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What if Dupilumab Breaks the Rules? A Case Report and Review in Psoriasis-Atopic Dermatitis Overlap

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Abstract

A 33-years-old woman entered the dermatological departments with numerous itchy nodular manifestation all over the entire lower surface of the legs. The patient reported intense itching also present around the body particularly in the flexor areas. She also presented psoriasiform lesion in the pre-tibial area, which has always been recognized as a difficult to treat area in psoriasis. Treatment with both topical and systemic steroids caused only temporary improvement. Histological esamination reported psoriasiform dermatitis associated with spongiosis phenomena in dermis, confirming a clinical overlap psoriasis-atopic dermatitis. Traditional systemic therapies and JAK-inihibitors were controindicated. Therapy with Dupilumab demonstrated efficacy in both psoriasiform and atopic clinical manifestations, despite the limited evidence in literature. We present our experience with literature revision.

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Keywords: Atopic Dermatitis, Psoriasis, Dupilumab, Prurigo Nodulare, Overlap Syndrome

Abbreviations

AD	Atopic Dermatitis
JAK	JAnus Kinase
IL	Interleuchine
Interleuchine	Italian Medicine Agency

Introduction

Atopic dermatitis is the most common inflammatory dermatitis all over the world with 5-25% of prevalence and variability within childs and adults in therms of prevalence and clinical manifestations [1]. Prevalence is in fact most elevated in childs [2]. The main clinical sign of AD is represented by widespread eczema all over the body mainly affecting flexor areas particularly in young-adults. The main symptoms include incessant and intermittent itching of the skin accompained by cutaneous burning sensation. General symptoms include 78 different manifestations, also including sleep disturbance, difficult in mantaining concentration and even keratocone [3]. AD is related to immune dis-regulation with an increased Th2-mediated response with production of cytokines such as IL-4, IL-5, IL-13 and IL-31 whose regulation is related to JAK-STAT pathway such as in other inflammatory diseases. Juvenile variants of atopic dermatitis may include nodular prurigo in which chronic scratching causes the formation of skin nodules that are resistant to topical therapies and unable to respond to systemic therapies for AD such as Dupilumab, again due to the dysregulation of the Th2-related inflammatory axis unlike the elderly variant in which prurigo is triggered mainly by stressors and chronic scratching [2]. Differential diagnosis include Psoriasis that represents one of the most common inflammatory diseases particularly in our latitudes. Psoriasis is related to immune dis-regulation with an increased Th1-Th17-mediated response with production of cytokines such as IL-12, IL-23, IL-17, TNF-alpha and IL-22 whose regulation is also related to JAK-STAT pathway such as in atopic dermatitis [4]. Clinical and hystological manifestations include erythematous-desquamative plaques mainly affecting the exstensor areas of the body (such us knees and elbows) without hystological response of spongiosis like in AD, except for pustolosis psoriasis [4]. Recently more and more cases of overlap syndrome are being diagnosed, in which psoriasis and atopic dermatitis arise together, constituting a clinical challenge for dermatologist and an obstacle to therapy, which often has to be combined for both pathologies and tailored to the individual patient. Literature studies based on clinical exeprinences around the years showed particular clinical improvement in patients treated with Dupilumab for AD however, causing a worsening of psoriasis due to the imbalance in the Th2-Th17 axis with necessity of overlap biological therapies for both inflammatory diseases [5]. We want to describe our experience on a case of overlap-syndrome Psoriasis-AD (nodular prurigo variant) in which the use of Dupilumab caused improvement on Th2-symptoms without worsening in Psoriasis clinical signs in constrast to literature reports.

Case Report

A 33-year-old female patient presented to the dermatological emergency department with diffuse nodular plaques on xerotic skin, predominantly affecting the peri-malleolar areas and bilateral calves (Img.1). At the same time, the same patient presented with rare and erythematous-nodular plaques on the kness and the pre-tibial areas, not specifically indicative for psoriasis (Img.2) although present in an area that is difficult to treat in psoriasis. The patient reported intense itching all over the day; in fact she showed diffuse scratching lesions with intense bleeding around affected areas and also all over the body, scratching principally at night. Medical history was negative for general pathologies except for seasonal allergies. Dermatoscopic examination was negative for scabies or other infective rashes.

Familiar anamnesis included positivity for psoriasis (grand-father) and first-grade positivity for thrombotic phoenomenons (father); the patient also presented platelets at the upper limits and non-specific alterations of coagulation indices, in particular elevated INR.

Incisional biosy was performed of both pre-tibial and peri-malleolar areas bilaterally with histological

response indicative for diagnosis of psoriasis-form dermatitis with diffuse signs of AD: "…skin with irregular epidermal hyperplasia with a thickened suprapapillary plaque, hyperparakeratosis, mild signs of suprapapillary spongiosis and phenomena of neutrophilic exocitosis and exoseroses. Superficial dermis also showed a moderate peri-vascular lymphocitic inflammatory infiltrate... ".

The clinical and histological signs lead us to the diagnosis of overlap syndrome Psoriasis-Atopic Dermatitis (with clinical prevalence of AD) and the controindications to prescription of systemic conventional therapies (cyclosporine) in addition to the warning on JAK-inihibitors lead us to toward therapeutic training with Dupilumab 600mg at time 0 and 300mg every two weeks, that is also indicated and prescribable for prurigo nodular variant of atopic dermatitis.

The patient underwent regular monthly check-ups starting from pharmacological induction (September 2025) with EASI score of 17.5, NRS score of 10, and DLQI score of 30, achieving excellent clinical benefit at 3 months with significant improvement of the inflammatory nodules on her legs bilaterally (Img. 3) and also on psoriasiform plaques on the pre-tibial areas, a reduction in the number of nodular lesions, and no psoriasis flare-ups related to the Th1-Th2 imbalance (Img. 4). At 3 months, she presented with an EASI of 8.8, NRS of 2, and DLQI of 5. No drug-induced side effects have been recorded.

The patient is continuing treatment and is experiencing daily clinical improvements as demonstrated by remote follow-ups also in AD and psoriasiform lesions.

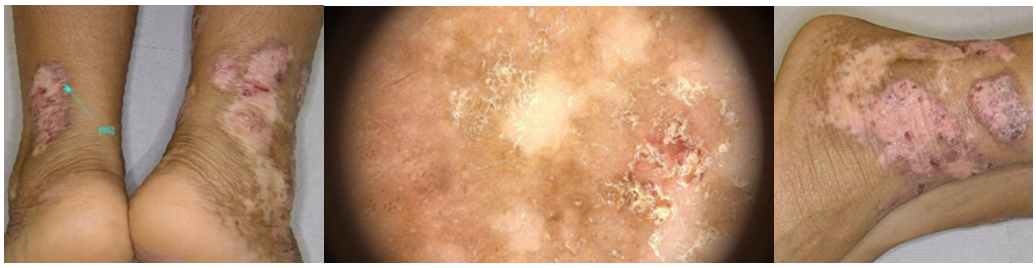

Figure 1: Clinical and Dermatoscopic Presentation on Peri-Malleolar Areas at Time 0, Before Terapeutical Goals.

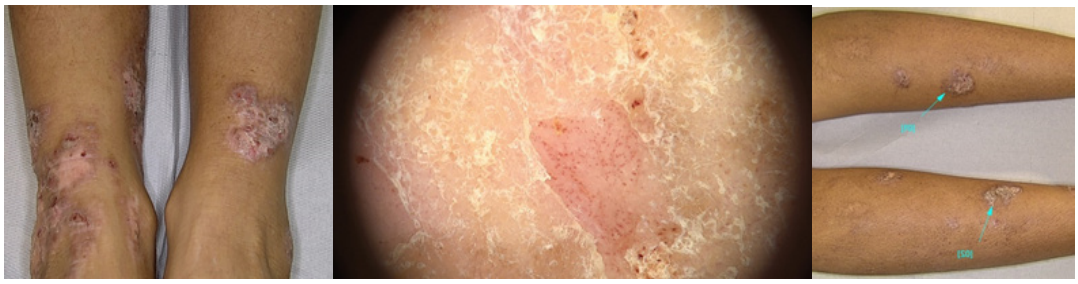

Figure 2: Clinical and Dermatoscopic Presentation on the Pre-Tibial Areas at Time 0 Before Terapeutical Goals.

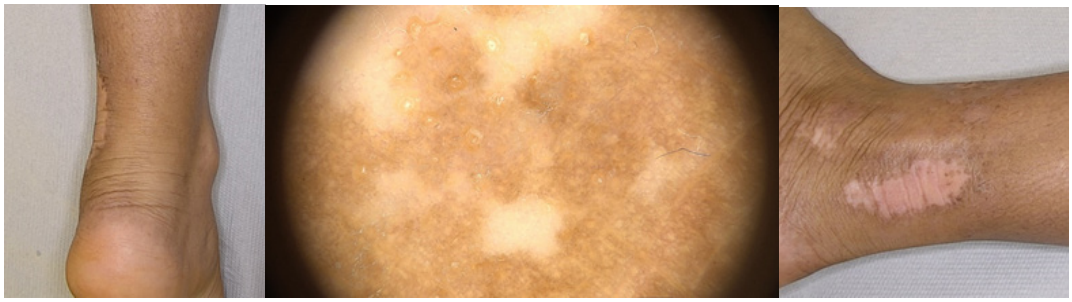

Figure 3: Therapeutic Goals at 3 Months Therapy on Peri-Malleolar Areas Bilaterally.

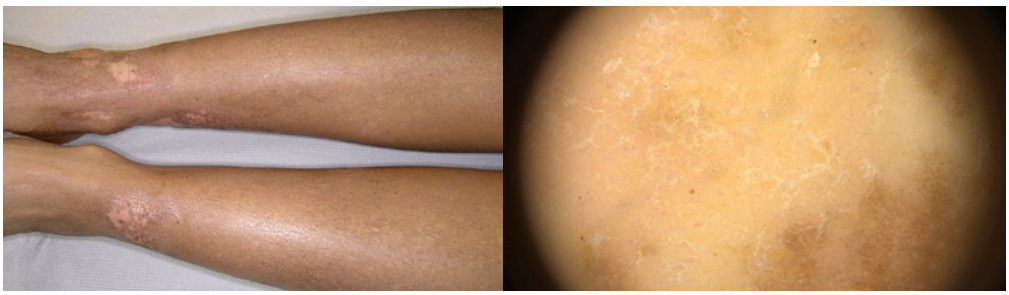

Figure 4: Therapeutic Goals at 3 Months Therapy on Peri-Malleolar Areas Bilaterally.

Discussion

In recent dermatological literature, the coexistance of DA and Psoriasis is increasingly recognized beyond rare caser reports, challenging the traditional view of these two conditions as mutually exclusive. Emerging observational data indicate that overlap phenotypes occur with notable frequency in clinical settings despite their distinct immunopathological profile (Th2 vs Th17 dominant, respectively).

A recent retrospective cohort study conducted between 2021 and 2024 at a tertiary dermatology center registered a prevalence of 5.1% of patients with confirmed diagnosis of overlap AD-Psoriasis with concurrent signs and symptoms. This suggests that overlap cases are not as rare as you might think and it often requires histological assessment to confirm the diagnosis e profile the therapy on patient as in our case, in which the patient was treated with Dupilumab by her general and dermatological conditions [6].

Reported prevalence estimates of AD-Psoriasis overlap show wide variability largely dependent on diagnostic criteria, with figures ranging from about 0.2% to 16.5% in different cohorts [6].

These results in scientific literature renforce the concept that Psoriasis and AD may share overlapping inflammatory pathways and phenotypes rather than representing strictly separate immunomediated diseases. This help in profile patients and in the choose of correct therapy in every one.

In the current therapeutic options, Dupilumab represents a foundamental biologic option for adult AD, as it is formally approved and reimbursed in Italy for the treatment of moderate-to-severe AD in adults eligible for systemic therapy, according to AIFA determines [7]. In recent years Dupilumab has also gained regolatory approval for the treatment of prurigo nodularis (PN) in adults, representing the first and currently only targeted therapy indicated specifically for this cronic inflammatory condition characterized by intense itch and nodular lesions [8].

Dupilumab is not approved for treatment of psoriasis all over the world cause of its different physio-pathological mechanisms (Th2 for AD and Th1-Th17 for psoriasis).

Several observational series and case reports have in fact documented psoriasiform reactions or new-onset of psoriasis in AD patients treated with Dupilumab, indicating that IL-4/IL-13 blockade and consequent suppression of the Th2 pathway may unmask, cause or facilitate a shift toward Th1/Th17-mediated inflammatory pathway of psoriasis. In narrative reviews, multiple patients developed “de novo” psoriasis or flares of pre-existing psoriasis during dupilumab therapy with a typical latency of weeks or months [5].

For instance, Napolitano et Al reported approximately 3.3% of adult AD patients trated with Dupilumab developed psoriasiform manifestations, and subsequent case series described a range of clinical presentations, often improving after discontinuation od Dupilumab or switching therapy [9].

In a comprehensive case series review Tare et al. reported that of 112 patients with AD and treated with Dupilumab, 101 developed de novo psoriasis and 11 experienced flares of pre-existing psoriasis during therapy with a latency of 5 years, confirming that Th2 inihibition may predispose to Th1/Th17 driven psoriasis phenotypes [10].

Kinoshita et al. demonstrated that a patient with developed psoriasiform eruption after dupilumab treatment

for AD rapidly improved his condition after switching therapy with baricitinib, renfoircing the hypotesis that disregulation of Th2/Th17 balance may underlie paradoxical psoriasis-like reactions [11]. However, in our patient's case, contraindications to JAK inhibitor therapy guided our therapeutic choice toward dupilumab, which, however, did not cause paradoxical psoriasis, as in many cases reported in the literature. The choice was also guided by the prevalent phenotype (AD).

With the help of artificial intelligence (IA) searching the main bibliographic databases, we have observed that there is currently no solid evidence in the scientific literature (such as large controlled clinical trials) that dupilumab is effective as a treatment for classic psoriasis. Indeed, the available data, as just reported, demonstrate exactly the opposite, since dupilumab may be associated with the de novo development of psoriasis or psoriasis flare-ups in patients also treated for atopic dermatitis.

Conclusion

AD and Psoriasis represent the main important dermatological inflammatory diseases in therm of prevalence and inbalance on quality of life, principally in Italy and in caucasian population. Recent reviews reported many cases of overlap syndrome AD-Psoriasis, challenging the traditional view of these two conditions as mutually exclusive. Dupilumab represents one of the most important drug for clinical improvement in AD, blocking Th2 inflammatory response thanks to its blockade on Il-4 and IL-13 citokines. Dupilumab is approved in Italy for treatment of AD both in adults or childs and for treatment of Prurigo Nodularis variant in adults. Actually no evidence of improvement in psoriasis are available; in fact difference review on use of Dupilumab confirmed as imbalance on Th2-Th17 inflammatory pathways may cause worsening or new onset of psoriasis. Many patients require both biological treatment for psoriasis and AD often causin difficult in therapy management.

Our case represent probably the first case in literature in which a patient with overlap syndrome AD-psoriasis, also confirmed by hystological response, manifested improvement in both AD and psoriasis dermatitis without any confirm in other case series or reports.

Further studies on clinical, histological and immunological parameters are needed to confirm our clinical response.

Conflict of Interests: None
Patient Consens: Yes

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