

## **Review for the Generalist: Cutaneous manifestations of juvenile systemic lupus erythematosus and juvenile dermatomyositis**

Arianna Vitale, Lucia Trail, Enrico Felici, Francesco Traverso, Alberto Martini, Angelo Ravelli

Dipartimento di Pediatria, Università di Genova, Unità Operativa Pediatria II, Istituto di Ricovero e Cura a Carattere Scientifico G. Gaslini, Genova, Italy

### **Correspondance:**

Angelo Ravelli, MD  
Pediatria II, Istituto G. Gaslini  
Largo G. Gaslini, 5  
16147 Genova, Italy  
Tel.: +39-010-5636386  
Fax: +39-010-5636211 or +39-010-393324  
E-mail: [angeloravelli@ospedale-gaslini.ge.it](mailto:angeloravelli@ospedale-gaslini.ge.it)

### **INTRODUCTION**

Cutaneous manifestations are among the most important clinical hallmarks of juvenile systemic lupus erythematosus (JSLE) and juvenile dermatomyositis (JDM). In both diseases, skin lesions are of great diagnostic help. Indeed, dermatologic features constitute 4 of the 11 the classification criteria for SLE (discoid rash, malar rash, photosensitivity, and oral/nasal mucocutaneous ulcerations) [1], and the presence of the typical skin rash is an essential requirement to diagnose JDM by the Bohan and Peter criteria [2,3].

In this paper, we review the distinctive cutaneous features of JSLE and JDM as well as the most recent advances in their management.

### **JUVENILE SYSTEMIC LUPUS ERYTHEMATOSUS**

Skin disease is common in JSLE both at disease onset and during disease exacerbations and is extremely heterogeneous [4,5] (Table 1). The most characteristic manifestation is the classic “butterfly” or malar rash (Figure 1), which is observed at onset in 30 to 50% of patients. Although not pathognomonic (as discussed below, a similar rash may occur in JDM), the malar rash is highly suggestive of SLE. It is characterized by symmetrical erythema and edema that is typically centered over the malar eminences and over the bridge of the nose, and sometimes extends to the forehead and the V area of the neck; the nasolabial folds are typically spared. The rash is usually confluent and well demarcated, and may be slightly raised. In most cases it is maculopapular with fine scales, but rarely results in scarring. Occasionally, the rash begins on the face as small, discrete macular and/or papular lesions that later become confluent and hyperkeratotic. The malar rash may be precipitated by exposure to sunlight (photosensitivity).



Figure 1 Juvenile SLE – Malar rash

**Table 1- Cutaneous manifestation of SLE**

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Acute manifestations

- Malar rash
- Photosensitivity
- Generalized erythema

Subacute manifestations

- Annular lesions
- Papulosquamous lesions

Chronic manifestations

- Discoid lupus erythematosus
- Lupus panniculitis
- Lupus tumidus

Non specific manifestations

- Alopecia
  - Urticarial lesions
  - Cutaneous vasculitis
  - Bullous lupus
  - Associated with antiphospholipid antibodies
    - Livedo reticularis
    - Leg ulcerations
    - Cutaneous necrosis or gangrene
    - Thrombophlebitis
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A number of other dermatologic manifestations can occur in JSLE. Maculopapular rashes resulting from vasculitis or perivasculitis may be seen anywhere in the body, particularly on sun-exposed areas, such as the face and the upper-anterior chest (Figure 2). These lesions are sometimes painful and may also involve the palms and soles. In most patients they heal without scarring or hyperpigmentation. More rarely, cutaneous disease may present as a more widespread morbilliform or exanthematous eruption or in an extremely acute form that can simulate toxic epidermal necrolysis. Petechial and purpuric eruptions may be related to perivasculitis or be secondary to thrombocytopenia.



**Figure 2 Juvenile SLE – Maculopapular rash over the upper back**

Discoid lupus (Figure 3) occurs rarely in pediatric patients [6]. It has been reported that only 2 to 3% of cases of discoid lupus have disease onset before the age of 15 years [7]. The discoid lesions consist of areas of flat or slightly elevated, sharply demarcated, red-purple, papulosquamous patches with adherent scales and follicular plugging, which most commonly occur in sun-exposed areas, such as the scalp and the limbs, in an asymmetric distribution. These lesions most commonly evolve into larger, coin-shaped (i.e. discoid) plaques, that can enlarge and merge to form larger, confluent, disfiguring plaques. They often leave atrophic scarring and alterations of skin pigmentation. Discoid lupus is more common in black children than in other ethnic groups. It is estimated that 7% of patients with discoid lupus will progress to systemic lupus over a period of 5 years [6] .



**Figure 3 Juvenile SLE – Discoid rash**

Alopecia is a common feature of JSLE. It is associated with disease activity and is usually characterized by diffuse hair thinning, which initially affects frontal hairs. The hairs become brittle and kinky and are prone to breaking off. This phenomenon is generally referred by the child or the parents as an excessive hair falling on the pillow, in the comb, or after shampooing. This alopecia is usually non-scarring and more often causes limited upset. In contrast, irreversible scarring alopecia from permanent follicular destruction is rare. Dystrophic nail changes may be seen in patients with long-standing disease.

Other uncommon cutaneous manifestations of JSLE are urticarial and bullous (pemphigoid-like) lesions. Finger, toes or face red-purple patches and plaques that are precipitated by cold exposure and are reminiscent of simple chilblains or pernio lesions are occasionally observed in children. Diffuse hyperpigmentation, usually most prominent on the light-exposed and extensor surfaces of the body, is another important, though rare, dermatologic feature of JSLE. The accumulation of excessive dermal mucin early in the course of a cutaneous lupus lesion can result in the development of succulent, edematous, urticarial-appearing plaques of "lupus tumidus". Lupus panniculitis is characterized by

inflammatory lesions in the lower dermis and subcutaneous tissue, which usually presents with deep, firm, 1- to 3-cm diameter nodules, often with normal-appearing overlying skin. As the lesion mature, the skin becomes attached to the nodular lesions and is drawn inward to produce deep depressions. Confluent involvement can simulate a lipoatrophy.

The so-called “subacute cutaneous lupus” begins with erythematous macules or papules that subsequently evolve into annular/polycyclic lesions with raised edges. They are localized on the trunk, limbs and face and may assume a scaly, hyperpigmented or atrophic appearance, but are nonscarring. Photosensitivity is common as well. Shallow, painful ulcers of the lips, gums, palate, and nasal mucosa occur in 10-15% of patients and frequently occur during disease exacerbations. Similar lesions are seen occasionally on the vulvar surface [8].

A number of skin changes that may develop in patients with lupus have been associated with the presence of circulating antiphospholipid antibodies [9]. They include leg ulcers, livedo reticularis, cutaneous necrosis, gangrene of the digits or extremities, thrombophlebitis, necrotizing purpura, and nailfold infarcts. Leg ulcers, which occur more often in the lower limbs, are painful and sharply marginated; they have a necrotic center or base and leave a white atrophic scar on healing. Livedo reticularis has been related to the stagnation of blood in dilated superficial capillaries and venules and affects primarily the skin of the thighs, shins, and forearms.

Deposition of immunoglobulins, usually of the IgG or IgM isotype, at the dermal/epidermal junction has long been recognized in lupus. For unknown reasons, these immunoglobulins may be identified in areas of skin than are not light-exposed, such as the buttocks, and in which there is no rash. This phenomenon is at the basis of the so-called lupus band test. Complement components may also be found at the dermal/epidermal junction.

### **JUVENILE DERMATOMYOSITIS**

A clear recognition of cutaneous features is essential for prompt diagnosis of JDM, especially in cases in which these manifestations are the initial or only findings (Table 2). Although dermatitis may precede the onset of myositis by several months or even a few years, it usually becomes evident in the first few weeks after the occurrence of muscle involvement. In some patients, skin disease can be the most active or severe disease complaint, failing to respond to therapeutic interventions that are adequate for myositis or other systemic involvement.

**Table 2 –Cutaneous manifestations of JDM**

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Heliotrope rash
Malar rash
V or shawl rash
Photosensitivity
Eyelids teleangiectasias
Gottron’s papules

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Gottron's sign  
Periungual erythema  
Cutaneous ulceration  
Calcinosis  
Lipodistrophy  
Mechanic's hand  
Poikiloderma  
Erythroderma

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In three-fourths of JDM patients, skin abnormalities are highly characteristic, whereas in the remainder a less characteristic rash is present [5,10]. The rash is photosensitive in up to 30% of patients. The three most typical, and most common, cutaneous manifestation of JDM are heliotrope discoloration of the upper eyelids, Gottron's papules, and periungueal erythema with capillary loop abnormalities. The heliotrope rash occurs over the upper eyelids and the periorbital region as a dusky, violaceous-reddish purple erythema, which may be associated with a malar rash resembling that of JSLE in its distribution, though less well demarcated, or to a more confluent erythema involving the entire face. The malar rash of JDM is also distinguished from that of JSLE by the involvement of nasolabial folds that is typically absent in lupus. In the acute phase, the heliotrope rash is often accompanied by edema of the eyelids or the face or both, resulting in sensation of tightness. Capillary teleangiectasias along the lid margin may persist long after the other sign and symptoms of disease activity have resolved (Figure 4).

Gottron's papules (Figure 5) are pink-red to violaceous, flat-topped papules and plaques that are located most commonly over the extensor surfaces of the proximal interphalangeal joints of the hands and less so over the metacarpophalangeal and distal interphalangeal joints. The skin over the thumbs is rarely, if ever, affected. The extensor surfaces of the elbows and knees and, less frequently, the malleoli and the vertebral apophyses may be involved as well. These papules may evolve over time to develop depressed atrophic, porcelain-white centers with prominent teleangiectasias. Occasionally, the lesions appear to be thickened and pale early in the disease course (hence the name "collodion patches"). Gottron's sign refers to the macular erythematous patches in a distribution similar to that seen for Gottron's papules. A photosensitive macular erythematous or violaceous eruption may involve discrete areas of the body, producing specific signs: the "V-sign" for the V of the neck and upper chest; the "shawl-sign" for the nape of the neck, upper back, and posterior aspect of the shoulders. In the most active and severe forms of JDM, the cutaneous rash may extend considerably and eventuate in total body erythema (erythrodermia). Pruritus is a common but underrecognized complaint of JDM patients, and is often associated with secondary skin findings of excoriations and erosions.



**Figure 4** JDM - Capillary telangiectasias along the lid

margin



**Figure 5** JDM – Gottron papules

Nailfold capillary abnormalities due to a widespread capillary vasculopathy, which is the underlying pathologic lesion of JDM [10], and periungueal erythema (figure 6) are detectable in 50 to 100% of patients with JDM. Careful examination with a water-soluble gel and a magnifying glass, an ophthalmoscope, or a stereomicroscope allows documentation of the presence of nailfold telangiectasias. The most common abnormalities are capillary dropouts, dilatation of isolated loops, thrombosis and hemorrhage, and arborized clusters of giant capillary loops, which are secondary to post-ischemic neovascularization and are distinctive of JDM. These changes have been correlated with a more severe disease course or with the development of cutaneous ulceration or calcinosis, and have been found to abate with disease remission [5,11]. Cuticular dystrophy, that leads to overgrowth of the cuticle is also well described in JDM and may reflect disease activity. Occasionally, telangiectasias similar to those seen in the periungual beds may occur on the anterior gingival margin.

The development of cutaneous ulceration has been well-recognized in JDM. The ulcers are thought to be vasculitic in nature and may locate at the corners of the eyes, in the axillae, in the upper part of hips, over the elbows or pressure points and over stretch marks (Figure 6). These lesions likely mean more severe vascular pathology, and may herald serious internal organ involvement, such as intestinal ulceration or perforation. Some authors believe that their presence may constitute an indication to treatment with intravenous cyclophosphamide [10]. It has been reported that children who develop a generalized rash and skin ulcerations may have the poorest prognosis, although this may not always be true [5]. "Vasculitic" ulcers must be distinguished from those caused by the

extrusion of calcium deposits in patients with calcinosis.



**Figure 6 JDM – Periungual**

### **erythema**

Late in the course of JDM, other cutaneous and subcutaneous changes may occur. A persistent rash may eventuate into poikiloderma, which is characterized by mottled hypo- and hyperpigmentation, fine teleangiectasias and atrophy, with or without scale. Mechanic's hand, which is rarely observed in JDM, consists of hyperkeratosis, scaling and fissuring of the fingers and palms of both hands; it can be mistaken for contact dermatitis.

The existence of an "amyopathic" form of JDM (dermatomyositis sine myositis) [12] is still controversial and, in particular, it is still unclear whether it represents a distinct entity or is simply at one end of a spectrum of disease severity. Furthermore, although some patients may present with rash alone, or muscle disease may not be initially documented, some authors believe that these children eventually develop myositis if followed for long enough [5]. There are, however, a few children with JDM who have persistently normal levels of serum muscle enzymes.

Lipodystrophy has been reported to occur in as many as 20% of JDM patients [5]. It can be generalized, partial, or localized and is characterized by a progressive, slow, and symmetrical loss of subcutaneous fatty tissue, which is often most noticeable over the face and the limbs (Figure 7). Lipodystrophy is often associated with other manifestations resulting from metabolic derangement, such as hirsutism, acanthosis nigricans, clitoral enlargement, hepatomegaly, insulin-resistance, and hypertriglyceridemia. The loss of subcutaneous fat over the masseter area and the arms and legs allows clear definition of muscle groups, giving a false impression of muscle hypertrophy. Abdominal muscle tone may be quite reduced and, therefore, the child may have difficulty in sitting-up, even if muscle strength is normal elsewhere [13]. The loss of abdominal muscle tone is associated with increased abdominal fat, leading to the development of a "pot belly". Insulin-resistance in patients with JDM has been related to muscle damage, probably because skeletal muscles are the main site of insulin-mediated glucose disposal [14].



**Figure 7 JDM Lipodystrophy over the**

**face**

Calcinosis is one of the most important sequelae of JDM, which occurs in approximately one-third of patients. Since this complication has been discussed in an excellent review, which appeared recently in the *Pediatric Rheumatology Online Journal* [15], it will not be addressed.

#### **MANAGEMENT**

The treatment of skin disease in SLE and JDM is similar and, therefore, the two diseases will be discussed together. The goal of management is to improve the patients' appearance and to prevent development of scars, atrophy, or pigmentation changes [5,16,17]. Because skin lesions are photosensitive in many patients, adequate protection from sunlight must be advised. A cornerstone of therapy is represented by the sunscreen, which should have a broad spectrum and be water-resistant. Unfortunately, no sunscreen is able to block all UVR that might exacerbate cutaneous rash and, therefore, patients should also be encouraged to use other sun-protective measures, including wearing clothes, hats and sun-glasses that protect the sun-exposed areas of the body from UVR.

Topical corticosteroids are sometimes prescribed, particularly in patients with discoid lupus, although the experience with their use is probably much greater in adults than in children. An appropriate topical corticosteroid is selected based on the area of the body to be treated as well as on the type of lesions that are present. Facial lesions should be treated with low- to mid-potency agents, whereas trunk and arm lesions deserve mid-potency agents; rashes located on the palms or soles and hypertrophic lesions must be managed with the most powerful topical corticosteroids. In general, ointments are more potent and are possibly more effective than creams. Intralesional injections of corticosteroids are often effective in patients with rashes that are refractory to topical corticosteroids. Again, these procedures may be indicated in adult patients with the most severe and disfiguring lesions, whereas their use in children is at least very limited. In some patients with lupus or dermatomyositis, including a few children, who displayed

cutaneous lesions that were refractory to conventional therapies, tacrolimus ointment was tested with some success [18-21].

When skin lesions are not controlled with topical agents, are associated with visceral involvement or are particularly severe or vasculitic in nature, systemic therapy is indicated. Beside treatment for the underlying disease, which can be itself effective on skin disease, the first-line therapy of dermatitis is often represented by the use of hydroxychloroquine, which reaches its maximal efficacy in 4 to 8 weeks. Because hydroxychloroquine may cause ocular toxicity, including irreversible retinopathy, patients must undergo an ophthalmologic screening at baseline and then every 6 months. This side effect is, however, very rare when the drug is used in a dose of less than 6.5 mg/kg/day [16,17].

In patients with urticarial vasculitis or bullous lesions there are reports of successes using dapsone. In recent years, thalidomide has been increasingly used for cutaneous lupus disease that is refractory to traditional therapies. The mechanism of action of this drug, which should be taken at bedtime, is believed to involve the inhibition of inflammatory mediators, particularly tumor necrosis factor alpha [22]. Evidence has been provided that up to 90% of patients who are able to tolerate the drug experience significant improvement [16]. The most important side effects of thalidomide are the neuropathy that may be reversible but may also progress despite stopping the drug, and the teratogenicity. Therefore, all patients receiving thalidomide must be questioned about the appearance of numbness, tingling or pain in both hands and feet and have the sensory nerve action potential amplitudes and, perhaps, nervous conduction velocity checked every 6 months. Furthermore, female with childbearing potential should practice adequate contraception and men must always use latex condoms during sexual intercourse because it is unknown whether thalidomide is present in the ejaculate [22]. Pregnancy tests should be done monthly. In patients with "recalcitrant" skin involvement, various immunosuppressant medications, including methotrexate, azathioprine, cyclosporine, intravenous immunoglobulins, and mofetil-mycophenolate have been tried with conflicting results. The role of the new biologic agents (e.g. tumor necrosis factor antagonists, rituximab) has not yet been defined.

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