections (Tuberculosis or Crohn's disease after biologic treatment), screening for liver disease (in systemic treated patients with methotrexate), and kidney disease etc.

4.1 Ocular involvement assessment

Ocular findings are common in 10% of patients, and the skin is usually affected first and afterwards the lid, conjunctiva and cornea. Blepharitis is the most common ocular finding in psoriasis patients, followed by dry eyes with lower incidence. Blepharitis is diagnosed by clinical examination, slit-lamp examination or swabbing the skin for bacterial and fungic testing.

Psoriasis may determine madarosis, cicatricial ectropion and trichiasis, even loss of the lid tissue, chronic nonspecific conjunctivitis (pink eye) and conjunctival hyperemia, and corneal dryness with a frequent punctate keratitis (inflammation of the cornea) and corneal melt [42, 43].

Acute anterior uveitis is usually associated with psoriatic arthritis and tends to be bilateral, prolonged, and more severe than nonpsoriatic cases. Diagnostic of acute anterior uveitis is challenging and it is performed based on clinical aspect, examination with slit-lamp (white blood cells accumulate in the fluid filled space in the front of the eye, in the anterior chamber) and basic workup for syphilis and sarcoidosis testing, for HLA-B27, tuberculosis or viral etiology screening (herpes simplex, herpes zoster, cytomegalovirus) [44].

4.2 Joint involvement assessment

Psoriatic arthritis affects approximately 10–30% of psoriasis patients and is characterized by stiffness, pain, throbbing, swelling, tenderness of the joints and progressive joint damage. Peripheral arthritis, spondylitis, enthesitis (inflammation of the sites where tendons insert into the bone), arthritis in the fingers and dactylitis (profuse swelling of the fingers or toes) are the most common manifestations.

The large joints are occasionally affected, but the distal joints, such as the fingers, toes, wrists, knees, and ankles are most often involved. In more than 20% of the cases, arthritis symptoms occur before the psoriasis ones [2].

Psoriasis severity and certain locations (the scalp and intergluteal and/or perianal region) have been associated with the development of psoriatic arthritis (PsA) [45]. Also, a retrospective study from 2014 on more than 4000 patient's reports that nail involvement in psoriasis was a significant predictor of the patient also having psoriatic arthritis [46]. Earlier age of onset of psoriasis had a positive correlation with the development of PsA, suggesting that the disease duration and inflammatory burden over time have an important part [47]. Arthritic changes cannot be reversed and may be mutilating and debilitating, suggesting the need of early treatment initiation. Patients who suffer also of osteoarthritis or rheumatoid arthritis of the finger joints have a higher risk to develop arthritis mutilans, in which bones are resorbed, leading to a collapse of the soft tissue (telescopic fingers of the hands).

Radiographs of affected joints can facilitate the diagnosis of psoriatic arthritis. Bone scans usually identify early joint involvement. Arthritis patients must be periodically screened with review of systems and physical examination and imaging tests.

The differentiation of psoriatic arthritis from rheumatoid arthritis and gout can be facilitated by the absence of the typical laboratory findings of those conditions and the radiographic aspect of the affected joints. Overlap with other arthritic syndromes is also possible.

4.3 Screening for cancers

The risk of cancer in patients with psoriasis remains a cause of special concern. The risk of carcinogenesis can occur due to the chronic inflammatory nature of psoriasis, the type of treatment applied (past immunosuppressive therapies such as MTX and cyclosporine immune-suppressive, PUVA or phototherapy), the increased prevalence of comorbid and other risk factors for cancer (smoking and obesity) [48, 49].

Cutaneous malignancies (melanoma and non-melanoma skin-cancer) seem to be directly related to phototherapy performed by the psoriasis patients. A significantly increased risk for SCC and BCC was detected in psoriasis patients treated with higher doses of PUVA compared to lower doses [52]. Scientists suggested that this malignancy risk can be decreased by using sunscreen or trying to stay out of the sun, and cease smoking, a risk factor for both psoriasis patients and skin cancer. Malignancy records for psoriasis patients also mention the development of leukemia, prostate, pancreatic, breast and colon cancer.

Latest data suggests patients with more severe psoriasis have an increased risk of cancer-related mortality, this association being the strongest for lymphoproliferative malignancies and cutaneous malignancies [50, 51]. The increased risk is likely linked to male gender, advancing age or COPD in patients with psoriasis arthritis [53].

Even though long-term control trials and observational studies are still needed, the addition of malignancy as a potential adverse event has been added in the medication packaging of biological therapies [48, 54]. Specific medications have raised concern in concurrent use, being suspected to increase the risk of malignancy: the addition of a biologic agent to potent immunosuppressive treatments, also the use of AZA, 6-MP, cyclosporine, or cyclophosphamide with TNF blockers [48]. According to published guidelines, a history of lymphoma, represents an absolute

contraindication to TNF-antagonist therapy, while biologic therapy is contraindicated in patients with an active or recent (within 5 years) history of malignancy, with the exception of treated nonmelanoma skin cancers.

For cutaneous malignancy detection, skin self-examination would be the first step, followed by complete skin examination performed by the dermatologist, with the use of dermoscopy and histopathological results confirmation after excision of the lesion.

For both Hodgkin and non-Hodgkin types of lymphoma, a specific screening test is not available and for a definitive diagnosis a biopsy is required. For leukemia, no screening test is available, but the condition may be detected through a Chest X-ray or CAT scan (showing swollen lymph nodes or signs of infection), Spinal tap (presence of leukemia cells in the cerebrospinal fluid), Bone marrow aspiration and biopsy from the hip bone (the existence of leukemia cells in the bone marrow).

The lung cancer screening is recommended to be performed each year by Low-dose helical or spiral computed tomography (CT) scan. to people aged 55 to 80 who have smoked for 30 pack years or more or who have quit within the past 15 years. People who routinely used tobacco products and/or drink alcohol should receive general health screening examination at least once a year for the detection of head and neck cancer.

Breast cancer screening should start with the patient's self-examination, followed by clinical breast examination and mammography over the age of 45 years old, and in some cases magnetic resonance imaging is used.

Screening and diagnostic of prostate cancer is recommended over the age of 50 years old and it is performed by digital rectal examination and prostate-specific antigen test.

According to the latest recommendations, for patients over the age of 50 years old, colorectal cancer screening primary tests should be used (guaiac-based fecal occult blood test or fecal immunochemical test every year), followed by flexible sigmoidoscopy every 5 years or colonoscopy every 10 years [54].

4.4 Screening for active and chronic infections

Mild to serious secondary infections can occur directly related to the immune-suppressing medication during psoriasis treatment.

People with HIV seem to be more likely to develop psoriasis. Clinical observation suggests that HIV-1 infection can trigger new-onset psoriasis or exacerbate existing psoriasis. As HIV-1 infection progresses and CD4+ T cell counts decrease, psoriasis can worsen. According to the Centers for Disease Control and Prevention HIV screening should be performed at least once by patients over 13 years old and pregnant women and more often for people with risk factors such as: having unprotected sex with positive or unknown HIV status subjects or multiple partners, injecting drugs and sharing needles, syringes, etc. There are three testing methods for HIV: antibody tests (detect HIV infection from blood or saliva about 3 to 12 weeks from the time of infection), combination tests (antibody/antigen tests detect HIV infection from blood about 2 to 6 weeks from the time of infection) and the very expensive nucleic acid tests (NATs) (detect HIV infection from blood sample about 7 to 28 days from the time of infection). The combination of two methods is highly accurate and recommended for all patients.: if antibodies are detected by initial ELISA method testing, the second test will be performed using the Western blot procedure [55].

Literature data indicate that immunosuppressive and immunomodulatory therapies for psoriasis and psoriatic arthritis are risk factors for allowing latent TB

to transform into active TB in some patients. The consensus statement from 2008 of the National Psoriasis Foundation recommended all patients to be screened for latent TB infection prior to initiating any immunologic therapy with systemic and biologic agents, also recommended that delaying immunologic therapy should be performed until latent TB infection prophylaxis is completed [56].

4.5 Screening for liver disease

Dermatologists should also screen psoriasis patients for hepatitis B virus (HBV) using triple serology testing: hepatitis B surface antigen, hepatitis B surface antibody, and hepatitis B core antibody, before beginning treatment with tumor necrosis factor (TNF) inhibitors or biologics (including ustekinumab and secukinumab), according to the latest recommendations.

If the patient is at risk for reactivation of HBV, liver function tests, hepatitis B surface antibody, hepatitis B core e antigen, and HBV DNA should also be tested. Routine follow-up with testing for reactivation should continue for at least 6 months after the TNF inhibitor is discontinued. In case of patients suffering of chronic HBV for whom biologics are considered, etanercept is recommended as first-line therapy [56].

As far as the systemic treated patients with methotrexate are concerned, the screening should be made in order to evaluate the liver injury. Besides the liver function tests, the liver biopsy was performed, but it was associated with significant morbidity and mortality. A recent Australasian position statement recommends transient elastography (which measures the speed of shear waves used to estimate hepatic tissue stiffness) for monitoring methotrexate therapy, repeated every 3 years if kPa < 7.5 and yearly if kPa > 7.5 [57].

4.6 Screening for kidney disease

The association of psoriasis with kidney disease in recent studies expands the list of bodily systems that psoriasis is affecting beyond the skin. The kidney seems to be both a target of classic cardiovascular risk factors and susceptible to the toxic effects of psoriasis traditional drugs. Medication such as cyclosporine and methotrexate may have contributed somewhat to the increased frequency observed [58].

Moderate to severe psoriasis, affecting over 20% of patients worldwide has been linked to a higher risk of kidney disease. The analysis performed on 143,883 psoriasis medical records in the United Kingdom concluded that severe psoriasis subjects were twice as likely to acquire chronic kidney disease compared to those with mild psoriasis or no psoriasis at all. Latest reports show that psoriatic arthritis is an independent predictor of renal damage in patients with psoriasis [59].

Several studies demonstrated a greater incidence of proteinuria and elevated creatinine in patients suffering from psoriasis [60]. Patients with psoriasis and/or psoriatic arthritis, particularly when they are candidates for systemic therapy, should be screened for an underlying renal damage by laboratory tests including glomerular filtration rate and a simple urine test to screen for albuminuria (albumin/creatinine ratio).

4.7 Screening for gastrointestinal disease

Gastrointestinal disease screening is indicated in patients with decreased growth rate, unexplained weight loss, or symptoms of inflammatory bowel disease. Celiac

disease, sclerosis and the inflammatory bowel disease (Crohn's disease) are autoimmune disorders, which may be present in psoriasis patients.

In **Celiac disease**, an autoimmune gluten-induced bowel disease, the small intestine is affected, leading to gastrointestinal manifestations (diarrhea and steatorrhea, weight loss) and malabsorption-related problems (folic acid, calcium, vitamin D and selenium malabsorption, copper and zinc deficiencies, iron deficiency or megaloblastic anemia) [61]. Celiac patients have an increased risk of developing adenocarcinoma and lymphoma of the small bowel. Screening for Celiac disease is performed with anti-transglutaminase and anti-endomysial antibodies, both having high sensitivity to diagnose patients with classic symptoms and complete villous atrophy and also 50% of the patients with minor mucosal lesions with normal villi. Professional guidelines recommend that a positive blood test must be followed by endoscopy/gastroscopy and biopsy. Checking total serum IgA level is also indicated and if negative, anti-DGP antibodies (antibodies against deamidated gliadin peptides) should be determined [62].

Crohn's disease, a type of inflammatory bowel disease (IBD), may affect any part of the gastrointestinal tract and presents gastrointestinal, systemic and extraintestinal manifestation. The diagnosis of Crohn's disease can sometimes be challenging and may take several years. A colonoscopy with a biopsy is the recommended test for diagnosis and it is approximately 70% effective in diagnosing the disease [63]. It allows direct visualization of the colon and the terminal ileum, identifying the pattern of disease involvement and presentation: stricturing, penetrating or inflammatory type. Modern investigation options of the small-bowel disease are the computed tomographic enteroclysis (hybrid technique that combines the methods of fluoroscopic intubation-infusion small bowel examinations with that of abdominal CT) and the capsule endoscopy, with a specific role in the investigation of Crohn disease. Blood determinations for anemia or infections are recommended, as well as a total blood count, erythrocytes sedimentation rates, body mineral levels and protein levels determination. Stool samples are checked for occult blood loss or infectious microbes. Expert guidelines do not currently recommend antibody or genetic testing for Crohn's disease, but the *Saccharomyces cerevisiae* antibodies (ASCA) and anti-neutrophil cytoplasmic antibodies (ANCA) are used to identify inflammatory diseases of the intestine and to differentiate Crohn's disease from ulcerative colitis [64].

Folate or acid folic deficiency represents the deficiency of B9 vitamin, vital for proper nerve function and preventing birth defects, also normalizing the high levels of homocysteine, which can increase the risk of heart disease. Folate deficiency is common in subjects with celiac disease or Crohn's disease. Patients with severe psoriasis seem to have a higher risk of developing folate deficiency [65]. The mechanism is believed to be an impaired absorption of folate and an excess loss of folate in the skin scales of patients suffering from psoriasis and mycosis fungoides [66]. In the screening of acid folic deficiency, ruling out cobalamin deficiency (vitamin B12) is important, as both cause megaloblastic anemia and neurologic manifestations, the serum folate level cannot be used alone to establish the diagnosis of folate deficiency. Additional follow-up tests include serum homocysteine (which is elevated in vitamin B-12 and folate deficiency) and serum methylmalonic acid (which is elevated in vitamin B-12 deficiency only). A recent study pointed out that 75% of the psoriasis patients treated with methotrexate in UK receives folic acid supplementation. Literature confirms a reduction in the adverse effects of MTX, but it questions if this may impact efficacy [67].

4.8 Screening for Parkinson's disease

Patients with psoriasis have a higher risk of developing Parkinson's disease probably due to the detrimental effect of chronic inflammation on the neuronal tissue [68]. Risk factors for this association from FDA reports would be: male gender, age over 60 years old, previous Azilect treatment and presence of high blood pressure. Latest findings suggest that an immune response to alpha-synuclein proteins (which accumulate inside the brain of Parkinson's disease patients) play a role in the disease, suggesting an autoimmune etiology. Diagnosis of Parkinson disease is challenging because of the highly variable clinical aspect and lack of reliable objective test. Still it is the updated diagnostic criteria that must guide the clinician [69].

4.9 Screening of polycystic ovary syndrome

Polycystic ovary syndrome (PCOS) in female psoriasis patients has a remarkably higher prevalence than in age- and BMI-matched control women. Women who present both PCOS and psoriasis are more likely to have insulin-resistance, hyperinsulinemia, reduced HDL cholesterol levels and a more severe degree of skin disease, compared to patients who suffer only of psoriasis. Similar to psoriasis, the components of metabolic syndrome seem to be closely related to PCOS as well. The ovulatory phenotype of the disease seems to be associated with milder psoriasis forms, while the phenotypes with oligoamenorrhea with higher severity scores of disease [70].

For PCOS screening and diagnosis two of the following criteria are sufficient: oligo- or anovulation, biochemical or clinical hyperandrogenism, and polycystic ovaries on ultrasound examination [71].

4.10 Screening of metabolic syndrome

Genetic susceptibility, inflammatory pathways and common environmental factors (tobacco smoking, alcohol consumption, psychological stress and low physical activity) are responsible for the development of psoriasis and metabolic comorbidities. These disorders share similar pathophysiological phenomena: chronic inflammation with high production of pro-inflammatory cytokines (especially TNF-alpha, IFN-gamma, IL-1, IL-2, IL-6, IL-8 and IL-17) that induces angiogenesis, adipogenesis, oxidative stress, insulin signaling, lipid metabolism and immune cell traffic [72, 73]. Metabolic aspects of chronic inflammation Th-1/Th-17 in psoriasis would have a role of predisposition and reciprocal aggravation on other conditions, such as obesity, diabetes and atherosclerosis [74].

Literature data prove in large observational studies the association of psoriasis to increased prevalence of metabolic syndrome, as well as its individual components: central obesity, atherogenic dyslipidemia, hypertension and insulin resistance [75, 76]. Severe psoriasis cases present higher chances for the development of metabolic syndrome, compared to mild forms of the disease [77].

Obesity or weight gain has been shown to be an independent risk factor for psoriasis. As obesity is also associated with reduced efficacy of psoriasis treatment, weight loss intervention programs should be included in psoriasis management.

Latest review on the topic emphasize the critical need for providers to screen psoriasis patients for cardio metabolic diseases, using the criteria abdominal circumference (>102 cm in males, >88 in females) plus two of the following: low

HDL-cholesterol (<40 mg/dL men, <50 mg/dL in women), hypertriglyceridemia (≥ 150 mg/dL), high blood pressure ($\geq 130/85$ mmHg) or high fasting glucose (≥ 110 mg/dL). The guidelines recommend annual measuring of waist circumference, quarterly determination of fasting lipids and glucose, monthly measurement of weight, body mass index and blood pressure. Screening is useful in patients with risk factors: female gender, advancing age, illiteracy, unemployment, positive family history, obesity and a sedentary lifestyle [78].

4.11 Screening for diabetes mellitus type 2

It is believed that fat cells in psoriasis patients secrete cytokines that raise insulin resistance in the liver and muscle, which initiates the destruction of the insulin-producing beta cells in the pancreas [79].

Several observational studies have investigated the association between diabetes mellitus type 2 and psoriasis or psoriatic arthritis (PsA). The highest risk for diabetes mellitus type 2 was detected for patients suffering from PsA. Literature data indicated a dose effect in the risk of suffering from type 2 diabetes mellitus, as patients having severe psoriasis had higher risk [80].

Screening of patients for diabetes mellitus type 2 is recommended annually in patients over 45 years or in patients younger than 45 years with major risk factors (positive family history, overweight, high blood pressure, etc.), and every 3 years for obese patients regardless of risk factors. Guidelines recommend a diagnostic of diabetes mellitus to be established with: single random plasma glucose level ≥ 200 mg/dL plus typical symptoms of hyperglycemia, while determinations should be repeated on the next day for the following situations: a fasting plasma glucose level ≥ 126 mg/dL; an A1C level of 6.5% or greater; a random plasma glucose level ≥ 200 mg/dL; a 75-g 2-hour oral glucose tolerance test with a plasma glucose level ≥ 200 mg/dL [81].

4.12 Screening for cardiovascular diseases

Psoriasis seems to be associated with cardiovascular and metabolic comorbidities, particularly in young patients and patients with more severe forms of the disease. Psoriasis patients have a twice as high risk to develop a cardiovascular disease, maybe due to the increased burden of subclinical atherosclerosis and vascular inflammation [76]. Psoriasis seems to be associated with atrial fibrillation and stroke, which may be aggravated in young patients. Studies noted significantly higher levels of serum lipids, including triglycerides and total cholesterol in psoriasis patients compared to healthy controls [82].

For screening of cardiovascular diseases (coronary artery disease being the most common heart disease) the completion of the Framingham 10 Year Risk of General Cardiovascular Disease Score and the dosing of the following parameters are necessary: LDL cholesterol and HDL cholesterol (every 4–6 years for normal risk patients), blood glucose level (start annual screening at 45 years old if normal weight or at 40 years old if obese) and amount of high-sensitivity C-reactive protein (used for those with intermediate risk, up to 20%, of having a heart attack within the next 10 years), blood pressure level determination (every 2 years if values are under 120/80 mmHg). Additional testing is required in the presence of risk factors (increased cholesterol, increased high blood pressure, diabetes, obesity, cigarette smoking, family history of premature disease in a first-degree relative) and it includes: electrocardiography (ECG), exercise cardiac stress test, echocardiography, coronary CR angiography, etc.

4.13 Screening for nonalcoholic fatty liver disease

Observational studies suggest that patients with psoriasis are up to threefold more likely to have fatty liver disease over controls. An explanation could be the fact that proinflammatory adipokines or skin-derived cytokines may lead to insulin resistance and hepatic lipid accumulation [83].

Patients with nonalcoholic fatty liver disease and psoriasis have more severe skin disease and are at higher risk of severe liver fibrosis than patients without psoriasis.

The risk was significantly correlated with obesity, insulin resistance, and metabolic syndrome and psoriatic arthritis [84].

As nonalcoholic fatty liver disease causes no symptoms in most cases, it is frequently diagnosed without this certain purpose. Liver screening includes liver enzyme and liver function tests, tests for chronic viral hepatitis (hepatitis A, hepatitis C and others), plain ultrasound showing steatosis. A liver biopsy is necessary in order to distinguishing NASH from other forms of liver disease. Non-invasive diagnostic tests are available: FibroTest for estimating liver fibrosis and SteatoTest for estimating steatosis [85].

4.14 Endocrine assessment in psoriasis

It is well known that the nervous system, the endocrine system and the skin have the same embryological origin, from the ectoderm [86]. Also, the function and the normal development of the skin are influenced by hormones, among them sex hormones, thyroid hormones or stress hormones [87]. Literature data present different endocrine conditions in association with psoriasis onset or exacerbation. Thus, a complete assessment of psoriatic patients should be performed, in order to identify concomitant disorders that can sustain or trigger psoriasis.

4.14.1 Estradiol

The involvement of sex hormones in psoriasis was taken into consideration due to the fact that the incidence of this chronic disease is higher in time periods characterized by hormonal imbalance, such as puberty, postpartum or menopause [88–90].

Thus, a significant correlation was found by Murase et al. between estradiol and psoriasis body surface area (BSA), with the improvement of the disease during pregnancy [7]. Also, a cohort study, published in 2016, suggested a possible association between hormonal imbalance, induced by irregular menstrual cycles or surgical menopause, and psoriasis risk in women [91].

Testing the level of estradiol in male patients with psoriasis, Cemil et al. found an inverse correlation between the severity of the disease, evaluated by PASI score, and the level of hormones [92].

4.14.2 Prolactin (PRL)

This pituitary hormone involved in reproduction and lactation exerts immunomodulatory effects also, being considered a member of type I cytokine family [93]. Several observations that sustain the role of PRL in psoriasis pathogenesis are linked, first, with the exacerbation of the disease due to prolactinoma development, secondly, with lesions remission in the context of bromocriptine administration, a dopaminergic inhibitor of PRL secretion [87].

The level of PRL in psoriasis patients was assessed in different studies and compared with controls. The correlation with PASI score was also evaluated, but

the results were contradictory, as it is shown in the first meta-analysis regarding this topic. However, the conclusions of this recent study sustain the significantly increased level of PRL in psoriasis patients compared to controls and the positive association with PASI [94].

4.14.3 Thyroid and thyroid hormones

The involvement of thyroid hormones in skin homeostasis is suggested by the variety of modifications associated with thyroid disorders, whether hyperthyroidism or hypothyroidism. Moreover, literature data confirm the presence of thyroid hormones receptors in the skin and the stimulatory effect upon epidermal growth factor, with the consequent keratinocytes hyperproliferation [95].

Thus, in several studies, an evaluation of thyroid function was performed in patients with psoriatic disease. Among these studies some case reports suggest the benefits of antithyroid drugs (e.g. propylthiouracil) in psoriasis evolution, or resolution of the disease after thyroidectomy [87].

Recent data presented a higher incidence of new cases of thyroid disorders (small thyroid, positive antithyroidperoxidase antibody-AbTPO, hypothyroidism) in patients with psoriatic arthritis, particularly in women, compared to control group. The females at risk are those with a level of thyroid-stimulating hormone (TSH) at the superior limit of the normal range, positive AbTPO or a small volume of thyroid gland [96]. The association between autoimmune thyroid disease and the prevalence of psoriatic disease was also suggested as a conclusion in a meta-analysis from 2017, due to Th1 immune predominance and high circulating levels of CXCL10 [97].

4.14.4 Stress hormones

Stress is one of the major factors that may trigger/exacerbate psoriasis lesions. The mechanisms include the activation of hypothalamic–pituitary–adrenocortical (HPA) axis and the sympathoadrenomodulatory system (SAM), with the consequent release of proinflammatory cytokines. Cortisol is an indicator of HPA activity. In patients with psoriasis the cortisol response to stress is lower than in controls [87]. Also, they present increased levels of epinephrine and adrenocorticotrophic hormone, which seem to be involved in maintaining and exacerbation of psoriasis lesions [98]. Moreover, the cutaneous glucosteroidogenesis is also defective in patients with psoriasis, which favors the specific clinical aspect of the lesions [99].

5. Diseases severity evaluation using common scales

5.1 Dermatologic assessment of disease severity

For psoriasis severity assessment, more than 40 different tools have been used. Commonly used measures by the dermatologist include: the Psoriasis Area and Severity Index (PASI), body surface area (BSA), the Physician Global Assessment (IGA) or the simplified Lattice-System Physician's Global Assessment (LS-PGA) and The Nail Psoriasis Severity Index (NAPSI) [100]. The patients can also assess the disease, using the Self-Administered PASI (SAPASI). Unfortunately, none of the currently published severity scores for psoriasis meets all the criteria required for an ideal score, and for a reliable assessment of psoriasis severity several independent evaluations are performed simultaneously [101].

Mild psoriasis is considered if it covers less than 3% of the body, moderate form, if 3–10% of the body has psoriasis lesions, and severe if psoriasis lesions are

present on more than 10% of the body. Disease severity cohorts were categorized based on PASI severity scores as follows: mild disease with PASI up to 5, moderate form with PASI score from 5 to 12, severe form between 12 and 20 PASI score, very severe over 20.

5.1.1 Psoriasis area and severity index (PASI) and BSA

PASI represents the most widely used tool for the measurement of the physical extent and severity of the disease (higher PASI scores indicate more severe psoriasis). PASI calculation consists of two major steps: calculating the BSA covered with lesions and the assessment of the lesions severity. The affected area and lesion characteristics generate a score from 0 to 72.

The amount of disease (BSA covered with lesions) is estimated by determining what percentage of the skin on a person's body is affected, with the size of the palm of the hand equal to about 1 percent of the skin. The body of the patient is divided into four sections, each scored by itself: head (H) -representing 10% of the skin surface, arms (A) (20%), trunk (T) (30%), legs (L) (40%). For each section, a grade from 0 to 6 is attributed for the percent of skin involved: 0—0% involvement, 2—less than 10%, 3—between 10 and 29% of involved area, 4—between 30 and 49%, 5—between 50 and 69%, 6—between 70 and 89%, 7—between 90 and 100%.

Within each area, the lesions severity is estimated by: erythema (redness), induration (thickness), desquamation (scaling), the severity of each parameter are noted on a scale from 0 (none) to 4 (maximum). The sum of all three severity parameters is then calculated for each section of skin, multiplied by the area score for that area, then multiplied by the weight of respective section (0.1 for head, 0.2 for arms, 0.3 for body and 0.4 for legs) [101, 102].

PASI scores are used at baseline for entering a trial, and at follow-ups, to assess treatment efficacy and outcomes, usually expressed as a percentage response rate; for example, PASI 50, PASI 75, PASI 90, PASI 100. The PASI assessments were found to be non-reproducible and it was noticed that the physician's estimations of the psoriatic lesion area tended to be overestimated.

The modified PASI which involves the computerized measurement of the area on the digital photograph is called Computer aided psoriasis continuous area and severity scores (cPcASI) and was successfully used in several clinical trials [103].

5.1.2 Physician global assessment (PGA)

Physician Global Assessment (PGA) is also called Investigator Global Assessment (IGA) and represents a 5 or 6-point ordinal rating scale, ranging from clear to severe psoriasis.

Score 0 means Cleared psoriasis, with no plaque elevation, erythema or scaling, but hyperpigmentation may be present. Score 1 means Minimal psoriasis, with minimal plaque elevation ($=0.25$ mm), faint erythema, minimal scaling with occasional fine scale over $<5\%$ of lesion. Score 2 means Mild psoriasis with mild plaque elevation ($=0.5$ mm), light red coloration, fine scales predominates. Score 3 means Moderate psoriasis with moderate plaque elevation ($=0.75$ mm), moderate red coloration, coarse scale predominates. Score 4 means Marked psoriasis, with moderate plaque elevation ($=1$ mm), bright red coloration, thick, nontenacious scales predominates. Score 5 means Severe psoriasis, with severe plaque elevation (>1.25 mm), dusky to deep red coloration, very thick and tenacious scale predominates [101, 102].

5.1.3 Nail psoriasis severity index (NAPSI)

Nail Psoriasis Severity Index (NAPSI) represents a numeric, reproducible and objective tool used to evaluate the severity of nail bed psoriasis and nail matrix psoriasis by area of involvement in the nail unit., which is divided into quadrants by imaginary longitudinal and horizontal lines. The Nail plate is assessed for nail matrix psoriasis by the presence of: nail pitting, leukonychia, red spots in the lunula, and crumbling in each quadrant of the nail. The nail bed psoriasis is assessed by the presence of: onycholysis, oil drop (salmon patch) dyschromia, splinter hemorrhages, and nail bed hyperkeratosis in each quadrant of the nail. Score 0 means the findings are not present, Score 1 means they are present in one quadrant of the nail, Score 2 if present in two quadrants of a nail, 3 if present in three quadrants of a nail, and 4 if present in four quadrants of a nail. Each nail has a matrix score (0–4) and a nail bed score (0–4), and the total nail score is the sum of those two individual scores (0–8). The sum of the total score of all involved fingernails is the total NAPSI score of the psoriasis patient [104].

5.2 Assessment of psoriasis arthritis

Accurate and reliable methods are needed to measure disease activity, progression, and change with therapy in psoriatic arthritis (PsA). Some evaluation tools have been developed specifically for PsA, while others were borrowed and adapted from the fields of rheumatoid arthritis, ankylosing spondylitis, and psoriasis. Key domains of interest for psoriasis arthritis assessment are joints, skin, enthesitis, dactylitis, spine, joint damage evaluated from the radiological, quality of life and functioning point of view. In 2007, the GRAPPA-OMERACT achieved consensus on 6 core domains that should be assessed in trials on subjects with PsA (peripheral joint activity, skin activity, pain, patient global assessment (PGA), physical function, and health-related quality of life) and other important but non mandatory domains (spinal disease, dactylitis, enthesitis, fatigue, nail disease, radiography, physician global assessment, and acute-phase reactants). Most of the clinical trials have used: the ACR scoring system, VAS scores of patient pain, patient global, physician global, the Health Assessment Questionnaire (HAQ), and acute phase reactant, C-reactive protein (CRP) or erythrocyte sedimentation rate (ESR) [104, 105].

A PsA specific response index was developed and then improved and renamed as PsA specific response criteria PsARC. Two of the following were needed to achieve response in a psoriatic arthritis patient: a joint count and no worsening of any measure (tender or swollen joint count improvement of at least 30%, patient global improvement by one point on a five point Likert scale, or physician global improvement on the same scale).

Unlike the ACR criteria (only measuring change in disease activity), the DAS evaluation was useful in determining the current amount of disease activity. as well as the change of disease activity with therapy in RA. The original DAS used the Ritchie Articular Index (RAI), swollen joint count (SJC), ESR, and general health status (GH) (VAS) [106, 107].

5.3 Psychological assessment

Latest literature data report that psoriatic patients have a higher incidence of depression, anxiety, low self-esteem and social withdraw or isolation. Depression affects a high percentage of psoriasis patients and leads to chronic fatigue, loss of interest in life and everyday activities, appetite changes, sleep disturbances and negative coping mechanisms (use of alcohol and/or drugs, self-harm or other

high-risk behavior). Psoriasis patients may also face feelings of guilt, shame, embarrassment or helplessness and stress (which can trigger flares of psoriasis). Sexual dysfunction may occur due to self-consciousness or painful lesions, which can also interface with activities of daily living, including dressing, bathing and sleeping. Psoriasis determines a negative impact on the patient's family functioning, including financial hardship and degeneration of patient-family relationships. It may also generate decreased vocational opportunities due to discrimination or perceived restrictions on career choices, which can lead to employment and economic difficulties. According to a national survey performed in USA on patients with severe forms of psoriasis: 20% said that their psoriasis contributed towards the loss of a job or resignation; 25% believed that their psoriasis has caused an intimate relationship to end; 43% said psoriasis had prevented them from making new friends; 83% expressed dissatisfaction with their current treatment [108].

Even if the dermatological condition can improve under treatment, the emotional problems may persist or aggravate in some patients. Suicidal ideation, occurred in up to 10% of psoriasis patients. A significant number of psoriasis patients reported a negative mental and physical impact that is similar to cancer, hypertension, heart disease, depression and diabetes.

The negative impact of psoriasis can be measured by using the following instruments: Dermatological Quality of Life Index (DQLI), Psoriasis Disability Index (PDI), The Family Psoriasis Index (PFI-14) questionnaire, the Health-Related Quality of Life (HRQoL) or SkinDex 29 or 17 [108].

6. Other laboratory studies

Laboratory studies and findings for psoriasis patients may include the following: test for rheumatoid factor (RF) (usually negative result), erythrocyte sedimentation rate (usually normal, except in pustular and erythrodermic psoriasis), uric acid level (may be elevated especially in pustular psoriasis, causing confusion with gout in psoriatic arthritis). If fluid is collected from the pustules, the results will indicate a sterile fluid with neutrophil infiltrate. Fungal studies can be performed, especially important in cases of hand and foot psoriasis that seem to be worsening with the use of topical steroids.

If starting systemic therapies such as immunological inhibitors, consider obtaining baseline laboratory studies in pretreatment and when indicated by medical history or physical examination findings (usually every 2–5 months): blood count (Hb, Htc, leucocytes, platelets, differential blood count), CRP, liver enzymes (ALT, AST, AP, γ GT), serum creatinine/eGFR, urine status (including urine pregnancy test in females), as for hepatitis B, C, tuberculosis and HIV testing, they are optional only in some cases. Further specific testing may be required according to clinical signs, risk, and exposure.

7. Evaluation algorithm regarding treatment

There are three different algorithms regarding the evaluation of psoriasis patients related to treatment: pre-treatment, during-treatment and post-treatment.

Pre-treatment evaluation indications include: medical history (also checking for comedication) and physical examination with the objective assessment of the disease with specific scales (PASI/PGA, DLQI, etc.), performing laboratory controls (pregnancy test included), checking for skin cancer, evidence of active and chronic infection (exclusion of tuberculosis), checking for hypersensitivity, metabolic,

gastrointestinal and renal disorders, underweight or depression, check for contraception and breastfeeding, need of vaccines.

During treatment evaluation indications include: medical history and physical examination (focusing on malignancies, infections, contraception, depression, anxiety) including the objective assessment of the disease with specific scales (PASI/PGA, DLQI, etc.), performing laboratory controls only when indicated on medical history or physical examination (tuberculosis testing included).

Post-treatment evaluation indications: discussing contraception (which can be pursued at least 20 weeks after discontinuation of biological treatment), continuing follow-up focusing on malignancies, infections, etc.

8. Conclusion

As a conclusion, care for psoriasis patients require more than the management of the skin lesions and of the joint involvement. The complexity of the disease requires a holistic approach of the patient, performed with utmost attention. Screening at regular intervals for associated diseases and prevention of comedication interactions, as well as recognition and avoidance of trigger factors, are essential. Psychosocial interventions, such as patient education and psychological treatment, may be needed in psoriasis management.

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