What's new this month?

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What's new this month?

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Epidermolysis bullosa (EB) is a rare genetic disease causing chronic and painful wounds with a significant impact on patients' quality of life. There is currently no specific treatment, although some clinical studies are focusing on gene and cell therapy. This approach is, however, at a very early stage. In this issue of *The European Journal of Dermatology*, Yang *et al.* [1] reviewed the properties of thymosin β4 and its potential to treat wounds, especially those associated with EB. Thymosin β4 is a regenerative protein present in several cells and body fluids, including wound fluids. It is inter alia related to promotion of tissue repair, tissue regeneration, reduction of inflammation and oxidative stress, decrease in apoptosis, and promotion of angiogenesis. Preclinical studies on various animals have shown its potential to accelerate dermal repair in normal and impaired healing. Safety of topically and intravenously delivered thymosin β4 has been demonstrated in Phase 1 studies in over 40 patients. Phase 2 trials of 71 patients with pressure wounds and 72 patients with venous stasis ulcers showed that topical thymosin β4 accelerated wound healing compared to placebo groups. Another study including 30 patients with EB used three dosages of topical thymosin β4 (0.01, 0.02 and 0.10%). At Day 15, all three formulations tended towards better efficacy compared to placebo for all wound sizes. No adverse effects have been reported. Awaiting the development of gene therapy, topical thymosin β4 could be a useful, simple, and safe therapeutic tool to improve quality of life for patients with EB. Systemic use could also be considered in the future, as thymosin β4 may repair and regenerate tissues in patients with internal injuries. It could also be useful in the treatment of other wounds, such as traumatic or surgical wounds.

Dermatomyositis (DM) is an autoimmune inflammatory disease with various cutaneous, muscular and pulmonary manifestations. Specific autoantibodies are detected in the serum of DM patients and correlate with clinical features and prognosis [2]. In this issue, Motegi *et al.* [3] investigated, based on a retrospective monocentric analysis, the clinical features of anti-melanoma differentiation-associated gene 5 (MDA5) antibody (Ab)-positive DM patients and the risk factors potentially associated with a poor prognosis. Among 75 Japanese patients included, 28 (37.3%) were positive for anti-MDA5 Ab, and 100% of these patients had interstitial lung disease (ILD). Clinical and biological features were compared between: anti-MDA5 Ab-positive patients and other DM patients; anti-MDA5 Ab-positive patients and rapidly progressive ILD (RP-ILD) and others; and anti-MDA5 Ab-positive patients and RP-ILD, survivors and non-survivors. The results suggest that anti-MDA5 Ab might be associated with clinically amyopathic DM, ILD, progression to RP-ILD, high serum ferritin levels, and certain skin manifestations (Gottron's papules, violaceous palmar macule, and antihelix/helix violaceous macules). For anti-MDA5 Ab-positive patients, clinical features do not appear to be different between patients with or without RP-ILD. However, high serum ferritin levels and low partial pressure of arterial oxygen (PaO_2) at diagnosis might be associated with progression to RP-ILD and poor prognosis. This study suggests that in cases of RP-ILD, the administration of initial intensive immunosuppressive triple therapy (high-dose prednisolone, calcineurin inhibitor, and intravenous cyclophosphamide) might improve prognosis. This study is a retrospective study based on a small number of patients, but the results are consistent with those from other studies published and highlight important characteristics that can aid in making an early diagnosis and initiating adequate treatment.

Pityriasis rubra pilaris (PRP) is a rare inflammatory disease affecting the skin, and sometimes the nails and eyes, with no consensus on treatment. Six subtypes are described, depending on the age at onset, clinical appearance, and the course of the disease [4]. Skin lesions are characterized by reddish-brown follicular keratotic papules, which can coalesce into hyperkeratotic plaques. Palmoplantar keratoderma and erythroderma may occur. In this issue, Engelman *et al.* [5] reviewed reported treatments for PRP type I. A total of 105 articles were included, but no randomized controlled clinical trials were found. The authors suggest a therapeutic algorithm based on their review. They recommend a basic therapy with a topical treatment (salicylic acid, vitamin D analogues, calcineurin inhibitors or topical corticosteroids) together with phototherapy. In addition, a systemic treatment should be considered; a systemic retinoid as first-line treatment. In case of a lack of efficacy, methotrexate, cyclosporine A or azathioprine should be added. If this second-line therapy fails, biological therapy can be used; ustekinumab and TNF-alpha antagonists (etanercept, infliximab and adalimumab) are reported with often good results. Since this review included only reported cases and some retrospective trials, it is difficult to draw any precise recommendations. The authors also point out that the lack of a standardized assessment scale for the severity of this skin disease makes it difficult to define a specific indication for any particular treatment. The risk of bias is

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also increased by the fact that the published cases generally correspond to patients who responded to treatment. However, this systematic review is the first for PRP type 1 and allows the various treatment options to be ranked.

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Dermpath & Clinic: Multiple nodules in the axillae: is it that old chestnut Hidradenitis suppurativa again?

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A 23-year-old female patient presented to our department with subcutaneous, indolent tumours in both axillae (*figure 1A, B*). The patient reported that similar lesions had occurred in the past, leading to numerous consultations with dermatologists. So far, no topical treatment has improved the skin lesions, which were yellowish to skin-coloured nodules, lacking a central pore. The patient's family history was negative for similar skin lesions. No nail changes were found. The patient denied smoking and had no history of other diseases. Initial differential diagnoses included hidradenitis suppurativa, epidermal inclusion cysts, tumours of the follicular infundibulum, and vellus hair cysts. A biopsy was obtained and histopathology revealed a thin-walled cyst, filled with horn material and homogeneous sebum. The lining of the cyst was composed of a stratified squamous epithelium consisting of a few cell layers while the *stratum granulosum* was absent. In addition, numerous sebaceous glands in or adjacent to the cyst wall were present (*figure 1C, D*). Based on these findings, the diagnosis of steatocystoma multiplex (SM) was made.

SM (OMIM184500) is a rare malformation of the pilosebaceous unit, characterized by the eruption of numerous sebum-containing dermal cysts that are usually dome-shaped, yellow nodules, varying in size and number. It commonly presents on areas with densely concentrated pilosebaceous units such as the trunk, proximal extremities, axillae, face, and scalp [1]. It most frequently occurs in adolescence or early adulthood and affects both sexes equally [2]. Although sporadic presentation is most often reported in SM, familial cases with autosomal dominant inheritance with a mutation involving keratin 17 (K17) are documented [3-5]. K17 is a type I keratin expressed in a number of epidermal appendages, such as the nail bed, hair follicles, and sebaceous glands. A heterozygous missense mutation, c.280C>T, in exon 1 of *KRT17* and other mutations in *KRT17* have already been described, not only in patients with SM [5], but also in those with pachyonychia congenital type 2 (PC-2). PC-2 comprises a group of autosomal dominantly inherited diseases, characterized by hypertrophic nail dystrophy and varying features of ectodermal dysplasia [4]. It is still under discussion whether SM is a variant of PC-2 or whether both diseases represent two distinct entities. Additionally, a relationship between SM and vellus hair cysts has been reported [6]. Steatocystomas share many characteristics with eruptive vellus hair cysts, such as age at onset, genetic mode of transmission, clinical appearance, and distribution. Hybrid lesions with histological features of both conditions have been described [7], and it has thus been suggested that the two conditions may lie along a spectrum for the same disease. Alternatively, it has been hypothesized that the two conditions are distinct based on the expression of different keratins. SM expresses K10 and K17 in contrast to eruptive vellus hair cysts, which only express K17 [8]. Although there are several hypotheses to explain the aetiopathogenesis of SM, such as originating from sebaceous retention cysts, or representing a naevoid malformation of the pilosebaceous duct, the exact cause of SM remains unclear [1].

With regards to our initially suspected diagnosis of Hidradenitis suppurativa (HS), the rare association between SM and HS suggests a shared genetic background [9, 10].

A skin sample has to be taken if malignancy is suspected or if, as demonstrated in our case, physical examination and history cannot exclude differentials such as vellus cyst, epidermoid or dermoid cyst, hidradenitis suppurativa, milia, follicular infundibular tumours, or lipomas [11]. Histologically, steatocystomas are mid-dermal cysts lined by an eosinophilic, undulating epithelial lining. Flattened, sebaceous lobules are usually present close to or within the cyst wall which is characteristic of steatocystoma and differentiates it from epidermal inclusion cysts and vellus hair cysts. Steatocystoma contains cellular debris and exhibits connections to the epidermis, but often these connections are a few straight epithelial cords rather than the multiple small connections seen in tumours of the follicular infundibulum [1].

Clinically, the lesions are asymptomatic and pose no malignant potential, however, patients often seek dermatological or surgical consultation owing to psychological distress [12]. The lesions lack central pores but may exude a creamy or oily fluid when punctured. There are few satisfactory treatment options [13]. Needle aspiration may decrease the size of lesions with good cosmetic outcome, but is associated with an extremely high recurrence rate [14]. The