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Morphea in Saudi Arabia, a Clinical Study of 64 Patients

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Received: 13 September, 2017; Accepted: 22 September, 2017; Published: 02 October, 2017

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Abstract

Morphea is a cutaneous disorder characterized by excessive collagen deposition leading to thickening of the dermis, subcutaneous tissue or both. Clinically, it is classified into circumscribed, generalized including coalescent plaque and pansclerotic, linear, mixed and rarely guttate type. Morphea can present with laboratory abnormalities including positive antinuclear antibodies. Here we represent a clinical review of morphea in Saudi Arabia.

Keywords: Morphea; Scleroderma; Saudi Arabia;

Introduction

Morphea is a chronic idiopathic inflammatory disease characterized by excessive collagen deposition of the skin. It affects primarily the dermis and may extend to subcutaneous structures. Unlike systemic sclerosis, morphea lacks internal organ involvement. It may affect adults or children, and is slightly more common in females than males. Most previous studies have been performed in Caucasian patients, and few studies have investigated Asian populations. As of our knowledge, this is the first clinical study of morphea in Saudi population.

Material and Methods

We retrospectively reviewed 64 morphea cases that were diagnosed histologically 2006 to 2016 in King Khalid University Hospital, a tertiary hospital in Riyadh, Saudi Arabia. We went through each patient's medical record and retrieved data about gender, age, lesion body distribution, associated systemic diseases and serology. Morphea classified based on Laxer and Zulian's classification into circumscribed including superficial and deep, generalized including coalescent plaque and pansclerotic, linear, mixed and rarely guttate type. All the six cases that were not confirmed by histopathology were excluded from the study. Hence, the diagnosis of these morphea cases was based on the clinical presentation and histopathological features.

Result

Out of the 58 patients studied 34 (59 %) were females and 24 (41%) were males (figure 1). Localized, linear and guttate morphea were the types observed in our study and their histological details were studied separately. Most of our cases were seen between 20-50 years of age group (table 1) with a mean of 36 and a standard deviation 15. Also, there is decrease in cases on both age extreme. Plaque localized morphea was seen in most of our patients (48 patients, 83%) (figure 3,5). Linear morphea seen in three patients, two of them were females 19 and 27-year-old and one 23-year-old male (figure 4). Guttate type observed in only one patient, a 30-year-old male. Systemic Scleroderma diagnosed in six patients (figure 2).

Out of the 26 patients with serological tests, 13 patients (50%) have ANA positive. Only three of those patients with positive ANA are sclerodermic, with age ranges between 8 and 45 years, all were females except one.

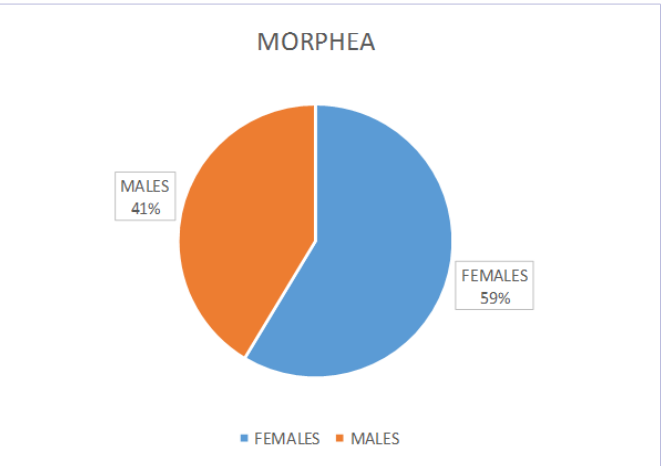

Figure 1: Females and males percentages

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Table 1: Patients data categorized based on gender, age, distribution and serology

Case #	Gender	Age	Body distribution	Serology	Diagnoses
1	M	34	Back and lower limbs	Not available	Morphea
2	M	48	Upper back	Not available	Morphea
3	M	41	Bilateral shins	Not available	Morphea
4	M	51	Abdomen	Not available	Morphea
5	M	30	Upper limbs	**-ANA & Scl-70** negative	Morphea
6	M	48	Left buttock	Not available	Morphea
7	M	18	Abdomen and back	Not available	Morphea
8	M	21	Trunk and upper extremities	Not available	Morphea
9	M	55	Upper back	**-ANA** 1:40 speckled	Morphea
10	F	29	Affecting > 80% of body surface area	**-ANA** negative	Scleroderma
11	M	27	Trunk and upper extremities	**-ANA** negative	Morphea
12	M	29	Left forearm	Not available	Morphea
13	M	48	Abdomen	Not available	Morphea
14	M	36	Right knee	Not available	Morphea
15	M	26	Lower limb	Not available	Morphea
16	F	17	Left forearm and arm	**-RF** 29 IU/ml **-ANA** 1:640 C.speckled (0-1.2) **-Smith ab** negative **-CCP** 389 Ru/ml **- dsDNA** ab negative **-Scl70**	Morphea
17	F	70	Trunk	- **Scl70,histone,ANA,dsDNA** negative	Morphea
18	F	43	Lower abdomen and upper back	Not available	Morphea
19	F	16	Back	**-ANA** 1:40 C.speckled **-Rf** 16 IU/ml **-Compl 3** 1.59g/l(0.7-1.7) **-compl4** 0.23g/l (.18-.5) **-dsDNA** negative **-Scl70** pending	Morphea

20	F	51	Back and Extremities	Not available	Morphea
21	F	48	Abdomen	**-ANA,Scl70** negative	Morphea
22	F	55	Bilateral hands	Not available	Morphea
23	M	38	Right arm	**-ANA,Scl70** negative	Morphea
24	M	39	Trunk & thighs	Not available	Scleroderma
25	F	8	Abdomen	**-Scl70** 21(0-20) **-RNP** 79.2 (0-20) **-ANA** 1:80 DS (0-1.2) **-smith, SSA,SSB** negative	Morphea
26	F	22	Trunk	Not available	Morphea
27	F	30	Abdomen	Not available	Morphea
28	M	61	Upper back	Not available	Morphea
29	F	53	Right arm	**-RF** <9.38 **-ANA, dsDNA** negative **-CRP** 20.6 mgs/l	Morphea
30	M	31	Lower limbs	**-ANCA** 1:20 (0-1:40) **-ANA** 1:40 F.S+nuclear (0-1.2) **-IgA** 10.7g/l (0.9-4.5) **-dsDNA** negative	Morphea
31	F	50	Right flank	Not available	Morphea
32	F	39	Trunk and abdomen	**-ANA** 1:40 F speckled (0-1.2) **-RF** negative	Morphea
33	F	19	Left lower limb	Not available	Morphea
34	F	60	Upper back	**-RF** negative	Morphea
35	M	19	Scalp	Not available	Morphea
36	M	19	Let flank	Not available	Morphea
37	F	31	Left breast, left thigh and left forearm.	**-RF , ANA,dsDNa, Scl70** negative	Morphea
38	M	38	Left leg	Not available	Morphea
39	F	32	Left flank	**-RF , ANA, dsDNa, Scl70** negative	Morphea
40	F	41	Right hip and buttocks	**-ANA** 1:40 nuclear(0-1.2) -**Rf, CRP** negative	Morphea
41	F	27	Scalp	**-ANA** 1:640 homogenous (0-1.2)	Morphea
42	F	35	Upper abdomen	**-Ana, dsDNA** negative	Morphea
43	F	9	Right Forearm	**-ANA** 1:512 nuclear **-RNP, Scl70, dsDNA,SSA,SSB,Smith ab,dermatomyositis, histone** negative **- IgG,IgM,IgA,IgE** normal limits	Scleroderma

44	F	47	Right arm	**-ANA** 1:40 nuclear (0-1.2) **-Scl70, RF** negative	Morphea
45	F	37	Right leg	Not available	Morphea
46	F	73	Upper chest	Not available	Morphea
47	M	22	Right arm	Not available	Morphea
48	M	22	Back	Not available	Morphea
49	F	7	Left upper arm	**-RF,ANA,Smith ab,SSA,SSB,RNP,Scl70,dermatomyositis,dsDNa,Histone** negative	Scleroderma
50	F	23	Abdomen	**-ANA** 1:40 nuclear	Morphea
51	F	45	Left arm	**-ANA** 1:640 homogenous **-Scl70** 62IU/ml (0-20) **-RNP** 99 IU/ml (0-20) **-SSA** 117 IU/ml (0-20) **-SSB** 40 IU/ml (0-20) **-Smith ab,dsDNA ab** negative	Scleroderma
52	F	56	Lower limbs	**-Anticardiolipin IgM** 7 MPL/ML -**Anticardiolipin IgG** 32 (6-12) GPL/ML **-RNP** 21 (0-20) **-Rf,ANA,dsDNA,SSA,SSB,Scl70** negative **-Anticardiolipin ab IgA** negative **-Complement3** 2.34g/l(0.7-1.7) **-Complement4** 0.57g/l (0.18-0.5)	Morphea
53	F	36	Right shoulder	-**ANA** negative	Morphea
54	F	42	Left flank	-**ANA** 1:280 homogenous (0-1.2) -**Rf** 16 IU/ml	Scleroderma
55	M	23	Legs and Arms	Not available	Morphea
56	F	40	Neck	Not available	Morphea
57	F	30	Left leg and bilateral arms	Not available	Morphea
58	F	48	Abdomen	Not available	Morphea

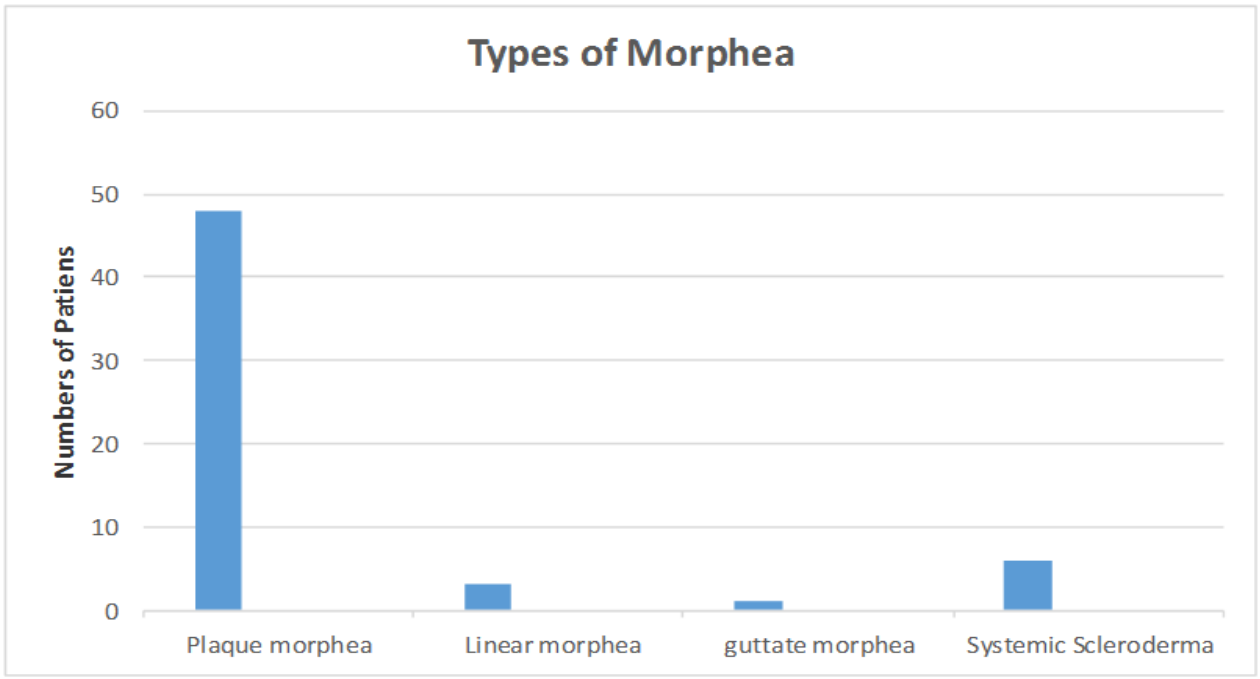

Figure 2: Types of morphea

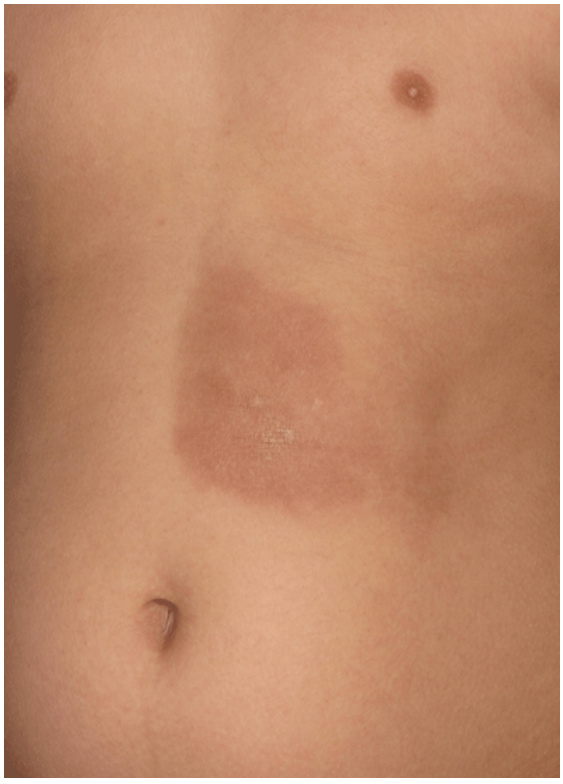

Figure 3: Localized plaque morphea

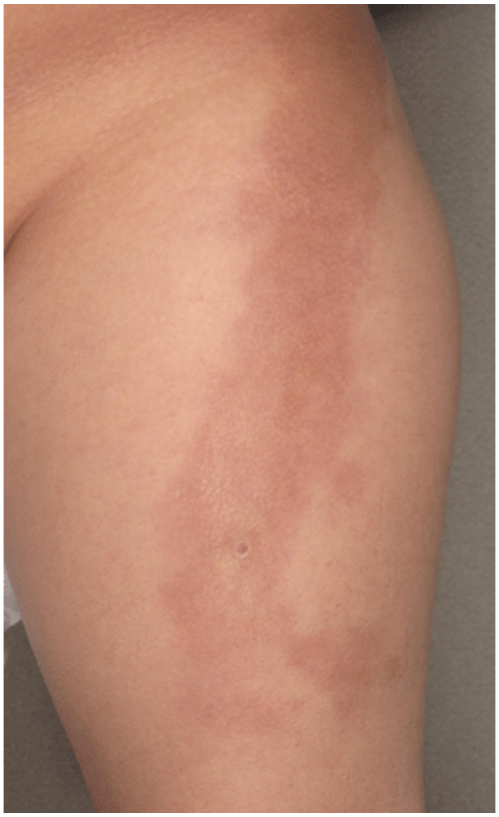

Figure 4: Linear morphea involving the left thigh

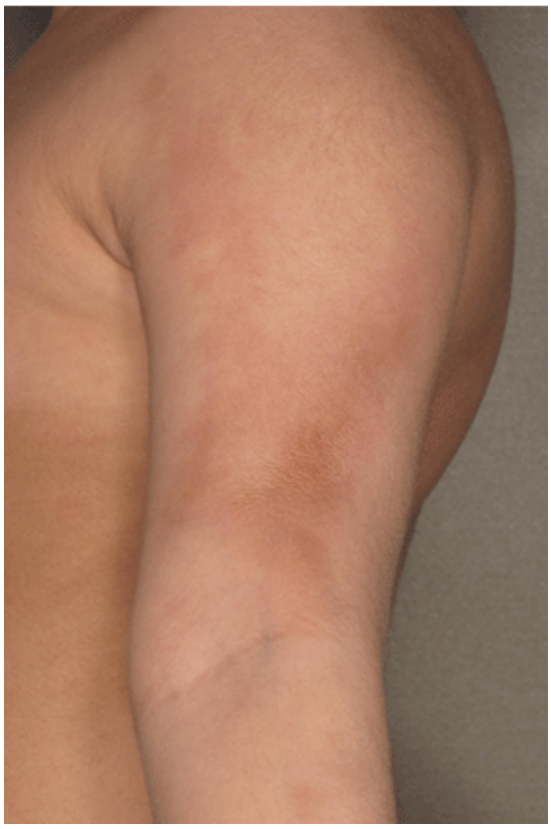

Figure 5: Plaque morphea in a 7-year-old child

Discussion

Scleroderma is a group of diseases in which there is deposition of collagen in the skin and sometimes other organs as well. When the disease limited to the skin and subcutaneous tissue, the term "morphea "is used. Morphea can also affect rarely the underlying fascia, muscles and bones. The presence of Raynaud's phenomenon and involvement of internal organs like lung and gastrointestinal tract allows separation of systemic sclerosis from morphea [1]. In small percentage of patients, skin sclerosis may lead to significant contractures or growth retardation, handicapping the affected individual for life, thus, prompt treatment is indicated [2].

Overproduction of collagen, particularly types I and III collagen, by fibroblasts in affected tissues is common to all forms of morphea. Three components are involved in the pathogenesis of morphea/scleroderma: vascular damage, lymphocyte activation, and altered connective tissue production. It has been proposed that endothelial cell damage may represent the initial step in morphea and systemic sclerosis. Early lesions are characterized by the influx of large amounts of mononuclear lymphocytes (usually activated T lymphocytes), histiocytes, eosinophils and plasma cells. There is inflammatory reaction in morphea patients (elevated ANAs, cytokines, and adhesion molecules). These cytokines (especially IL-4) upregulate transforming growth factor-β (TGF-β), initiating a cascade of events resulting in increased production of collagen and other extracellular matrix components via induction of connective tissue growth factor, platelet-derived growth factor, and matrix metalloproteinases [3,4].

Estimated incidence of morphea range from 0.5 to 2.7 per 100,000 with a female: male ratio of 2-3:1. In our study, the ratio was 1.5:1. The disease affects all ages; nonetheless, the peak incidence is seen between the ages of 20 and 40 years. Almost similar result was observed in Saudi Arabia. 20-30% of morphea begins in childhood.

The frequency of the different types varies between studies. This is possibly due to use of different classification systems. In our study, we used Laxer and Zulian's classification. One study revealed 56% of patients had plaque-type, 20% linear, 13% generalized, and 11% deep morphea. The most common pediatric subtype is linear morphea then En coup de sabre. In adults, circumscribed and generalized subtypes predominate. Deep morphea/morphea profunda is uncommon in both adults and children. The plaques of morphea most commonly develop on the trunk and are between 2 and 15 cm in diameter [5,6]. In our cases, plaque type was noted in most of the patients 83%. Linear morphea was seen in 5% while guttate type observed in one case.

The presence of ANA or antibodies to ssDNA and histones are unusual in patients with plaque-type morphea. They are more frequent in linear and generalized morphea, where ANA can be found in high titers in 40–80% of patients. About 40% of children and adolescents with morphea have elevated ANA titers [7]. In this study 26 patients were tested for ANA serology, 50% of them were positive.

The microscopic feature of morphea varies depending on the stage of the disease and the biopsy site. The peripheral border may show inflammatory cells, comprised chiefly of lymphocytes and plasma cells, located in the lower dermis and scattered in the interstitium. Initial collagen changes are seen in the lower part of the dermis and subcutaneous tissue, then later affect the whole of the dermis; they include thickened collagen bundles with diminished spaces among fibers. Morphea profunda shows thickened subcutaneous fibrous septae with mononuclear infiltrate mix with many plasma cells. Excessive sclerosis and hyalinization of connective tissue may involve the underlying fascia [8]. The histopathological features of our cases were almost similar to the previously investigated studies.

In Conclusion, Morphea is an inflammatory disease characterized by excessive dermal and subcutaneous collagen production. This is the first study investigating the clinical types of morphea in Saudi patients.

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