Answer to Dermacase *continued from page 1667*

3. Morphea

Morphea is a relatively benign, well circumscribed localized scleroderma, characterized by ovoid or, less commonly, linear plaques. The lesion typically begins as an erythematous, red- or lilac-coloured, swollen, smooth, non-pitting area with centrifugal expansion. As the lesion progresses, the centre assumes a yellowish-white tone and undergoes gradual depression with induration and atrophy.[1] It is different from systemic scleroderma in that it is not accompanied by Raynaud's phenomenon, acrosclerosis, and systemic organ involvement, thus the prognosis for the patient is good.

Morphea is classified based on clinical morphologic findings into 5 groups: generalized, plaque, bullous, linear, and deep.[2]

Generalized morphea. Generalized morphea is the severe form of the local disease with widespread involvement of the skin. Eventually, multiple indurated plaques with hyperpigmentation occur, with some degree of muscle atrophy.[1]

Plaque morphea. This form is superficial and confined to the dermis. It might involve only 1 or 2 areas, or present as multiple small, flat, or slightly depressed patches. Sometimes it presents as flat-topped white papules that might coalesce to form plaques.[1]

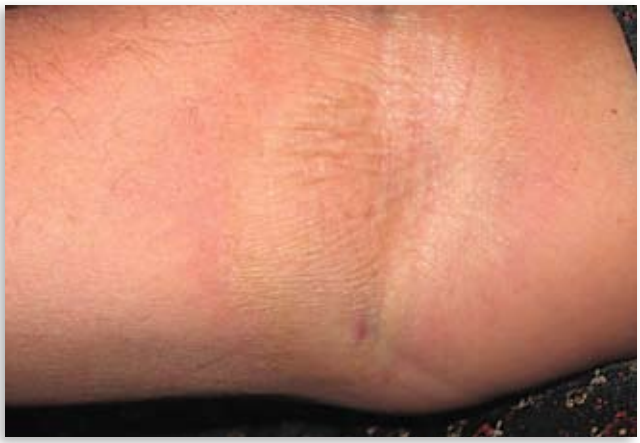
Bullous morphea. This form presents as coexisting, tense, subepidermal bullae together with typical plaque morphea.

Linear morphea. This form usually occurs in children as single linear and unilateral bands occurring most frequently on the limbs, sometimes on the forehead, and most rarely on the anterior trunk. On the limbs it could contribute to progressive and long-lasting induration of the skin and subcutaneous tissue. It can cause deformity, growth retardation, joint contractures, muscle atrophy, and in severe cases flexion deformities, limb atrophy, and poorly healing ulcerations.

Deep morphea. Deep morphea involves the deep dermis, subcutaneous tissue, fascia, or muscles, typically with diffuse lesions. Because the inflammation is deep, the typical skin-colour changes of localized morphea are usually absent.[1]

Epidemiology

The annual incidence is 2.7 per 100 000.[1] The disease affects all ages, with peak incidence affecting patients between the ages of 20 and 40. Linear morphea is more common in children under the age of 10, whereas plaque morphea is frequently encountered in adults. Morphea affects women 2 to 3 times more frequently than men.



Pathophysiology

Morphea is histologically characterized by fibrosis of the skin with accumulation of extracellular matrix components, particularly collagen in the dermis. Its etiology remains in question, despite circumstantial evidence pointing to hereditary, infective, autoimmune, drug-induced, traumatic, postirradiation, and malignant factors as causative agents.[3-6]

Many dermatologists favour the autoimmune hypothesis, which suggests that morphea is one of the organ-specific autoimmune disorders targeting skin. It stipulates that the mechanism of pathology is an autoimmune dysregulation of fibroblast activity, aberrations of the endothelial cells, and abnormal cytokine production, namely transforming growth factor β and connective tissue growth factor.[4] These act in concert to promote tissue repair and regeneration via increased collagen production, leading to fibrosis and sclerosis. Because many findings suggest an immunologic basis for the disease, it might be indicated that patients with morphea should be investigated for other autoimmune disorders. Association between morphea and vitiligo has been suggested,[3,7] and vitiligo itself has been associated with certain organ-specific autoimmune diseases.

Investigations

Although there are no serologic tests that confirm the diagnosis of morphea, frequent abnormalities include an eosinophilia, positive antinuclear antibodies, anti–single-stranded DNA antibodies, and antihistone antibodies.[8] In addition, radiographic studies might be abnormal if deeper tissues are involved. Morphea must also be differentiated from systemic scleroderma and sclerodermoid syndromes.[9]

The characteristic skin biopsy is that of a "square biopsy" that shows lymphocytes located in the deep dermis and scattered among the collagen bundles. The initial collagen changes are seen in the lower part of the dermis and subcutaneous tissue, but later affect the whole of the dermis; they include eosinophilia of the collagen and broadening of the collagen bundles with

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diminished interbundle spaces. Eccrine glands are often entrapped by collagen and lose their adventitial fat. Inflammatory changes disappear as morphea progresses, and are replaced by hyalinized dermal collagen.

Treatment

The treatment of sclerosing skin diseases remains a great challenge. Management of morphea involves reassurance that the process is benign and often arrests spontaneously, along with a course of either one or several of the following: general measures (regular massage or physiotherapy, warmth, protection from trauma and cold, avoidance of smoking); topical agents (corticosteroids, calcipotriene, and imiquimod); phototherapy (UVA, UVA1, psoralen–UVA[PUVA]); or oral systemic therapy (steroids, low-dose methotrexate, antimalarials, colchicine, D-penicillamine, sulfasalazine).[1,4,10-13] The age of the patient, area of the body affected, percentage of the body surface area involved, subtype of morphea, and comorbidities are used to gauge the aggressiveness of treatment.

With phototherapy and photochemotherapy, UVA or PUVA therapy provides clearance of early inflammatory lesions and softening of sclerotic lesions but without full reversion to normal skin.[10] Even low-dose UVA and UVA1 phototherapy has been found to be highly effective for sclerotic patches, including advanced and rapidly evolving lesions.[13] In PUVA therapy, the photosensitizing psoralen can be administered orally or topically (either by application of a psoralen-containing cream or by immersion in an aqueous psoralen bath), followed by a low-dose UVA irradiation to induce PUVA erythema. The restriction of topical PUVA treatment to a selective lesional area is better for patients presenting with single lesions only, as it is associated with fewer systemic side effects.[11] PUVA therapy and UVA1 phototherapy exhibit a tolerable risk-benefit ratio[11] and are not of great concern if treatment courses are of short duration.[10]

The immunomodulation treatments work by modifying the immunological response. Treatment with an interferon-γ inducer, such as imiquimod 5% cream, has been shown to successfully reduce dyspigmentation, induration, and erythema, decrease dermal thickness and fibrosis with appreciable positive changes in inflammation and contour, and result in overall improvement of morphea lesions.[4] The efficaciousness of the treatment is due to interferon-γ inhibiting profibrotic cytokines along with transforming growth factor β. Novel treatment considerations also include topical photodynamic therapy with 5-aminolevulinic acid.[14]

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Competing interests

None declared

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