The Pathognomoncity of Gottron's Sign

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Summary

This article presents the case of a previously healthy 43-year-old female who presented with a 3-month history of progressive, symmetrical, bilateral, proximal muscle weakness accompanied by a violaceous-to-erythematous rash involving her hands, arms, thighs, chest, and face. She had conspicuous non-edematous periorbital violaceous patches with telangiectasia and prominent warm violaceous macules overlying the metacarpophalangeal (MCP) and proximal interphalangeal (PIP) joints. Muscle biopsy confirmed dermatomyositis.

Gottron's sign is the most specific cutaneous finding of dermatomyositis and is present in at least 70% of patients. The lesions begin as non-palpable flat macules or patches (Gottron's "sign") or are firm and raised (Gottron's "papules"), but the lesions eventually coalesce into raised non-blanching plaques that occur over bony prominences – typically the MCP, PIP, and/or distal interphalangeal joints. Gottron's sign (and papules) are pathognomonic for dermatomyositis, although some other conditions may have similar presentations. Gottron's sign must always be explained, as dermatomyositis may be primary or secondary to malignancy or other connective tissue diseases, and none of the conditions that make up the differential diagnosis are benign.

Résumé

Cet article décrit le cas d'une femme de 43 ans dotée auparavant d'une bonne santé, affligée depuis trois mois d'une myopathie proximale symétrique bilatérale progressive, accompagnée d'une éruption de taches violacées érythémateuses sur les mains, les bras, les cuisses, le thorax et le visage. La femme présente des plaques violacées manifestes sans oedème périorbitaire mais avec télangiectasies, ainsi que des macules remarquables de couleur violacée qui recouvrent les articulations métacarpo-phalangiennes (MCP) et interphalangiennes proximales (IPP). Une biopsie musculaire a confirmé la présence d'une dermatomyosite.

Les lésions cutanées sont la manifestation la plus spécifique d'une dermatomyosite et celles-ci sont présentes chez au moins 70 % des patients. Les lésions débutent comme des macules ou des plaques planes et non palpables (« signe de la manucure ») ou des élevures solides (« papules » de Gottron), mais elles finissent par se fondre en plaques élevées qui ne pâlisent pas à la vitropression et qui sont localisées sur les proéminences osseuses – en général les articulations MCP, IPP et/ou interphalangiennes distales. Le signe de la manucure et les papules sont pathognomoniques de la dermatomyosite, même si d'autres pathologies se présentent de façon similaire. Elles doivent toujours être investiguées, car la dermatomyosite peut être primitive ou secondaire à une affection maligne ou à d'autres maladies des tissus conjonctifs, et aucune des pathologies sur lesquelles repose le diagnostic différentiel n'est à caractère bénin.

Case

A previously healthy, 43-year-old female presented with a 3-month history of progressive, symmetrical, bilateral, proximal muscle weakness (hips to shoulders), dysphonia, dysphagia, and odynophagia. Of note, her muscle weakness was accompanied by a non-pruritic, non-blanching, macular-to-papular, violaceous-to-erythematous rash involving her hands, arms, thighs, chest, and face. On physical examination, she was febrile (38.2°C) and looked unwell. She had very conspicuous non-edematous periorbital violaceous patches with telangiectasia and similar, but more erythematous patches involving the “v-neck,” shoulders, and anterior chest wall. Most striking, she had very prominent warm violaceous macules overlying the metacarpophalangeal (MCP) and proximal interphalangeal (PIP) joints of both hands (Figure 1). Her musculoskeletal examination revealed 3/5 bilateral weakness in her deltoids, hip flexors, and abductors as well as bilateral joint swelling of her wrists and second, third, and fourth MCP joints. The rest of her detailed physical examinations were unremarkable.

The only laboratory abnormalities were elevated creatine kinase (588 U/L; normal <146 U/L) and lactic dehydrogenase (919 U/L; normal <225 U/L). Immunologic markers including anti-Jo1, rheumatoid factor, anti-nuclear antibodies, and extractable nuclear were negative, and her erythrocyte sedimentation rate (ESR) was normal. Chest radiographs and electrocardiograms were normal.

Muscle biopsy showed moderate to severe inflammatory myopathy most consistent with dermatomyositis, confirming our clinical initial suspicion.

After 3 days of intravenous treatment with human immunoglobulin (100 g daily) and high-dose pulse methylprednisolone (1 g daily), our patient's weakness improved and there was marked improvement in the erythematous components

of her various skin manifestations, including those limited to the MCP and PIP joints. She was discharged home on 50 mg daily of prednisone, and she underwent outpatient malignancy workups with her family physician and follow-up with her rheumatologist.

Discussion

Dermatomyositis

Dermatomyositis is a rare autoimmune inflammatory myositis affecting both adults and children, with an incidence of about 10 per million.^{1,2} It is often idiopathic but can be drug induced, paraneoplastic (most commonly ovarian, gastrointestinal, lung, and breast adenocarcinomas), or part of the initial presentation for other autoimmune diseases.^{2–4} It is characterized by symmetrical, bilateral, proximal muscle weakness (usually progressing over weeks to months), an elevation of serum muscle enzymes, and a muscle biopsy with distinct characteristics. Dermatomyositis also has very specific (and frankly pathognomonic) cutaneous features – namely a periorbital “heliotrope” rash and so-called Gottron's sign (or Gottron's papules if palpable). The heliotrope rash can also be rarely observed in systemic lupus erythematosus (SLE) or scleroderma, but is present in one third of patients with dermatomyositis.¹ Other cutaneous findings not specific for dermatomyositis include periorbital edema, periungual erythema or telangiectasia, cuticular hypertrophy, poikiloderma in sun-exposed areas (v-sign, shawl sign), panniculitis, and either generalized or localized photosensitivity.^{1,2}

Clinical-Pathological Findings of Gottron's Sign

Gottron's sign is the most specific cutaneous finding of dermatomyositis that has been reported, and is present in at least 70% of patients.¹ Gottron first reported his eponymous sign in 1930, wherein he described violaceous to erythematous

lichenoid macules or patches covering bony prominences – and he considered them a specific hallmark of dermatomyositis.⁵ The lesions typically begin as non-palpable flat macules or patches (Gottron's *sign*) or are firm and raised (Gottron's *papules*), but the lesions eventually coalesce into raised, non-blanching plaques that occur over bony prominences – typically the MCP, PIP, and/or distal interphalangeal (DIP) joints.³ Less commonly, the lesions have been reported on the extensor surfaces of elbows or knees, and telangiectasias may be present.^{3,6}

Figure 1. Gottron's sign in a 43-year-old woman presenting with dermatomyositis. *A*, Violaceous macules overlying the metacarpophalangeal and interphalangeal joints represent Gottron's sign, a cutaneous finding pathognomonic for dermatomyositis. This is distinct from Gottron's papules, which are violaceous papules (i.e., palpable) overlying the same distribution. *B*, Infrared rendition of panel *A* highlighting the erythema overlying the metacarpophalangeal and interphalangeal joints. Of note, the patient did have low-grade fever when the photograph was taken.

Table 1. Differential Diagnosis of Gottron's Sign

Primary Dermatomyositis	Secondary Dermatomyositis	Not Dermatomyositis
Classic adult	Drug-induced:	Systemic lupus erythematosus
Paraneoplastic	• Statins	Lichen planus
Amyopathic	• Nonsteroidal anti-inflammatory drugs	Psoriasis
Juvenile	• Chemotherapeutics	Polymorphic light eruption
As part of an "overlap syndrome"	• Antibiotics: penicillin, isoniazid, sulphonamides	Granuloma annulare
	• D-penicillamine	Dermatitis:
	Infection-related:	• Contact dermatitis
	• Human immunodeficiency virus	• Seborrheic dermatitis
	• Herpes simplex virus	• Atopic dermatitis
		Trauma-related knuckle pads

Histologically, Gottron's cutaneous lesions are characterized by atrophy of the epidermis, basement membrane thickening, vacuolar degeneration of the dermal-epidermal junction, perivascular lymphocytic infiltrates, and mucin deposition.^{6,7} The individual changes are not unique to dermatomyositis, as SLE, discoid LE, and lichen planus may produce some of these features, although the constellation of findings is quite typical for dermatomyositis.⁶ There are, however, several important differences that are not found in dermatomyositis: in SLE, the dermatitis often extends into the hair follicle and may appear interphalangeal, and direct immunofluorescence staining is often positive; in discoid LE, pilosebaceous atrophy is often present; and in lichen planus, irregular epidermal "saw-toothed" hyperplasia and a dense lichenoid infiltrates are present.⁷

Differential Diagnosis of Gottron's Sign

Gottron's sign (and papules) are widely considered pathognomonic for dermatomyositis, although some other conditions may have similar presentations (Table 1). In our experience, SLE with rash affecting the dorsum of the hands is the most common differential diagnosis for Gottron's sign. That said, SLE almost always spares the skin overlying articular surfaces.² Lesions resembling Gottron's papules may be present in patients with undifferentiated connective tissue diseases, as part of an adverse drug effect, and with certain viral infections (e.g., human immunodeficiency virus, herpes simplex virus), and skin conditions such as lichen planus, psoriasis, or other dermatidities^{2,8} (see Table 1). Gottron's papules (and other hallmark cutaneous lesions of dermatomyositis) may present without other clinical features such as muscle weakness or enzyme changes. When this occurs, the patient is said to have amyopathic dermatomyositis.⁹

Conclusions

To summarize, Gottron's sign is highly specific and virtually

pathognomonic for dermatomyositis, and it is clinically easy to recognize. The differential diagnosis is very limited, and a thorough history and physical examination are often sufficient to rule out other conditions. Perhaps most importantly, Gottron's sign must always be explained, as dermatomyositis may be primary or secondary to malignancy or other connective tissue diseases, and none of the conditions that make up the differential diagnosis could be considered benign (see Table 1).

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References

1. Dourmishev LA, Dourmishev AL. Dermatomyositis: Advances in Recognition, Understanding and Management. Berlin, Germany: Springer-Verlag; 2009.
2. Kovacs SO, Kovacs SC. Dermatomyositis. Am Acad Derm 1998;39:899–920.
3. Callen JP. Dermatomyositis. Lancet 2000;355:53–7.
4. Zampieri S, Valente M, Adami N, et al. Polymyositis, dermatomyositis and malignancy: a further intriguing link. Autoimmun Rev 2010;9:449–53.
5. Gottron H. Hautveränderungen bei Dermatomyositis. VIII Congres Intern. Dermatol. et Syphilogr., Copenhagen, 1930 August 5–8, Compt rend Seancy, Ed. S.Lomholt, Copenhagen 1931; 826–30.
6. Stone JH, Sack KE, McCalmont TH, Connolly MK. Gottron's papules? Arthritis Rheum 1995;38:862–5.
7. Mahalingam M, Mendese G. Histopathology of Gotton's papules – utility in diagnosing dermatomyositis. J Cutan Pathol 2007;34:793–6.
8. Dourmishev LA, Dourmishev AL. Activity of certain drugs in inducing of inflammatory myopathies with cutaneous manifestations. Expert Opin Drug Saf 2008;7:421–33.
9. Sontheimer RD. Dermatomyositis: an overview of recent progress with emphasis on dermatologic aspects. Derm Clin 2002;20:387–408.