CASE REPORT

Plaque-type morphea in children

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Abstract

We present the case of a girl, aged 8-year-old, with a history of acrocyanosis and repeated respiratory infections with beta-hemolytic streptococcus, which was consulted for the presence of skin lesions in the right buttock area. Clinical examination showed, in the right buttock region, an oval plaque with a diameter about 12 cm, hard, well defined, with irregular outline. The biopsy was performed and it revealed typical aspects of plaque-type morphea. The epidermis was mostly atrophic, with areas of ridge reduction; an important proliferation of collagen fibers within superficial and deep dermis and an abundant lymphocytic inflammatory infiltrate throughout the dermal thickness reaching hypodermic level and infiltrating it. General treatment consisted of antibiotics; vitamin E; local treatment with topical cortisone; analogues of vitamin D3 to which we associated topical adjuvants with repairing and healing role applied to the biopsied area. Evolution was favorable after three months of treatment, with obvious improvement of skin lesions; skin became more elastic and the purple red contour ring disappeared.

***Keywords*:** children, plaque-type morphea, skin, histopathology.

Introduction

Scleroderma is a chronic disease of autoimmune etiology affecting microcirculation and lax connective tissue, characterized by fibrosis and obliteration of regional blood vessels. It is classified into two main categories: localized scleroderma (morphea) and systemic sclerosis, which is characterized by diffuse sclerosis of the skin associated with internal organ damage [1].

Localized scleroderma is the form of scleroderma that affects almost exclusively the skin, subcutaneous tissue and sometimes-adjacent muscles, without the Raynaud phenomena, acrosclerosis or the internal organ involvement. The disease is chronic, self-limiting and its development is mostly favorable [2].

Although there are few studies on incidence and prevalence of localized scleroderma that was observed in children, although it is an unusual presence, morpheme occurs 10 times more frequently than juvenile systemic sclerosis. Many children diagnosed by dermatologist with morphea never arrive in pediatric rheumatology services due to mild disease development considerations, so that only 2% of the patients seen by the rheumatologist have localized scleroderma [3].

Patient and Methods

We present the case of a girl, aged 8-year-old, with a history of acrocyanosis and repeated respiratory infections with β-hemolytic streptococcus, which was consulted for the presence of skin lesions in the right buttock area.

The lesion appeared three months ago in the right buttock region where could be seen a straight lilac red plaque well demarcated, slightly edematous, non-itching, with irregular edges, of about 4 cm in diameter. Subsequently the lesion had a tendency to peripheral extension, becoming yellowish-white in center with purple-lilac outlines.

It was made a skin biopsy from an atrophic lesion of the right buttock region. Skin fragment was then processed by conventional techniques including paraffin, then were executed three-micron sections. Those were stained by usual Hematoxylin–Eosin (HE) staining, in the Department of Pathology of Emergency County Hospital in Craiova.

Results

From personal pathological history, we noted that at the age of four the child presented a bradycardia crisis for which she was hospitalized in Timisoara, and a possible heart disorder was excluded.

Clinical examination showed, in the right buttock region, an oval plaque with a diameter about 12 cm, hard, well defined, with irregular outline, with infiltrated shiny waxy yellowish skin above (Figure 1). Plaque's edges were surrounded by a purple red halo (Figure 2). Underlying muscles were not affected.

Laboratory investigations: hematological, biochemical, immunological tests were performed and only ASLO was increased, also ESR was initially increased but it has normalized after treatment, anti-*Borrelia burgdorferi* were negative, nasal and pharyngeal exudates negative.

Imaging exams (CT scan, cerebral MRI and right leg MRI) and neurological investigations were normal, without revealing lesions of the underlying bones.

Histopathology revealed several aspects. The epidermis was mostly atrophic, with areas of epidermal ridge reduction, alternating with areas of almost completely disappeared ridges (Figure 3).

In the dermis were revealed most of the changes, affecting both stroma and glands. Both in the superficial and deep dermis there was an important proliferation of collagen fibers. Those were arranged in thick bundles having a parallel layout to the skin surface. Also of interest, hair follicles in dermis were affected, collagen fiber bundles being arranged around them (Figure 4).

Very important for diagnosis an abundant lymphocytic inflammatory infiltrate was evident throughout the dermal thickness reaching hypodermic level (Figure 5), and infiltrating it latter (Figure 6). Inflammatory infiltrate was predominantly perivascular ordered (Figure 7), but was found also around sweat glands (Figure 8). Blood vessels were rare inside the sclerotic collagen, with thickened walls caused by the collagen fibers deposited at this level, having narrowed lumina.

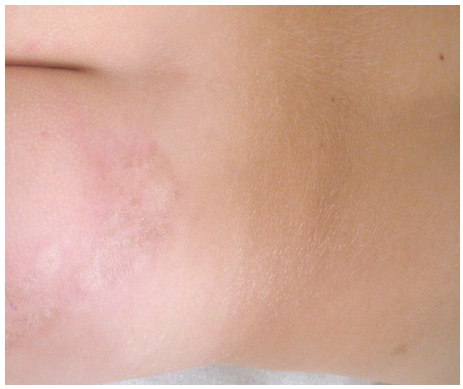

Figure 1 – ***Posters of the child's plaque-type morphea.***

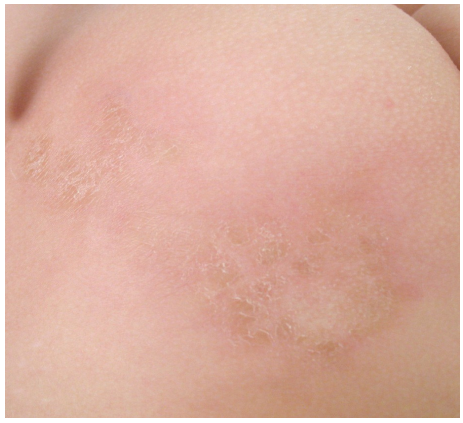

Figure 2 – ***Plaque morphea, detailed clinical appearance: skin atrophy and lilac "ring" at the periphery.***

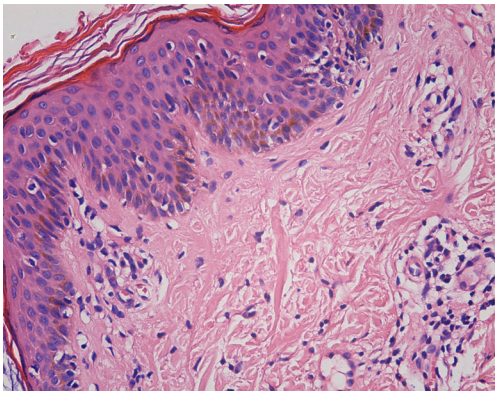

Figure 3 – ***Atrophic epidermis with focal deletion of the epidermal ridge (HE stain, ×200).***

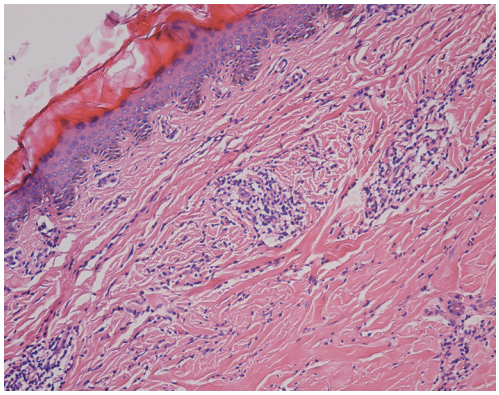

Figure 4 – ***Collagen in superficial dermis: thick collagen bundles lying parallel to the skin surface (HE stain, ×100).***

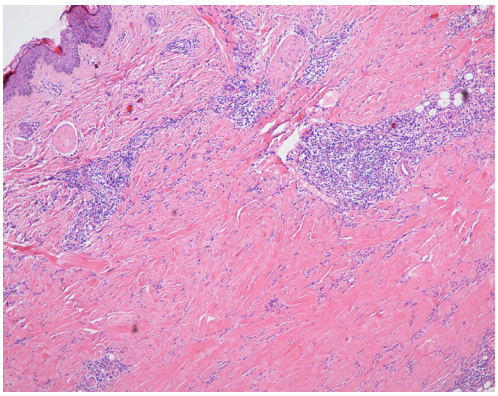

Figure 5 – ***Abundant inflammatory infiltrate around the dermal thickness (HE stain, ×40).***

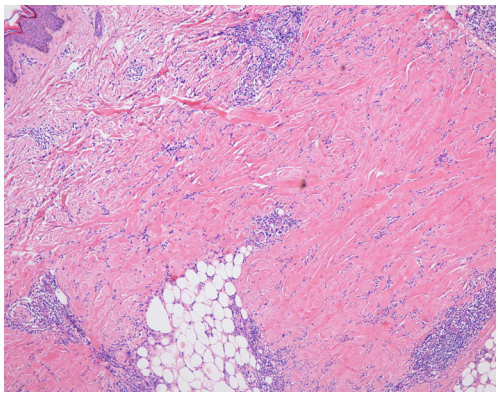

Figure 6 – ***Inflammatory infiltrate in the hypodermis (HE stain, ×40).***

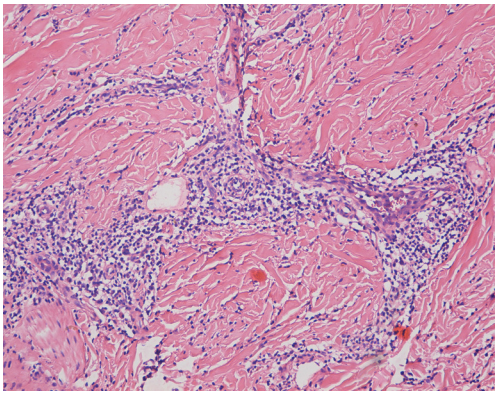

Figure 7 – ***Perivascular lymphocytic inflammatory infiltrate (HE stain, ×200).***

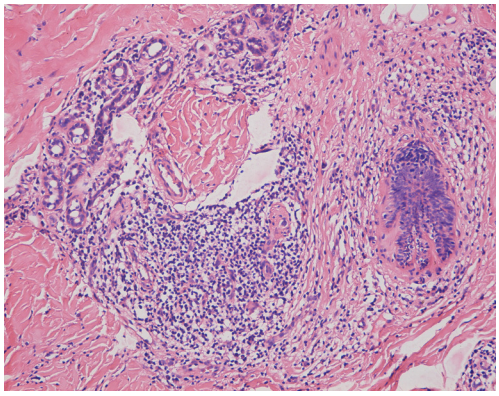

Figure 8 – ***Lymphocytic inflammatory infiltrate around sweat glands (HE stain, ×200).***

Regarding the glands, they presented some changes: very rare hair follicles, atrophic sweat glands and sebaceous glands absent in the biopsy fragment analyzed.

Therefore, based on clinical examination, paraclinical and histopathological tests the diagnosis was plaque morphea.

General treatment consisted of antibiotics (i.m. Moldamin, 6 MU/week) Piascledin; vitamin E; local treatment with topical cortisone (Dermovate, Locoid); analogues of vitamin D3 – Calcipotriol (Daivonex) to which we associated topical adjuvants with repairing and healing role (Cicabio, Cicalfat) applied to the biopsied area.

Evolution was favorable after three months of treatment, with obvious improvement of skin lesions; skin became more elastic and the purple red contour ring disappeared.

Discussion

Morphea, also known as localized scleroderma, has as particular clinical feature: the cutaneous sclerosis present is of well-defined shape and variable size, not associated with visceral involvement [1].

Morphea incidence in the U.S. was estimated at 25 cases/one million inhabitants per year, two thirds of adults with morphea plaque lesions, half of those cases occurring in pediatric patients. Among children predominates linear morphea (two thirds of cases), followed by subtype plaque morphea (25%) and generalized morphea (5%) [2]. Although, it affects all races, it seems that most commonly affects white race, with a predisposition for female gender, with a W:M ratio of 3:1, excepting linear form which has only a slight female predominance. Linear morphea usually occurs in children and adolescents; two thirds of cases before the age of 18 years, other subtypes have the highest incidence in three and four decades of life [2].

A variety of clinical entities are classified as morphea, all with the common feature induration and thickening of skin and subcutaneous tissue as a result of excessive collagen deposition [4].

Excess collagen production in lesional fibroblasts [5] is common in all forms of morphea, but the exact mechanism is unknown. Pathogenesis is still unclear, involving vascular or immunologic changes, and metabolic changes of the conjunctive tissue.

It turned out that early vascular alterations favor the formation of dermal mononuclear cell infiltrates [6]. These cells, particularly T-cells will release activating (TGF-β, interleukins 1 and 4) or inhibitory (interferon γ) substances for the metabolic activity of fibroblasts. If one accepts the assumption of a normal balance of cytokines in the dermis, it can be assumed that it is affected in scleroderma dermis [7].

The trigger factor acts on a genetically predisposed field and it could be infectious type (Epstein–Barr virus infection, varicella, measles, borreliosis, after BCG vacin), traumatic or toxic [2, 3, 8, 9].

Regarding infectious factors are discussions in literature about how infection with *Borrelia burgdorferi* is transmitted through tick bites [9], but the usefulness of serological tests for Lyme disease in juvenile morphea cases is true only for cases that have been in an endemic area [3].

The most widely used classification divides morphea into five general subtypes: plaque morphea, generalized morphea, linear scleroderma, bullous morphea, and deep morphea [10].

I. Plaque morphea is characterized by superficial dermal location of the lesion, rarely touching the surface of the hypodermis. There are several clinical forms of plaque morphea:

1. *Plaque morphea itself*, which starts as well demarcated erythematous plaque, round-oval, infiltrative-edematous aspect, non-depressible, evolving towards sclerosis (skin color: waxy white or yellow-orange) and central atrophy, keeping only inflammatory purple red ring edges (lilac ring).

2. *Guttate morphea* is characterized by small size of several millimeters of the lesions that are grouped, pearly white, shiny, slightly depressed without sclerotic characteristics. Location of choice is at chest level.

3. *Ring morphea* – circular layout sclerosis situated mostly at the extremity of a member, rarely affecting foreskin.

4. *Keloid morphea* – typical plaque morphea lesions with isolated nodules or united nodules with keloid scar appearance.

5. *Lichen sclerosus et atrophicus* – clinical atrophic macules and small plaques, bright white.

6. *Atrophoderma of Pasini and Pierini* is considered a form of morphea with questionable category [8]. This

presents as asymptomatic, hyperpigmented atrophic patches with well demarcated "cliff drop borders" on the trunk the trunk and proximal parts of limbs. No pronounced inflammatory or sclerotic changes are present.

II. Generalized morphea form of the disease is more severe, characterized by extension of skin damage and its association with muscle damage.

III. Bullous morphea is characterized by tense subepidermal bullae in the presence of typical morphea or deep morphea.

IV. Linear scleroderma is characterized by one or more linear streaks and induration that can involve dermis, subcutaneous tissue, muscle, and bone. It occurs on the extremities, face, or scalp of children and adolescents.

V. Deep morphea – subcutaneous morphea, morphea profunda, disabling pansclerotic morphea of childhood, and eosinophilic fasciitis.

The context of the classification of forms of morphea is still questionable and because mixed juvenile localized scleroderma forms in which different types of injuries occur in the same individual are not included, there are new projects required to achieve this new criteria classification for juvenile localized scleroderma [3].

Morphea diagnosis is primarily clinical, sometimes supplemented by biopsy of skin and subcutaneous tissue. According to the literature, the disease can develop in two phases [11]. Initial inflammatory phase, collagen bundles in reticular dermis are thickened and there is an interstitial and perivascular lymphocytic inflammatory infiltrate. It can also affect the subcutaneous adipose tissue, and replace it with thickened trabeculars of new formed collagen. In the late sclerotic phase, the inflammatory infiltrate is reduced. The reticular dermis collagen bundles become thick, arranged in bundles, and having few cells and many eosinophiles. In papillary dermis, normal fibers may be replaced by uniform collagen [11]. In linear, segmental, subcutaneous and generalized types, fascia and subjacent skeletal muscles may be affected by vacuolation, separated from each other by edema and inflammatory cells [12].

The differential diagnosis is complex: sclero-atrophic lichen, carcinoid syndrome vitamin K injection, chronic discoloration, basal cell carcinoma, after exposure to chemicals or toxins, annular granuloma, migratory erythema, eosinophilic fasciitis, keloid and hypertrophic scars, scleredema, scleromyxedema [1, 2].

Morphea must be differentiated of stiff syndrome (SSS – *Stiff Skin Syndrome*) which can sometimes be difficult because of the clinical similarities between the two diseases. However, histopathological aspects are distinct. In SSS, there is fascial sclerosis with slightly increased number of fibrocytes and thickened collagen fibers that can sometimes be present in reticular dermis and / or subcutaneous septa; in a characteristic way, inflammatory infiltrate is absent and are no changes regarding glands [13].

Evolutionary clinical markers are represented by lilac ring extension of the initial lesion, the appearance of new lesions. Reduction of skin sclerosis is a sign of involution of the disease [14].

For a correct histopathological diagnosis of plaque morphea deep biopsy is necessary. Sometimes histological changes are minimal, while clinical diagnosis is obvious [7]. Most frequently first is the edema, the homogenization and later a dermal fibrosis associated with collagen vascular changes.

Accumulation of collagen and glycosaminoglycans has been reported from studies of cultured dermal fibroblasts that came from patients with linear scleroderma [5].

Although biological balance is not usually required, some authors require antinuclear antibodies, anti-denatured DNA, rheumatoid factor. Erythrocyte sedimentation rate is usually normal but may be increased in patients with eosinophilic fasciitis or active morphea. Peripheral eosinophilia may be observed in patients with recent morphea, active, of any kind [2].

Antinuclear antibodies with fluorescence stained nucleolar or rarerly nuclear can be present in some forms of morphea, ranging from 23–73% [2].

Denatured DNA antibodies are positive in approximately 50% of cases and should be a correlation between their level and disease progression [2–4]. Not reported the presence of antibodies and anti anti-centromer SCL70 [8] or occurs in less than 5% of patients with morphea [2]. Complement is generally normal and anti superoxide dismutase Cu/Zn appear in 90% of patients with morphea [2].

Anticardiolipin antibodies have a prevalence of 13% in children with localized scleroderma and their presence is not correlated with increased risk of thromboembolic accidents and coagulation abnormalities [3]. RF is present in 25–40% of patients, high levels being correlated with joint and severe skin damage.

Techniques as skin thermography, skin ultrasound, twistometria, are useful for determining the disease activity in some forms of morphea but often are not available. Of the imagistic techniques, X-ray can be useful in cases of linear morphea and MRI is important to establish CNS and eye damage [3, 14].

Regarding the evolution and prognosis, plaque is a self-limiting disease with a tendency to slow involution over time, duration of disease activity is on average of 3–5 years and may resolve spontaneously leaving hypo- or depigmented areas. Risk of systemic sclerosis transformation is absent regarding localized morphea.

Treatment of localized scleroderma in children should be individualized according to clinical type morphea, given that most patients have benign forms, remission can be spontaneous and that systemic treatment may have potential toxicity. Of course, that forms like deep, linear, the ones that have osteo-articular implications and possible functional impotence a systemic therapy, and physical and occupational therapy is considered [3]. Plaque morphea is self-limiting and has more aesthetic implications and first line of treatment is local using: topical corticosteroids can reduce inflammation and prevent progression, vitamin D analogue (Calcipotriol) which inhibits the activity of fibroblasts and production of TGF-β, with anti-inflammatory effect and may apply on lesion to increase the drug absorption, local immunomodulators

(Tacrolimus 0.1%) under occlusion, Imiquimod 5% cream, emollient, ionization hyaluronidase, ultrasound therapy [1–3, 14–17].

Although promising clinical results were reported about photochemotherapy, phototherapy, PUVA, 5-aminolevulinic acid photodynamic therapy, or the 585 nm pulsed laser are required controlled, multicenter, randomized studies to assess their effectiveness in treatment of localized scleroderma in children [1–3, 18–20].

Conclusions

The diagnosis of plaque morphea, is based on clinical appearance of lesions but investigative balance requires interdisciplinary collaboration. Histopathology is useful in the diagnosis and to determine the depth effect and also for differential diagnosis with other skin disorders accompanied by sclerosis.

Given that this form of localized scleroderma has no evolution to systemic sclerosis, the existing balance is not exhaustive but clinical oriented.

Localized scleroderma therapeutic management should be individualized according to clinical type of morphea, plaque morphea benefiting of local treatment.

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Received: July 15th, 2010

Accepted: August 25th, 2010