A 74-year-old patient, suffering for 20 years from polycythemia rubra vera, was treated with hydroxyurea for 2 years. Intensive xerosis (ichthyosis-like) and violaceous papules on the dorsal hand surfaces were observed. There was also reddish purple periorbital erythema resembling “heliotrope erythema.” Such a disease pattern has been described as “hydroxyurea-induced dermatomyositis-like eruption” – a drug-adverse reaction associated with hydroxyurea therapy. The reaction has typical dermal features of dermatomyositis without any systemic symptoms (in the case of our patient, antinuclear antibodies absent and creatine phosphokinase within the normal range). The above reaction is associated with chronic hydroxyurea uptake and, after withdrawing the drug, alleviation of skin lesions usually takes place after 10 days to 18 months with no recurrences. In the case of our patient, we observed clinical improvement after 3 months; xerosis decreased, heliotrope erythema vanished, and there was also a decrease in both the number and intensity of violaceous papules on the dorsal hand surfaces.

**Introduction**

Hydroxyurea is a chemotherapeutic agent that inhibits DNA synthesis through its influence on ribonucleotide diphosphate reductase – an enzyme catalyzing conversion of ribonucleotides into deoxyribonucleotides and interfering with thymidine incorporation in DNA (1). Hydroxyurea is used for treatment of myeloproliferative disorders (polycythemia vera, chronic myeloid leukemia, and essential thrombocytosis), but also in therapy of sickle cell anemia and severe cases of psoriasis. Predominant adverse reactions associated with the administration of hydroxyurea include bone marrow suppression and various symptoms of the gastrointestinal tract. Cutaneous adverse reactions (nail hyperpigmentation, alopecia, mucocutaneous ulcerations, and erythema fixum) have been reported in 10 to 35% of patients, although the precise effect on skin and mucosal membranes has not yet been fully explained (2).
Case report

We present the case of a 74-year-old male patient that has been suffering from polycythemia rubra vera for 20 years and had been treated for the past 2 years with hydroxyurea. On the day of admission, the patient complained of persistent hand lesions of 2 months’ duration, together with marked dryness of the entire body surface. Regardless of the frequent use of various emollients, skin lesions became even more exacerbated shortly before consultation at the Department of Dermatology.

Thorough examination revealed intensive overall xerosis (ichthyosis-like), together with the presence of symmetrical red-violaceous papules, localized within the dorsal hand surfaces (particularly over the metacarpophalangeal and proximal interphalangeal joints) (Fig. 1). There was also purple periorbital erythema resembling “heliotrope erythema” (Fig. 2). Muscle examination yielded no abnormalities.

As a part of the diagnostic approach, we performed patch tests with hydroxyurea (1% in white petrolatum), which appeared to be negative after 48 and 72 hours. Moreover, serum antinuclear antibodies were absent and the creatine phosphokinase level was within the normal range. Histopathological examination (hematoxylin-eosin stain) of a skin biopsy taken from one of the violaceous papules revealed the presence of thin, atrophic epidermis with Civatte bodies (colloid bodies) and sparse perivascular, mixed dermal infiltrate.

After consulting the patient’s hematologist, hydroxyurea was withdrawn and replaced with alternative therapy. We observed gradual clinical improvement within 3 subsequent months: xerosis decreased, heliotrope erythema vanished, and there was also a resolution regarding both number and intensity of red-violaceous papules of the hands (Fig. 3).

Figure 1. 74-year old patient presenting symptoms of hydroxyurea induced dermatomyositis-like eruption: violaceous papules and plaques localized on the dorsum of right hand.

Figure 2. The same patient: "heliotrope-like" erythema around the eyes.

Figure 3. Clinical improvement after 3 months of hydroxyurea withdrawal – resolution of red-violaceous papules of the hands.
Case report: Hydroyxurea-induced dermatomyositis-like eruption

Discussion

The case presented above is an example of a condition previously described by other authors as hydroxyurea dermatomyositis-like eruption – an adverse reaction associated with prolonged hydroxyurea therapy (1). Other terms have also been applied: dermatomyositis-like lesions, pseudodermatomyositis, Gottron’s papules-like rash (GP-like rash), or hydroxyurea dermopathy (3–6). Usually after withdrawing from a suspected drug, alleviation of skin lesions takes place after 10 days to 18 months with no recurrences. The reaction has typical dermal features of dermatomyositis (scaly erythema on the dorsa of the hands with atrophic and telangiectatic changes) (2), but without any systemic symptoms. No proximal muscle weakness has been reported and the muscle enzyme level and electromyography are normal.

According to literature data, some other medications such as BCG vaccination, penicillamine, lovastatin, simvastatin, phenylbutazone, alfuzosin, phenytoin, and tegafur are also considered to be associated with dermatomyositis-like eruption (7–12). Although the pathomechanism of the reaction has not yet been fully revealed, such factors as the latency of onset and slow progression, together with subsequent healing after withdrawal of the culprit drug, are strongly suggestive of chronic cumulative damage to the basal layer of the epidermis. Moreover, GP-like rash has also been rarely described as a manifestation of non-dermatomyositis conditions: leishmaniasis, acanthosis nigricans, and arsenic poisoning (13). The clinical picture of hydroxyurea dermatomyositis-like eruption is variable as reported by different authors. Vassallo et al. (1) conducted a clinicopathologic study on over 500 patients affected by chronic myeloid leukemia and treated with hydroxyurea. Clinical findings especially included acral erythema, xerosis, telangiectasias, livedoid erythema of the heels, ichthyosiform lesions, and hyperpigmentation. According to the authors, mild xerosis and hyperpigmentation were specifically common findings in the group of patients analyzed. The exact cause of described hyperpigmentation is unknown, although it may be associated with increased activity of melanocytes, which are involved in reduction of free radicals, probably produced by drug direct toxicity on cells.

Haniffa and Speight (14) described painful leg ulcers and dermatomyositis-like skin changes on the hands of a 52-year-old woman treated with hydroxyurea for 5 years because of polycythemia rubra vera. Usually in such cases ulcerations are painful and tend to be localized over sites exposed to trauma: the dorsa of the feet, malleoli, toes, and shins. In some patients, ulcerations may also involve mucosal membranes. According to Best et al. (15), among 115 patients suffering from various lymphoproliferative disorders, 14 presented with hydroxyurea-induced leg ulcers. Unfortunately, the healing response after drug withdrawal is less predictable compared to dermatomyositis-like rash.

In the case of our patient, clinical findings of hydroxyurea dermatomyositis-like eruption were typical, although it must be emphasized that, among such features as xerosis and GP-like papules, “heliotrope-like” violaceous erythema of the periorbital area is described only rarely by other authors. Histopathological findings typically included vacuolization of the basal layer of the epidermis (colloid bodies present), together with mild hyperkeratosis and moderate dermal perivascular inflammatory infiltrate (13).

Regarding the differential diagnosis of hydroxyurea dermatomyositis-like eruption, we focused on remarks presented recently by Slobodin et al. (16): the similarity of the histological picture in hydroxyurea dermatomyositis-like eruption and true dermatomyositis may cause diagnostic difficulties. However, no abnormalities in laboratory findings and no systemic symptoms, together with the presence of marked xerosis and cutaneous atrophy (which are considered common features in hydroxyurea-treated patients) enabled us to establish the appropriate diagnosis. Furthermore, thorough analysis of all disease attributes mentioned above may be of indispensable help in differentiating dermatomyositis-like eruption in hydroxyurea-treated patients with myeloproliferative disorders from cases of neoplasia-related dermatomyositis.

References


Hydroxyurea induced dermatomyositis - like eruption


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