Acta Scientific PAEDIATRICS (ISSN: 2581-883X)

Volume 8 Issue 4 April 2025

Literature Review

Keloidal Morphea: A Systematic Review of The Literature

Mor Frisch[1], Noa Zur Aviran[1], Elena Didkovsky[2,3], Daniel Mimouni[1,2], Yael A Leshem[1,2], Omri Zidan[1] and Lihi Atzmony[4]*

[1]*Division of Dermatology, Rabin Medical Center, Petach Tikva, Israel*

[2]*Faculty of Medical and Health Sciences, Tel Aviv University, Tel Aviv, Israel*

[3]*Department of Pathology and Cytology, Rabin Medical Center, Petach Tikva, Israel*

[4]*Department of Dermatology, Yale School of Medicine, New Haven, CT, USA*

***Corresponding Author:** Lihi Atzmony, Department of Dermatology, Yale School of Medicine, New Haven, CT, USA.

Received: April 14, 2025

Published: April 25, 2025

Abstract

Background: Keloidal Morphea represents a rare and challenging variant within the spectrum of morphea and systemic sclerosis, characterized by keloid-like or hypertrophic scar like-nodules

Objective: We sought to assess the current evidence regarding keloidal morphea.

Methods: We conducted a systematic review of the literature available on PubMed, supplemented with four additional cases from Rabin Medical Center

Results: Our initial search yielded 812 results of whom, 52 reports met the inclusion criteria leading to a total of 69 cases. Keloidal morphea predominantly affects females (87%) and is most prevalent among individuals aged 30-50, with a notable prevalence in African Americans, highlighting a potential genetic predisposition to keloid formation in darker skin types. Keloidal morphea can occur alone or alongside systemic sclerosis, observed in 58% of the cases. The trunk and upper limbs are the most frequently involved areas. Both isolated and systemic sclerosis-associated keloidal morphea exhibit similar clinical and histological features, which suggests shared pathophysiological aspects. The complexity of these manifestations makes management challenging, with treatments ranging from steroids to phototherapy, yet often resulting in only modest improvements.

Limitations: Low quality of evidence, variability in the extent of data, lack of studies.

Conclusion: The presence of keloidal morphea in both isolated and systemic sclerosis contexts underscores the need for further research into its pathophysiology and treatment. This review aims to enhance understanding and guide future research efforts to improve the outcomes for keloidal morphea patients, emphasizing the importance of recognizing this condition in patients with systemic sclerosis and in populations with a predisposition to keloid development.

Keywords: Morphea; Keloid; Systemic Sclerosis; Scleroderma

Introduction/Background

Systemic sclerosis (SSc) is an autoimmune connective tissue disease of unknown etiology that affects the skin, blood vessels, and internal organs. The term "systemic sclerosis" is used to convey the systemic nature of the disease, which has two major clinical subtypes: cutaneous limited and cutaneous diffuse. Limited SSc is characterized by limited cutaneous sclerosis, while diffuse SSc is characterized by generalized cutaneous sclerosis [1].

Morphea, historically referred to as "localized scleroderma" or "circumscribed scleroderma", is characterized by circumscribed thickening and hardening of the skin resulting from autoimmune vascular changes, increased production of collagen, and extracellular matrix proliferation [2]. The histopathological features of morphea are indistinguishable from systemic sclerosis. Morphea has historically been subclassified based on clinical features to plaque-type, linear, generalized, and other less common variants such as deep, guttate, and profunda morphea [3-5].

Keloidal morphea (KM) is a rare variant of morphea, first reported by English physician Thomas Addison in 1854 [6]. Later on, in 1894, Unna named this condition "keloid-like scleroderma" [7]. The terms nodular morphea, KM, nodular scleroderma, and keloidal scleroderma have been used interchangeably without specific definitions. In addition to being a rare variant of morphea, this keloidal manifestation has been reported in systemic sclerosis. Previous studies did not specifically focus on differentiating between the systemic sclerosis and non-systemic sclerosis variants [8-13].

The aim of this systematic review was to evaluate the literature on KM and assess whether differences exist when it appears as part of systemic sclerosis versus as a standalone morphea.

Methods

We searched PubMed in March 2024 to identify all relevant English-language studies, regardless of publication status, or year of publication. The search strategy was (((morphea) OR (systemic sclerosis) OR (scleroderma)) AND ((keloid) OR (hypertrophic scar) OR (nodular) OR (nodule) OR (scar))).

Four cases of KM that were diagnosed and followed-up in Rabin Medical Center during 2003-2024 were added to the analysis.

Study selection criteria

Inclusion criteria

- **Language:** English
- **Relevance**: articles must have the term morphea or scleroderma or systemic sclerosis and also keloid or scar or nodule.
- **Study design:** Because of the anticipated low number of studies and lack of uniformity regarding disease definition, we elected to include all relevant published studies regardless of study design.

Exclusion criteria

Reviews or expert opinions that do not include specific case descriptions.

Study selection and data extraction

The titles and abstracts were screened by two authors (M.F. and N.Z.A.), who reviewed the full texts based on the eligibility criteria. Data were extracted onto an Excel (Microsoft, WA) extraction form, which included the fields shown in Table 1 and Supplementary Tables 1a, 1b, 2a, 2b. The publications were organized chronologically by their year of publication.

Study	Authors	Year	Article Type (No. of patients)
1	Li Yu [22]	2023	Case report (1)
2	Christina Marcelus [23]	2022	Case report (1)
3	Elena Castelli [24]	2021	Case report (1)
4	Fatma Hammarni [25]	2021	Case report (1)
5	Dongfung Yu [10]	2020	Case report (1)
6	Sahar Dadkhahfar [26]	2020	Case report (1)
7	Elena Campione [27]	2019	Case report (1)
8	Shinichi Nakazato [28]	2016	Case report (1)
9	Sama Kassira [14]	2015	Case report (1)
10	Daniel Torchia [29]	2015	Case report (1)
11	N.E Salmon [30]	2013	Case report (1)
12	El Khoury [31]	2012	Case report (1)

13	Hsien-Yi Chiu [32]	2011	Case report (1)
14	F.Kauer [33]	2009	Case report (1)
15	Kapil Jain [34]	2007	Case report (1)
16	Yoshinaga E [35]	2003	Case report (1)
17	Adrienne Rencic [8]	2003	Case Series (4)
18	J.Labandeira [36]	2003	Case report (1)
19	Sylvia Hsu [37]	1999	Case report (1)
20	Masahid Kubo [38]	1997	Case report (1)
21	C.Micalizzi [39]	1994	Case report (1)
22	Bettley FR [40]	1951	Case report (1)
23	RMC - CASE 1	2008	Our cases
24	RMC - CASE 2	2008	Our cases
25	RMC - CASE 3	2008	Our cases
26	RMC - CASE 4	2010	Our cases

Supplementary Table 1a: Studies Included in the systematic review: Morphea Group.

Study	Authors	Year	Article Type (No. of patients)
1	Kuzumi [41]	2024	Case report (1)
2	Sanchez NG [42]	2023	Case report (1)
3	Arghya Chattopadhyay [43]	2020	Case report (1)
4	Nina A. Richarz [11]	2020	Case Series (4)
5	Chutika Srisuttiyakorn [44]	2016	Case report (1)
6	David N. Lortscher [45]	2016	Case report (1)
7	Julia Spierngs [46]	2015	Case report (1)
8	Chayada Kokpol [47]	2015	Case report (1)
9	Barbara Stadler [48]	2013	Case report (1)
10	Moinzadeh P [49]	2013	Case report (1)
11	Sumit Sen [50]	2013	Case report (1)
12	Chika Ohata [12]	2013	Case report (1)
13	Candrice R. Heath [51]	2012	Case report (1)
14	Elizabeth N. LE [52]	2012	Case Series (2)
15	Wriston CC [53]	2008	Case Series (2)
16	Lucilla Melani [54]	2005	Case report (1)
17	Toshiyuki Yamamoto [55]	2005	Case Series (3)
18	Mittermayer Santiago [56]	2004	Case report (1)
19	Leander Cannick III [13]	2003	Case report (1)
20	Aviv Barzilai [21]	2003	Case report (1)
21	T.C Ling [9]	2003	Case report (1)
22	Adrienne Rencic [8]	2003	Case Series (2)

23	Hitoshi Mizutani [57]	1995	Case report (1)
24	James M Krell [58]	1995	Case report (1)
25	Toshiyuki Yamamoto [59]	1994	Case report (1)
26	Tetsuo Sasaki [60]	1992	Case report (1)
27	Jaime Perez-Wilson [61]	1992	Case report (1)
28	T A Akintewe [62]	1985	Case report (1)
29	Willian D James [63]	1984	Case Series (2)
30	Alan R. Cantwell [64]	1980	Case report (1)
31	Cameron Kennedy [65]	1979	Case report (1)

Supplementary Table 1b: Studies Included in the systematic review: SSc Group.

Case	Author (Year)	Type	Gender	Age	Ethnicity	Localization	Family or Personal history of Keloids	Pervious history of surgery or trauma
1	Li Yu/2023 [22]	case report	F	60	N/A	Trunk, upper limbs	no	N/A
2	Christina Marcelus/2022 [23]	Case report	F	27	N/A	Trunk, Lower limbs	N/A	N/A
3	Elena Castelli/2021 [24]	Case report	F	50	Caucasian	Trunk, Upper limbs	N/A	Yes
4	Fatma Hammarni/2021 [25]	Case report	F	52	N/A	Trunk	No	Yes
5	Dongfung Yu/2020 [10]	Case report	F	34	N/A	Trunk, Upper limbs, Lower limbs	N/A	N/A
6	Sahar Dadkhahfar/2020 [26]	Case report	F	54	N/A	Trunk, Upper limbs, Lower limbs	N/A	No
7	Elena Campione/2019 [27]	Case report	F	61	Caucasian	Lower limbs	N/A	No
8	Shinichi Nakazato/2016 [28]	Case report	F	42	Japanese	Upper limbs	No	No
9	Sama Kassira/2015 [14]	Case report	F	41	Afro-American	Trunk	N/A	N/A
10	Daniel Torchia/2015 [29]	Case report	F	18	Hispanic	Trunk, Upper limbs, Lower limbs	N/A	N/A
11	N.E Salmon/2013 [30]	Case report	F	11	Bangladeshi	Neck, Trunk, Upper Limbs, Lower Limbs	N/A	N/A
12	El Khoury/2012 [31]	Case report	M	16	N/A	Trunk	No	No
13	Hsien-Yi Chiu/2011 [32]	Case report	F	44	N/A	Trunk, Upper limbs	No	N/A
14	F.Kauer/2009 [33]	Case report	F	16	N/A	Trunk	No	No
15	Kapil Jain/2007 [34]	Case report	M	18	N/A	Lower limbs	No	No
16	Yoshinaga E/2003 [35]	Case report	M	45	Japanese	Trunk	no	N/A
17	Adrienne Rencic/2003 [8]	Case Series	F	41	Afro-American	Trunk	No	No

18	Adrienne Rencic/2003 [8]	Case Series	F	46	Afro-American	Trunk	N/A	N/A
19	Adrienne Rencic/2003 [8]	Case Series	F	50	Afro-American	Trunk, Upper limbs, Lower limbs	Yes	N/A
20	Adrienne Rencic/2003 [8]	Case Series	F	52	N/A	Trunk	Yes	No
21	J.Labandeira/2003 [36]	Case report	F	28	Caucasian	Trunk, Upper limbs, Lower limbs	No	No
22	Sylvia Hsu/1999 [37]	Case report	F	9	Afro-American	Trunk, Upper limbs	N/A	N/A
23	Masahid Kubo/1997 [38]	Case report	F	61	N/A	Face, Neck, Trunk	No	No
24	C.Micalizzi/1994 [39]	Case report	F	64	N/A	Trunk, Upper limbs	No	N/A
25	Bettley FR/1951 [40]	Case report	M	68	N/A	Trunk, Upper limbs	N/A	N/A
26	RMC - CASE 1	Our cases	F	54	Caucasian	trunk (bilateral breasts)	no	surgery (normal scar)
27	RMC - CASE 2	Our cases	F	67	Caucasian	trunk	no	yes
28	RMC - CASE 3	Our cases	F	53	Caucasian	trunk including breasts	no	no
29	RMC - CASE 4	Our cases	F	71	Caucasian	trunk, upper and lower limbs	no	no

Case	Author (Year)	Clinical Description	Histology	Abnormal Lab	ANA and titer	Treatments for skin lesions	Improvement yes/no
1	Li Yu/2023 [22]	multiple, infiltrated erythematous papules and plaques with sclerosis and tenderness	2 biopsies - nodular diffuse spindle cell infiltration with collagen hyperplasia and perivascular lymphocytic inflammation in the dermis. Negative CD34 and cytokeratin. Alcian blue staining positive for mucin. Verhoeff-Van Gieson - loss of elastin fibers.	N/A	1:320 (Pattern-N/A)	Mtx 7.5 mg weekly	N/A
2	Christina Marcelus/2022 [23]	Unilateral discrete nodules in a linear array – indurated. ivory colored plaque and multiple firm, tender, well-demarcated nodules in a linear distribution.	No. (1) Morphea, No. (2) inflammatory morphea showing dermal sclerosis with interstitial lymphoplasmacytic inflammation	Positive U1RNP antibodies.	Positive 1:80	Hydroxychloroquine- 400 mg/day X 3 months. Phototherapy UVA1 20 times	No
3	Elena Castelli/2020 [24]	multiple firm, linear or arciform, erythematous and slightly pigmented asymptomatic plaques of 2-3 cm in diameter and 2-3 cm in length	Thickened epidermis replacing subcutaneous fat, hypereosinophilic collagen bundles in papillary and reticular dermis	N/A	negative	N/A	N/A

4	Fatma Hammarni/2021 [25]	firm slightly itchy nodules	No. (1) morphea, No. (2) bundles of thick collagens in the dermis	N/A	Positive 1:640	Sulfasalazine	N/A
5	Dongfung Yu/2020 [10]	Annular plaques	marked fibrosis of mid to deep dermis with sparing of the papillary dermis, superficial and deep perivascular and peri eccrine lymphoplasmacytic inflammation	N/A	Positive greater than 1:1280 nuclear pattern	Oral steroids, TCS	yes
6	Sahar Dadkhahfar/2020 [26]	nodular lesions within the area of sclerosis	increased deposition of bundles of collagen extending from the mid-reticular dermis to the dermal-sub-cutaneous junction. Collagen bundles replaced adipocytes around the eccrine glans	N/A	N/A	Pulse methylprednisolone, Methotrexate, Cyclosporin, Intralesional Steroids	No
7	Elena Campione/2019 [27]	large, multinodular fibrotic skin lesions. Dermoscopy-white areas with high reflectance associated with dotted vessels on light erythematous background were detected	atrophy of the epidermis, a dense dermal sclerosis extended to a poor adipose tissue reaching the hypodermis, decreasing of lymphocytic peri adnexal infiltrate, few cells and large extracellular matrix deposits	increase of GGT, decrease of phosphorus and a decrease of serum vitamin D. ESR slightly elevated.	negative	Imiquimod 5%, Oral vitamin D	Yes (Imiquimod and vitamin D)
8	Shinichi Nakazato/2016 [28]	Linear band like skin induration with hyperpigmentation and skin atrophy. Nodules resembling hypertrophic scar were also noted.	No. (1) sclerotic skin and sclerotic collagen bundles in the dermis with mild perivascular infiltration of lymphocytes and plasma cells. Collagen bundles replaced adipocytes around eccrine gland and extended into the subcutis. reduction and atrophy of skin adnexa (morphea), No. (2) nodular lesion - hypocellular nodules in the deep dermis containing collagen fibers arranged in a haphazard manner, interspersed with plump fibroblasts (keloid)	N/A	negative	Intralesional Steroids, Oral tranilast, TCS	no
9	Sama Kassira/2015 [14]	dark brown indurated nodules with a slightly violaceous border with smaller hyperpigmented plaques. Hypertrophic, exophytic papule overlying a hyperpigmented plaque	Acanthotic epidermis with overlying basilar hyperpigmentation, dermis - proliferation of myofibroblasts and thickened collagen bundles. Lack of vertically oriented blood vessels and a lack of overlying epidermis	anti-RO LA - elevated.	Positive 1:1280	Methotrexate 17.5mg/week for 6 weeks	yes
10	Daniel Torchia/2015 [29]	segmental, sclero-atrophic, reddish, hyperpigmented, indurated plaque with small raised, pink, indurated nodules	Mainly broad, homogenous, eosinophilic, collagen bundles arranged in a haphazard pattern in the dermis.	N/A	negative	TCS, Oral steroids, Methotrexate, mycophenolate mofetil, Phototherapy	Yes (PUVA)

11	N.E Salmon/2013 [30]	Linear plaques	No. (1) -findings keeping with morphea. No. (2) further biopsies - a pattern of fibrosis that was more in keeping with scarring than with morphea.	mildly positive RF	negative	Oral steroids prednisolone 0.75mg/kg/day for 1 months	Yes (prednisolone)
12	El Khoury/2012 [31]	multiple well demarcated hyperpigmented indurated atrophic plaques. Within some skin-colored to hyperpigmened firm nodules were present, some of which in a linear pattern.	hypertrophic scar showing horizontal parallel collagen bundles, numerous plaques and perpendicularly oriented capillaries and a spars inflammatory infiltrate adjusted to area showing fetures of scleroderma. Diffuse dermal hyalinization on the collagen bundles, entrapment of the eccrine coils.	N/A	N/A	N/A	N/A
13	Hsien-Yi Chiu/2011 [32]	several irregularly shaped, firm nodules with hyperpigmentation and induration	Consistent with a diagnosis of keloid formation except for the presence of peri eccrine lymphocytic infiltration	N/A	negative	Multiple treatments (not specifying)	no
14	F.Kauer/ 2008 [33]	multiple progressive morpheic skin lesions	No. (1) Morpheic lesion - orthokeratosis, acanthosis, perivascular infiltrate of inflammatory cells, mostly lymphocytes and some plasma cells. the bundles of collagen were partially thickened hypereosinophilic and in parallel orientation. No. (2) Keloidal lesion - nodular dermal tumor and overlying epidermis with orthokeratosis and irregular acanthosis. In the dermis thickened and curly bundles of collagen parallel to the skin surface with many small vessels and discrete lymphocytic infiltrates.	Slightly elevated blood sedimentation	negative	TCS, IV Penicillin G 10 mega for 10 days, Crème-PUVA cumulative dose 2.32 J/cm^2	Yes (Penicillin, PUVA)
15	Kapil Jain/ 2007 [34]	multiple, firm nodules within the area of induration.	No. (1) classic histologic features of morphea. No. (2) hyalinized thick collagen bundles in the papillary dermis with abundant mucin throughout the reticular dermis consistent with morphea with dermal mucinosis	Leukocytosis with eosinophilia and raised ESR	negative	Oral steroids	No
16	Yoshinaga E/2003 [35]	discrete erythematous nodules on the breast, abdomen and upper arm. The lesion was elevated and sclerotic. On the fingers small firm papules and plaques.	thickened dermis extended to the subcutaneous fat and collagen fibers in the mid to lower dermis markedly homogenized. In the deep dermic whirl like pattern of collagen and atrophy of appendages elastic fibers in the dermis were decreased.	slightly abnormal lever function. Positive RF	N/A	N/A	N/A
17	Adrienne Rencic/2003 [8]	7X4 cm hyperpigmented, sclerotic, firm, tender keloidal plaque	Fibrosis of reticular dermis, perivascular lymphoid infiltrate, consistent with morphea	N/A	Positive titer 1:640	N/A	N/A

18	Adrienne Rencic/2003 [8]	multiple morpheaform plaques. keloid like nodules	Consistent with morphea	N/A	Positive titer 1:1280	N/A	N/A
19	Adrienne Rencic/2003 [8]	multiple large keloid-like nodules	Consistent with keloid	N/A	Positive titer 1:1560	N/A	N/A
20	Adrienne Rencic/2003 [8]	a large keloid	Consistent with keloid	N/A	Positive titer 1:640	N/A	N/A
21	J.Labandeira /2003 [36]	hemispherical papules. Plaques, nodules	Dermal sclerosis with thickened collagen bundles	N/A	Positive 1:100 homogenous pattern.	PUVA 4 time weekly, TCS, Topical Calcipitriol for 4 months	Yes (all of them)
22	Sylvia Hsu/1999 [37]	hyperpigmented, indurated papules and nodules in a linear distribution	sparse superficial and deep perivascular infiltrate of lymphocytes, compactly arranged collagen bundles in the upper part of dermis and abundant mucin throughout the dermis. To summery - morphea with no evidence of keloidal features.	N/A	N/A	N/A	N/A
23	Masahid Kubo /1997 [38]	irregularly pigmented sclerotic plaques nearly symmetrical Some of the lesions were elevated from the surrounding normal skin and appeared similar to keloid lesions	Thinned epidermis with basal pigmentation and a thickened dermis composed of overlying homogenized collagen fibers	N/A	negative	Oral Steroids for 50 week starting from 30mg/day to 12.5/day	yes
24	C.Micalizzi /1994 [39]	confluent plaques of sclerotic skin, some were skin-colored and others had an erythematous halo. In some of the plaques, particularly in the paravertebral region were papulo-nodular lesions.	No. (1) overlying homogenized collagen fibers and a moderate dermal perivascular mono-nuclear infiltrate, No. (2) thinned epidermis and thickened and homogenized collagen fibers with a band-like arrangement. the elastic fibers were fragmented in the upper dermis and absent in the mid and deep dermis	positive anti LA, weekly positive - anti RO, RNP, borrelia (were not considered significant).	Positive 1:160 speckled pattern	Penicillin, Doxycycline	No
25	Bettley FR/1951 [40]	ivory-colored nodules of firm consistency measuring 3-10 mm. some are elongated and tend to lie along the skin creases. Surrounded skin - normal	fibromatous type of collagen exhibiting massive hypertrophic bundles crossing in different directions containing many Spidle-shaped nuclei. Other findings compatible with scleroderma. mucin positive	N/A	N/A	N/A	N/A
26	RMC - CASE 1	on normal appearing skin sclerotic nodules, some arcuate, some figurative with hyperpigmented trail. Erythemal-brown color	Fibrosis in the papillary dermis with thickened collagen fibers. Perivascular infiltrates of lymphocytes, histocytes and plasma cells. Eccrine glands appear atrophic and trapped. negative for elastic fibers. mucin positive	normal autoimmune panel	normal	topical steroids	no

27	RMC - CASE 2	on both normal skin and linear surgical keloidal scar - sclerotic hyperpigmented nodules, some arcuate, some "horseshoe like", Erythemal-brown color	4 biopsies: First biopsy - in the upper dermis dilation of small blood vessels, in the middle and lower dermis thickened collagen fibers. Second biopsy - areas of keloids and adjacent areas of hypertrophic scar. Third biopsy - sclerosis of upper and middle dermis. thickened keloidal fibers, trapped adnexa with thickened dermis. negative for elastic fibers	normal autoimmune panel	normal	no	N/A
28	RMC - CASE 3	hyperpigmented nodules plaques and nodules, some arcuate, creating a large semi-annular ring on the lower abdomen	Thickened superficial and middle dermis, whorled collagen and fibroblasts. Sparse Lymphocytic perivascular infiltrate, perpendicular vessels compatible with scar and morpheic futures	normal autoimmune panel. Anti Borrelia antibodies - negative	normal	MTX, PUVA	no improvement
29	RMC - CASE 4	violet-brown plaques and nodules resembling Kaposi sarcoma, more prominent in lower limb while standing	few biopsies : findings in some compatible with LSA, and some with nodular scar. Thickened collagen fibers, normal adnexa. normal elastic staining	Anti-cardiolipin IgM: elevated (intermittently), Lupus anticoagulant: elevated (single test), Remaining autoimmune panel: normal. Borrelia antibodies – 5 times within 15 months: always IgM positive, IgG negative, without seroconversion (false positive results)	normal	TCS MTX 15 MG once weekly with tapering to 7.5 mg once weekly	mild improvement

Supplementary Table 2a: Morphea Group Characteristics.

Case	Author (Year)	Type	Gender	Age	Ethnicity	Localization	Family or Personal history of Keloids	Pervious history of surgery or trauma
1	Kuzumi/2024 [41]	case report	F	68	N/A	Trunk, upper limbs	N/A	N/A
2	Sanchez NG/2023 [42]	case report	F	27	Hispanic	trunk	no	no
3	Arghya Chattopadhyay/2020 [43]	Case report	M	47	N/A	Trunk	No	No
4	Nina A. Richarz/2020 [11]	Case Series	F	53	Caucasian	Trunk, Upper limbs	N/A	N/A
5	Nina A. Richarz/2020 [11]	Case Series	F	49	Caucasian	Trunk	N/A	N/A
6	Nina A. Richarz/2020 [11]	Case Series	F	25	Caucasian	Trunk	N/A	N/A
7	Nina A. Richarz/2020 [11]	Case Series	F	46	Caucasian	Trunk	N/A	N/A
8	Chutika Srisuttiyakorn/2016 [44]	Case report	F	50	N/A	Neck, Trunk	No	No
9	David N. Lortscher/2016 [45]	Case report	F	53	N/A	Trunk	N/A	No
10	Julia Spierings/2015 [46]	Case report	M	76	N/A	Trunk, Upper limbs	N/A	N/A
11	Chayada Kokpol/2015 [47]	Case report	F	63	N/A	Neck, Trunk	N/A	No
12	Barbara Stadler/2013 [48]	Case report	F	44	Afro-American	Neck, Trunk	N/A	N/A
13	Moinzadeh P/2013 [49]	Case report	F	50	N/A	Trunk, upper limbs	N/A	N/A
14	Sumit Sen/2013 [50]	Case report	F	26	N/A	Trunk, Upper limbs	No	N/A
15	Chika Ohata/2013 [12]	Case report	F	67	Japanese	Lower limbs	No	No
16	Candrice R. Heath/2012 [51]	Case report	F	13	Afro-American	Face, Neck, Trunk, Upper and lower limbs	N/A	No
17	Elizabeth N. LE/2012 [52]	Case Series	F	70	N/A	Neck, Trunk, Upper and lower limbs, Buttocks	N/A	N/A
18	Elizabeth N. LE/2012 [52]	Case Series	F	45	N/A	Neck, Trunk	No	No
19	Wriston CC/2008 [53]	Case Series	M	51	N/A	trunk	N/A	No
20	Wriston CC/2008 [53]	Case Series	F	30	N/A	Trunk, Upper limbs, Lower limbs	N/A	N/A
21	Lucilla Melani/2005 [54]	Case report	F	22	N/A	Neck, Trunk, Lower limbs	N/A	N/A
22	Toshiyuki Yamamoto/2005 [55]	Case Series	M	29	N/A	Trunk, Upper limbs	No	N/A
23	Toshiyuki Yamamoto/2005 [55]	Case Series	M	34	N/A	Trunk	No	N/A
24	Toshiyuki Yamamoto/2005 [55]	Case Series	F	60	N/A	Trunk	No	N/A
25	Mittermayer Santiago/2004 [56]	Case report	F	39	N/A	Neck, Trunk, Upper limbs	N/A	N/A

26	Leander Cannick III/2003 [13]	Case report	M	40	Afro-American	Trunk, Upper limbs	No	N/A
27	Aviv Barzilai/2003 [21]	Case report	F	62	N/A	Face (behind ears), Upper limbs,	No	No
28	T.C Ling/2003 [9]	Case report	F	53	N/A	Trunk	N/A	N/A
29	Adrienne Rencic/2003 [8]	Case Series	F	54	Caucasian	Trunk, Upper limbs	N/A	No
30	Adrienne Rencic/2003 [8]	Case Series	F	17	Arab	Trunk	N/A	No
31	Hitoshi Mizutani/1995 [57]	Case report	F	40	N/A	Trunk	No	No
32	James M Krell/1995 [58]	Case report	F	40	N/A	Neck, Trunk, Upper limbs	N/A	N/A
33	Yamamoto/1994 [59]	Case report	F	66	N/A	Trunk	no	N/A chemical exposure to silica
34	Tetsuo Sasaki/1992 [60]	Case report	F	44	N/A	Trunk	N/A	No
35	Jaime Perez-Wilson/1992 [61]	Case report	F	42	Caucasian	Trunk, Upper limbs	No	No (surgery in a different spot - normal looking linear scar)
36	T A Akintewe/1985 [62]	Case report	F	17	Nigerian	Neck, Trunk. Upper limbs	No	N/A
37	Willian D James/1984 [63]	Case Series	M	24	N/A	trunk, upper limbs	No	No
38	Willian D James/1984 [63]	Case Series	F	17	Caucasian	Trunk	Yes	N/A
39	Alan R. Cantwell/1980 [64]	Case report	M	66	N/A	Neck, Trunk, Upper limbs	N/A	N/A
40	Cameron Kennedy/1979 [65]	Case report	F	46	N/A	Lower limbs	N/A	N/A

Case	Author (Year)	Clinical Description	Histology	Abnormal Lab	ANA and titer	Treatments for skin lesions	Improvement yes/no
1	Kuzumi/2024 [41]	symmetrically distributed, numerous firm nodules on the chest, shoulders and upper arms,	dermal fibrosis with thickened collagen bundles and mild perivascular infiltration	positive Anti-topoisomerase	1:2560 (Speckled)	N/A	N/A
2	Sanchez NG/2023 [42]	on both normal and sclerotic skin, multiple (25-30) non-tender, firm. Hyperpigmented, well-circumscribed nodules, largest was 4.5 cm.	dermal fibrosis with haphazardly arranges thickened and compact collagen bundles with loss of interfibrillar space, sclerotic appearance and loss of adnexal structures.	N/A	N/A	N/A	N/A
3	Arghya Chattopadhyay/2020 [43]	multiple irregular elevated pinkish brown scars with pseudopod-like extensions, enlarging and hardening suggestive of a keloid	mild acanthosis with maintained rete ridges in the epidermis, upper epidermis with haphazardly arranged thick collagen bundles indicating keloid. Lower dermis arranged myofibroblasts and small interspersed capillaries, indicating scleroderma.	N/A	N/A	N/A	N/A

4	Nina A. Richarz/2020 [11]	firm exophytic nodules	dense collagen bundles resembling a hypertrophic scar	N/A	Positive (no titer) speckled	N/A	N/A
5	Nina A. Richarz/2020 [11]	Firm hyperpigmented nodules	Morphea-like sclerosis with septal distribution and mild inflammatory infiltrate	Positive anti RO	Positive (no titer) nucleolar	N/A	N/A
6	Nina A. Richarz/2020 [11]	mildly, firm, hyperpigmented plaques	dense collagen bundles with a mild perivascular inflammatory infiltrate consistent with morphea	N/A	Positive (no titer) speckled	N/A	N/A
7	Nina A. Richarz/2020 [11]	firm plaques and nodules over normal skin having the appearance of spontaneous keloids	morphea-like parallel collagen bundles in the upper dermis and aberrant enlarged collagen bundles resembling a keloid in the lower dermis	N/A	Positive (no titer) speckled	N/A	N/A
8	Chutika Srisuttiyakorn/2016 [44]	multiple asymptomatic papules	Thick sclerotic collagen fibers in the mid dermis	positive anti SCL70	Positive 1:320 homogenous pattern	N/A	N/A
9	David N. Lortscher /2016 [45]	symmetrically distributed hyperpigmented indurated annular plaques with raised borders	2 biopsies- increased deposition of collagen bundles extending from the mid reticular dermis to the dermal subcutaneous junction. marked increase in spindles fibroblasts within the fibrous tissue	anemia and moderate renal insufficiency,	Positive 1:640 anti-centromere pattern.	Intralesional Steroids	No
10	Julia Spierings/2015 [46]	multiple firm nodules some grouped and some disseminated	thick sclerotic patches of dense collagen bundles and loss of adipose tissue around the exocrine glands	N/A	N/A	N/A	N/A
11	Chayada Kokpol/2015 [47]	numerous well - circumscribed asymptomatic flesh-colored firm papules and nodules ranging from 2 to 20 mm in diameter	2 biopsies - homogenized collagen bundles with scattered plump fibroblasts in the lower reticular dermis.	positive anti SCL 70	negative	Intralesional Steroids (triamcinolone 5 to 10 mg/ml at 4 to 8 week interval), TCS	yes
12	Barbara Stadler/ 2013 [48]	numerous nodular lesions 2-3 cm in diameter not painful	2 biopsies - epidermis with acanthosis and hyperpigmentation at basal layer. Reticular dermis has increased thickness and sclerosis of collagen bundles. Collagen fibers exhibit parallel distribution. A discrete perivascular inflammatory process. Entrapment of eccrine glands and nerves. elastic fibers are seen.	N/A	Positive above 1:640 fine speckled pattern	Intralesional Steroids, systemic steroids, Methotrexate and phototherapy	No (injections) N/A for others

13	Moinzadeh P/2013 [49]	within sclerotic Skin more than 50 subcutaneous nodules in 8-10 mm averaged diameter.	Thickened collagen bundles in part hyalinized, in part irregularly distributed, and an unobtrusive papillary dermis. Extramodular areas appeared less fibrotic with low cell density, dense collagenous matrix with lympho-histiocytic infiltrates mainly surrounding blood vessels. Masson's trichrome - reduced number of elastic fibers only within nodules. Mucin - negative.	Positive SCL 70	positive (titer N/A)	N/A	N/A
14	Sumit Sen/2013 [50]	Flat itchy swellings - could clinically be diagnosed as keloids and also 2 small, non-itchy nodules	No. (1) - suggestive of keloid though it did not have the whorled pattern characteristic of keloid, No. (2) - hyperkeratosis, acanthosis and increased pigmentation of the basal layer. Dermal collagen is increased. features were suggestive of nodular scleroderma.	N/A	Positive 1:40 speckled pattern.	N/A	N/A
15	Chika Ohata/2013 [12]	Several red hard nodules 2 to 5 cm in size and some with subcutaneous indurations	No. (1) - effacement of rete ridges, sclerosis and marked telangiectasia in the upper part of dermis with no adnexa and closely spaced thick bundles of collagen organized parallel to the epidermis in the lower part of dermis. No. (2) - spaced thick bundles of collagen aligned along the long axis of septa in the subcutis	N/A	Positive 1:1280, speckled pattern	Intralesional Steroids,oral tranilast, D -penicillamine	No
16	Candrice R. Heath/2012 [51]	several keloidal scars arising in areas of previously normal-appearing skin	after revision - findings of nodular or keloidal-type scleroderma	N/A	Positive 1:1280 nuclear pattern	Intralesional Steroids, TCS	yes
17	Elizabeth N. LE/2012 [52]	numerous firm, fixed, skin colored nodules on from 0.5 to 1 cm symmetrically	Increased sclerotic, thickened wavy collagen fibers with increased number of admixed stellate spindled fibroblasts that spared the papillary dermis bur extended into the deep dermis with replacement of the subcutaneous fat	N/A	N/A	Surgical removal	Yes (hypopigmented scars)
18	Elizabeth N. LE/2012 [52]	multiple firm, fixed hyperpigmented dermal nodules up to 1 cm	increased wavy sclerotic collagen deposition with an increased number of admixed stellate spindle fibroblasts that spared the papillary dermis and extended into the deep dermis with replacement of subcutaneous fat. Beneath the nodule - thickened sclerotic collagen bundles that lacked an associated increased number of fibroblasts - typical scleroderma	N/A	N/A	hydroxychloroquine	no
19	Wriston CC/2008 [53]	multiple, firm, hyperpigmented, raised, well circumscribed nodules and plaques	dermal fibrosis with thickened keloidal collagen bundles. Hyalinized dermal collagen bundles were also present. Dermal sclerosis extended into the subcutaneous tissue and was evident between adipocytes. features of both scleroderma and keloid	N/A	N/A	Intralesional Steroids (10 mg/ml) every 6 weeks for 4 months	No

20	Wriston cc/2008 [53]	multiple indurated hyperpigmented papules and plaques	keloidal collagen only	N/A	Positive 1:2560	Intralesional Steroids (10 mg/ml) every 6 weeks for 6 months, TCS	Yes
21	Lucilla Melani/2005 [54]	multiple firm, raised, nontender, intensely red hyperpigmented nodules, well circumscribed and confluent (ranging 0.5 - 6 cm)	Thickened dermis with fibrous proliferation and a marked cellular fibroblaststic component, that extended to subcutaneous fat	U3-RNP ab and anti HCV, anemia, increased ESR and CRP,	Positive (no titer)	Steroids (not specifying how)	No
22	Toshiyuki Yamamato/2005 [55]	Nodular lesions	Dense deposition of thickened collagen bundles in the thickened dermis	N/A	Positive 1:160 speckled	N/A	N/A
23	Toshiyuki Yamamato/2005 [55]	a few firm hyperpigmented papules and nodules	Thickened collagen bundles in the dermis	N/A	Positive 1:2560	N/A	N/A
24	Toshiyuki Yamamato/2005 [55]	nodular changes	Dermal sclerosis with acellular thickened collagen bundles in the dermis to subcutis	Anti topoisomerase 1 and anticentromere - positive	Positive 1:1280, homogenous speckled pattern.	N/A	N/A
25	Mittermayer Santiago/2004 [56]	diffuse thickening with numerous indurated, non-tender well demarcated keloidal plaques measuring up to 12 cm in main diameter	2 biopsies compatible with scleroderma	N/A	Positive 1:40 speckled	D-penicillamine, azathioprine	No
26	Leander Cannick III/2003 [13]	discrete, irregular, hypertrophic plaques resembling keloids. Induration and keloidal nodules	No (1)- minimal superficial perivascular inflammatory cell infiltrate and fibrosis within the dermis consistent with SSC. No (2)- broad brightly eosinophilic collagen bundles typical of keloid	N/A	negative	N/A	N/A
27	Aviv Barzilai/2003 [21]	red linear and firm plaques, looking like keloids	Reticular dermis thickened by a linear fibrous proliferation, composed mainly of eosinophilic normal-appearing collagen fibers. Within the fibrous tissue, spindle and plump fibroblasts. Pure resemblance to a scar - parallel arrangement of the fibrous proliferation, the appearance of the collagen bundles and increased myofibroblasts	weakly positive anticentromere antibody test which turned negative when twice repeated	negative	N/A	N/A
28	T.C Ling/2003 [9]	nodules over sites of preexisting scleroderma	acellular, fibrous material in the dermis	Positive anti Ds-DNA anticentromere and anticardiolipin	Positive 1:10000 speckled	TCS, topical Calcipitriol, PUVA	Yes (PUVA)

29	Adrienne Rencic/2003 [8]	numerous flesh colored 3-10 mm nodules with normal surrounding skin	thick sclerotic collagen bundles in discrete fascicles consistent with keloid	N/A	Positive 1:1280 fine speckled and homogenous	N/A	N/A
30	Adrienne Rencic/2003 [8]	keloidal lesions on back, Discrete tender hyperpigmented plaques with telangiectasias and pseudopod-like extensions	Nodular dermal fibrosis with focal thickening, glassy eosinophilic collagen, plump fibroblasts, consistent with morphea	Anti-Ku antibody Creatine kinase 246	Positive 1:2560	N/A	N/A
31	Hitoshi Mizutani/1995 [57]	linear tender nodules	No (1)- In the mid dermis significantly thick collagen bundles proliferated in a whorl-like patten around vessels in a hematoxylin eosin section. fibrous nodules demarcated from dermal tissue. The upper and deep collagen bundles with a moderate thickness distributed in parallel to the epidermis, sandwiching the mid dermal whorl-like nodule. No (2)- density and thickness of collagen bundles in the nodule were decreased and highly compacted collagen in a concentric pattern in comparison to the first biopsy. reduces cells around vessels.	mild eosinophilia, gammaglobulinemia 22%, positive anti SCL-70,	Positive (no titer) speckled	5 years of TCS, D-penicillamine	Yes (TCS, D-penicillamine)
32	James M Krell/1995 [58]	hundreds of flesh to brown colored minimally tender firm nodules from 2 mm to 2 cm predominantly in areas not involved with cutaneous sclerosis. dusky sclerotic plaques.	No (1)- features of scleroderma. No (2) - diffuse sclerosis of dermal collagen with blunting of the dermal - subcutaneous interface. There we no hyalinized collagen fibers typical of keloids. sparse lymphocytic infiltrates in the deep reticular dermis.	hematocrit 30%, WBC 12.7, PLT 501, urea 41, creatinine 1.7, EST 55,	Positive 1:11280 speckled pattern.	Penicillamine	No
33	Yamamoto/1994 [59]	nodular scleroderma within an area of non-sclerotic skin: Numerous, reddish-brown, pea-sized nodules within non-sclerotic skin of the abdomen	Thick, hyalinized collagen bundles throughout the dermis. Silica was not identified with polarized light.	High levels of serum IGE, normal CBC. High ESR. Positive DS-DNA ab, SCL 70, RNP. Decreased creatinine clearance	positive 1:40,960 (Speckled)	N/A	N/A
34	Tetsuo Sasaki/1992 [60]	5 keloidal nodules	Nodular fibrosis in the mid dermis which consisted of fibroblastic cells and collagen fibers, mostly parallel to the skin surface.	positive RF, serum gamma globulin slightly increased.	Positive 1:80	D-penicillamine 200 mg/day	no
35	Jaime Perez-Wilson/1992 [61]	Multiple firm, raised, non-tender, well circumscribed papulo-plaques and nodules, 2-3 cm diameter	4 biopsies- thickened dermis with a fibrous proliferation that extended to the subcutaneous fat. Increased number of spindle cells and multiple disoriented collagen bundle, sometimes running parallel to the surface of the skin. In some specimens thick, homogenized and hyalinized collagen adopting a whirl-like pattern. A marked reduction of elastic fibers and atrophy of appendages.	N/A	Positive 1:40 speckled pattern.	N/A	N/A

36	T A Akintewe /1985 [62]	widespread hyperpigmented keloidal lesions	sclerotic features consistent with scleroderma	N/A	N/A	Oral steroids	N/A
37	Willian D James/ 1984 [63]	numerous firm hyperpigmented papules and plaques	widening of dermis by extension of fibrous tissue into the subcutaneous fat, trapping and atrophy of adnexal structures and a perivascular infiltrate of lymphocytes, histiocytes and plasma cells in the mid and deep dermis extending focally into the subcutaneous fat. focally withing the mid dermis were nodular areas with increased number of spindle cells, increased mucin, neovascularization, disorientation of collagen bundles in a whorl-like pattern and centrally broad hyalinized acellular fibrosis	N/A	Positive 1:640 nuclear pattern	N/A	N/A
38	Willian D James/ 1984 [63]	hard nodules within areas of thickened skin	N/A	N/A	Positive 1:640 speckled pattern	Systemic steroids	No
39	Alan R. Cantwell/ 1980 [64]	numerous, firm, raised, well-circumscribed asymptomatic nodules that averaged 1 cm in diameter	six skin bunch biopsy- consistent with scleroderma. Areas of mild edema of the upper dermis were seen, thickened dermis with thickened collagen bundles parallel to the epidermis, sometimes in a "whirling" pattern. The junction of the subcutaneous fat and dermis was focally flattened and areas of collagen in the upper subcutaneous fat. thickened walls of some blood vessels, atrophy and absence of the sebaceous glands and hair structures and a reduction in the number of sweat glands, which were surrounded by dense collagenous connective tissue, mild scattered perivascular and peri appendageal infiltrate compose of lymphocytes and histiocytes.	N/A	negative	N/A	N/A
40	Cameron Kennedy/1979 [65]	painless subcutaneous nodules 1-2 cm. These were not tender, partially fixed and freely movable	extensive areas of subcutaneous necrosis with fibrin deposition. At the periphery of this material was a scanty chronic inflammatory cell infiltrate surrounded by a zone of fibrosis. No evidence of vasculitis	N/A	Positive 1:100	D-penicillamine	N/A

Supplementary Table 2b: SSc Group Characteristics.

No- number, N/A data not available, Mtx- Methotrexate

Outcomes

- Clinical features of KM
  - Patient factors: Age, gender, medical history, splitting into two groups – KM with or without systemic sclerosis
  - Signs including location and morphology
  - Symptoms
  - The onset of morphea among patients with systemic sclerosis - was it before, after, or concurrent with systemic sclerosis?
- Histologic features of KM
- Treatment
  - Treatment modalities
  - Response to treatment
  - Duration of treatments and follow up

Data analysis

Data were combined at the aggregate level and presented using descriptive statistics. Continuous variables were reported as mean and standard deviation (SD).

Results

The search identified 812 citations (Figure 1). After reviewing titles and abstracts, 52 publications, all case reports/series met eligibility criteria for full-length review, encompassing 65 cases. Among these, 25 cases described morphea solely without SSc documentation (morphea group – Table 1a, supplement), while 40 cases described both morphea and systemic sclerosis (SSc group – Table 1b, supplement). In systemic sclerosis cases, four were limited, one was diffuse, and 35 were unspecified. Baseline characteristics for all patients are presented in Table 1. Tables 2a-2b (Supplementary Data) provide detailed information for each case**.**

Clinical features

Patient factors

The mean age of all cases was around 43 years, with 87% females. Among the patients, 8/43 (19%) were of Afro-American ethnicity.

Only 3/35 (9%) patients had a family or personal history of keloids, and 4/32 (13%) patients had a previous history of surgery or trauma at the affected site.

The mean age and female predominance were similar in the morphea and SSc groups: age of 43 vs. 44 and female predominance of 86% vs. 80%, respectively.

Family or personal history of keloids was observed in 2/18 (11%) patients in the morphea group compared to 1/17 (6%) patient in the SSc group.

Previous history of surgery or trauma at the affected site was present in 4/16 (25%) patients in the morphea group, compared to none in the SSc group.

Signs including location and morphology

Localization

The trunk was the most common site in both groups, observed in 62/69 (90%) patients (table 1). In the subgroup analysis, which incorporated both textual descriptions and clinical images, chest involvement was noted in 33 out of 69 cases (48%). Specifically, breasts were affected in 38% (11 out of 29) of cases in SSc group, compared to 10% (4 out of 40) in morphea group.

Morphology

The clinical presentation was similar in both groups. Lesions were keloid-like nodules on normal appearing skin or on top of sclerotic areas. lesions were either annular or elongated plaques or round nodules/infiltrated papules. The color varied from skin-colored to ivory, erythematous and dark brown. The size ranged from few millimeters in diameter to more than 10 centimeters. Skin lesions varied in number from discrete and several to multiple.

Among cases with breast involvement in morphea group and SSc group, 50% and 45% respectively, exhibited annular patterns. In our cases, two out of three cases involving the breasts displayed annular and arcuate patterns.

Symptoms

Itch was frequent in the SSc group (61%) while experienced in only 16% of the morphea group. Other symptoms such as pain, burning sensation were similarly distributed in both groups.

Morphea onset

Among the SSc patients with the known timing, KM appeared before SSc in 1/35 (3%) case, a childhood case. In 11/35 (31%)

cases it accrued together, in 23/35 (65%) cases KM appeared after SSc.

Histologic features

The histological characteristics were similar in both groups and are outlined in Supplementary Tables 2a and 2b. In general, some samples showed classic morphea features without keloidal features, some demonstrated a mixture of keloid scar and morphea features and some were described as "keloid".

Key histologic features include:

- Perivascular and perieccrine infiltrates of lymphocytes, eosinophils, plasma cells, and mast cells.
- Thickened collagen bundles oriented parallel to the dermal-epidermal junction.
- Atrophic eccrine glands trapped within the thickened dermis.
- Keloid-like features such as haphazardly arranged thick collagen bundles and reduced elastic fibers.

Most cases did not undergo special staining. Among those that were stained, some showed a decreased number of elastic fibers, while others exhibited a preserved number. Staining for mucin revealed the absence of mucin in some cases, while others exhibited abundant mucin throughout the dermis. Some cases did not specify the histological findings and only mentioned descriptions such as consistent with morphea or scleroderma, consistent with keloid or keloidal collagen, sclerosis, morphea-like sclerosis, or a mixture of keloid and morphea findings.

Treatment

Treatment modalities

Many therapeutic interventions have been reported (table 1).

The mean number of treatments was 0.97 ± 1.17, with the most common being topical steroids, systemic steroids and intralesional steroids.

The mean number of prior treatments in the morphea group was 1.24 ± 1.24 and 0.77 ± 1 in the SSc group. While most common treatments in the morphea group were topical steroids (37%), systemic steroids (31.5%), and phototherapy (26%), the most common treatments in the SSc group were intralesional steroids (37%), D-penicillamine (31.5%), topical steroids (26%), and systemic steroids (22%).

Response to treatment

Some degree of improvement in lesions was observed in 9/19 (47%) patients in morphea group and in 6/16 (38%) patients in SSc group. Overall, any positive clinical response was classified as improvement (Supplementary tables 2a and 2b). However, it is important to note that the observed improvements were mostly modest, with some lesions appearing softer in texture and flattened to some extent compared to the beginning of the therapy. Among the entire cohort, 15/35 (43%) patients showed any improvement in their lesions.

Treatments that achieved some measures of improvement were topical steroids, intralesional steroids, oral steroids, MTX, IV Penicillin G, PUVA, Surgical removal Imiquimod and oral vitamin D.

Duration of treatments

Data regarding the duration of follow-up was available for only 10/25 (40%) patients in the morphea group and 4/40 (10%) patients in the SSc group. The mean follow-up durations were 21 ± 54.31 months and 1.7 ± 6.5 months, respectively.

	Morphea group (n* = 29)	Systemic sclerosis group (n* = 40)	All patients (n*=69)
Characteristics	No. of patients (%)	No. of patients (%)	No. of patients (%)
Age (Years)	43.2 ± 18	44.12 ± 16.65	43.74 ± 17.3
Female	25/29 (86%)	32/40 (80%)	57/69 (87%)
Afro-American	5/29 (17%)	3/14 (21%)	8/43 (19%)
Family or Personal history of Keloids	2/18 (11%)	1/17 (6%)	3/35 (9%)
Previous history of surgery or trauma at the affected sites	4/16 (25%)	0/16 (0%)	4/32 (13%)
Localization of Involvement			

Face (including behind ears)	1/29 (3%)	2/40 (5%)	3/69 (4%)
Neck	2/29 (7%)	11/40 (28%)	13/69 (19%)
Trunk	25/29 (86%)	37/40 (93%)	62/69 (90%)
Upper limbs	14/29 (48%)	18/40 (45%)	32/69 (46%)
Lower limbs	10/29 (35%)	6/40 (15%)	16/69 (23%)
Buttocks	0/29 (0%)	1/40 (3%)	1/69 (1%)
Symptoms			
Itch	2/12 (16%)	11/18 (61%)	13/40 (33%)
Pain	1/12 (8%)	1/18 (6%)	2/30 (7%)
Burning	1/12 (8%)	1/18 (6%)	2/30 (7%)
Abnormal Capillaroscopy	1/8 (13%)	5/7 (71%)	6/15 (40%)
Positive ANA (≥1:40)	11/24 (46 %)	29/33 (88%)	40/57 (70%)
No. of Treatments	1.24 ± 1.24 (n= 19 patients)	0.77 ± 1 (n=19 patients)	0.97 ± 1.17 (n= 38 patients)
Topical Steroids	7/19 (37%)	5/19 (26%)	12/38 (32%)
Intra Lesional Steroids	2/19 (11%)	7/19 (37%)	9/38 (24%)
Systemic Steroids	6/19 (32%)	4/19 (21%)	10/38 (26%)
Phototherapy	5/19 (26%)	2/19 (11%)	7/38 (18%)
D-penicillamine	0/19 (0%)	6/19 (32%)	6/38 (16%)
Methotrexate	6/19 (32%)	1/19 (5%)	7/38 (18%)
Penicillin	2/19 (11%)	0/19 (0%)	2/38 (5%)
Hydroxychloroquine	1/19 (5%)	1/19 (5%)	2/38 (6%)
Mycophenolate Mofetil	1/19 (5%)	0/19 (0%)	1/38 (3%)
Surgical Removal	0/19 (0%)	1/19 (5%)	1/38 (3%)
Topical Calcipitriol	1/19 (5%)	1/19 (5%)	2/38 (6%)
Imiquimod	1/19 (5%)	0/19 (0%)	1/38 (3%)
Oral Tranilast	1/19 (5%)	1/19 (5%)	2/38 (6%)
Oral Vitamin D	1/19 (5%)	0/19 (0%)	1/38 (3%)
Sulphasalazine	1/19 (5%)	0/18 (0%)	1/38 (3%)
Doxycycline	1/19 (5%)	0/19 (0%)	1/38 (3%)
Cyclosporin	1/19 (5%)	0/19 (0%)	1/38 (3%)
Azathioprine	0/19 (0%)	1/19 (5%)	1/38 (3%)
Outcome of Treatment			
Any Improvement of lesions	9/19 (47%)	6/16 (38%)	15/35 (43%)

Table 1: Baseline characteristics of patients.

No. number, Data are presented as number and percent or mean and standard deviation.

* In cases where data were missing, n was smaller reflecting only cases with available data.

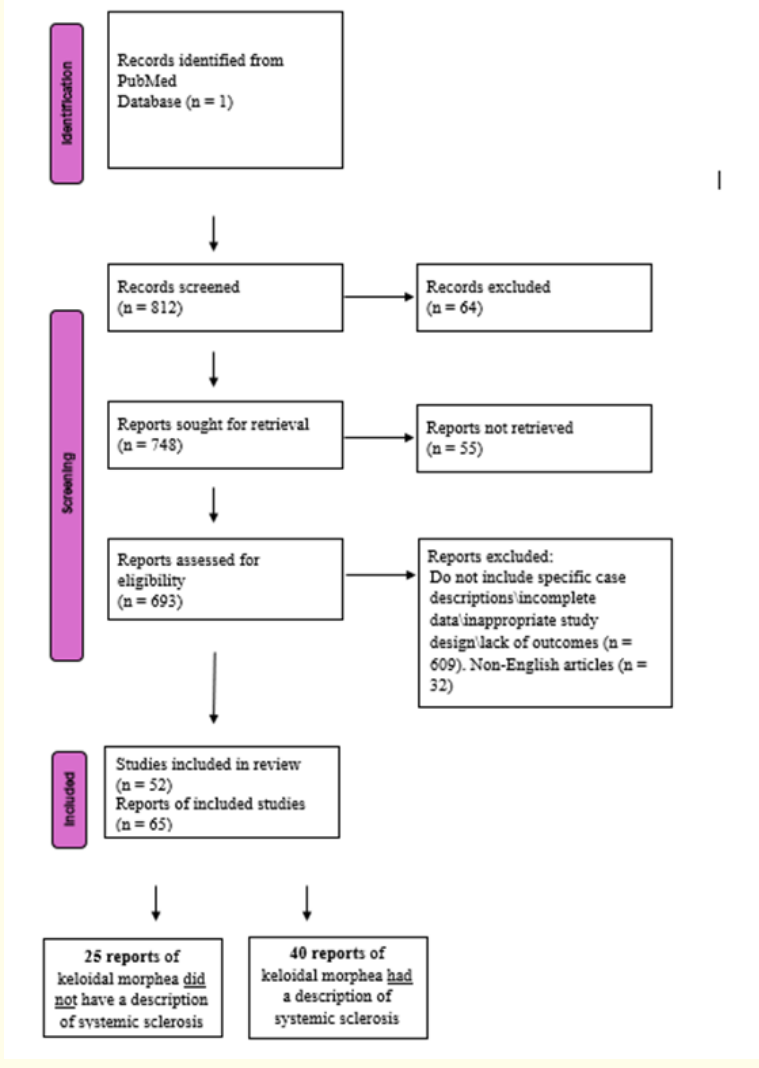

Figure 1: PRISMA flow diagram

Discussion

This systematic review consolidates and analyzes existing literature on KM, a rare variant within the spectrum of morphea and SSc characterized by keloid-like nodules or hypertrophic scars. Altogether, the aggregated data shows that KM predominantly affects females with a significant portion of patients being African American [14]. Although the age range of affected individuals spans from childhood to old age, the highest occurrence was in individuals aged 30-50, particularly in their forties. As in keloids without morphea or SSc, the trunk was the most commonly involved site, followed by the upper limbs.

It is notable that a subset of patients with SSc also exhibit characteristics of morphea. Published studies report that morphea occurs in approximately 3.6 to 6.7% of SSc patients [15,16]. In our analysis, we categorized the patients into two groups: those with and without SSc. Both groups showed similar clinical and histological features, indicating that systemic involvement does not significantly change the skin manifestations of KM. This suggests that KM in SSc patients represents a form of morphea, particularly in those prone to keloid or hypertrophic scar formation.

In the SSc group KM lesions typically developed either concurrently with or shortly after the onset of systemic symptoms with one patient developing KM lesions before the diagnosis of SSc. This temporal relationship emphasizes the importance of monitoring skin changes in systemic sclerosis patients to ensure timely intervention, potentially mitigating the progression and impact of KM.

Hypertrophic scars and keloids have a higher prevalence in individuals with darkly pigmented skin, including Africans and African Americans, with reported incidences between 4% to 16% [17,18], compared to a prevalence of 1% to 5% in Caucasian populations [19]. Similarly, the incidence of SSc among Black individuals is approximately 2.5 times that observed in Whites, quantified at 20 cases per million per year versus 8 cases per million per year [20]. Despite these findings, our literature review revealed no studies directly comparing the incidence of morphea in African Americans with that in Caucasians. Our data show that 17% of the patients in the morphea group and 21% in the SSc group were African American. This observation supports the hypothesis of a genetic predisposition that influences the higher incidence of these conditions in this population, akin to the predisposition observed in keloid formation without morphea.

The review indicated that histologically, KM exhibits characteristics of morphea, sometimes accompanied by signs of keloids or hypertrophic scars. However, some reports lack detailed histological descriptions, merely noting that the findings were consistent with "morphea" or "keloid". Barzilai et al. introduced a continuum hypothesis suggesting a range with nodular morphea or nodular scleroderma at one end (nodules that histologically resemble scleroderma) and KM or keloidal scleroderma at the other (nodules that histologically resemble keloids), with keloid-like scleroderma in between (nodules that histologically resemble hypertrophic scars) [21]. Another explanation for the variation in histological features among different samples may be due to differences in the age of the lesion or the site from which the sample was taken.

It is notable that the reported number of treatments for patients with morphea exceeded those for SSc. This discrepancy could be due to the fact that treatment data was available for less than 50% of the patients with SSc and for two-thirds of patients with morphea. Given that it is highly unlikely that SSc patients received no treatment, it is reasonable to infer that systemic treatments may have been underreported in the SSc group, rather than not utilized at all. Furthermore, the extensive range of treatment modalities described for KM reflects the challenges in finding effective therapy for the keloidal form of morphea.

Limitations

The primary limitation of this review is the variability in the extent and quality of data across the included case reports. Many cases lacked comprehensive follow-up information, limiting the ability to draw definitive conclusions about long-term outcomes and treatment efficacy. The lack of standardized outcome assessment instruments for keloidal morphea further hinders the ability to assess severity and treatment response.

Conclusion

This systematic review highlights the complex clinical and histologic features of KM, a rare and challenging variant of morphea. The similarities between isolated and systemic sclerosis-associated KM call for a unified approach in diagnosis and management. Clinicians should consider KM in the differential diagnosis of nodular skin lesions, particularly in patients with SSc. Long-term follow-up studies are essential to better understand the natural history of this condition and identify predictors of treatment response and disease progression. By consolidating existing knowledge, this review aims to enhance clinical awareness and guide future research efforts, ultimately improving the management and outcomes of patients with KM.

Funding

No sources of funding were used to conduct this study or prepare this article.

Conflict of Interest

Mor Frisch, Lihi Atzmony, Noa Zur Aviran, Elena Didkovsky, Yael A Leshem, Omri Zidan and Daniel Mimouni have no conflicts of interest that are directly relevant to the content of this article.

Ethics Approval

Not applicable.

Consent to Participate

Not applicable.

Availability of Data and Material

Not applicable.

Code Availability

Not applicable.

Author Contributions

All authors contributed to the gathering and writing of this article. L.A. and M.F. designed the study and wrote the first draft of the manuscript. M.F. and N.Z.A. collected and organized the information for this study. M.F. analyzed the gathered data. L.A., Y.A.L., E.D., O.Z., and D.M. revised the paper and provided important insights critical to its final version.

Bibliography

1. Sobolewski P., *et al*. "Systemic sclerosis - multidisciplinary disease: clinical features and treatment". *Reumatologia* 57.4 (2019): 221-233.

2. Bolognia JL., *et al*. "Dermatology". 4th ed., (2018): 693-721.

3. Fett NM. "Morphea (localized scleroderma)". *JAMA Dermatology* 149.9 (2013): 1124.

4. Sartori-Valinotti JC., *et al*. "Updates on morphea: role of vascular injury and advances in treatment". *Autoimmune Disease* 2013 (2019): 467808.

5. Mayes MD. "Classification and epidemiology of scleroderma". *Seminars in Cutaneous Medicine and Surgery* 17.1 (1998): 22-26.

6. Addison T. "On the Keloid of Alibert, and on True Keloid". *Medico Chirurgical Transactions* 37 (1854): 27-47.

7. Unna P. "Die histopathologie der hautkrankheiten". edn. berlin, hirchwald, (1894): 1119.

8. Rencic A., *et al*. "Keloid morphea and nodular scleroderma: two distinct clinical variants of scleroderma?" *Journal of Cutaneous Medicine and Surgery* 7.1 (2003): 20-24.

9. Ling TC., *et al*. "Keloidal scleroderma". *Clinical and Experimental Dermatology* 28.2 (2003): 171-173.

10. Yu D., *et al*. "Morphea With Keloidal Features: A Case Report and Review of the Literature". *American Journal of Dermatopathology* 42.10 (2020): 766-768.

11. Richarz NA., *et al*. "A review of the clinically distinguishing features of nodular or keloidal scleroderma in systemic sclerosis". *Australas Journal of Dermatology* 61.2 (2020): e269-e273.

12. Ohata C., *et al*. "Nodular morphea (NM report of a case of concurrent NM and morphea profunda associated with limited type systemic sclerosis, and overview and definition for NM". *European Journal of Dermatology* 23.1 (2013): 87-93.

13. Cannick L., *et al*. "Nodular scleroderma: case report and literature review". *Journal of Rheumatology* 30.11 (2003): 2500-2502.

14. Kassira S., *et al*. "Keloidal Scleroderma: Case Report and Review". *Case Reports in Dermatological Medicine* 2015 (2015): 635481.

15. Toki S., *et al*. "Clinical and laboratory features of systemic sclerosis complicated with localized scleroderma". *Journal of Dermatology* 42.3 (2015): 283-287.

16. Soma Y., *et al*. "Coexistence of morphea and systemic sclerosis". *Dermatology* 186.2 (1993): 103-105.

17. Alster TS and Tanzi EL. "Hypertrophic scars and keloids: etiology and management". *American Journal of Clinical Dermatology* 4.4 (2003): 235-243.

18. English RS and Shenefelt PD. "Keloids and hypertrophic scars". *Dermatology Surgery* 25.8 (1999): 631-638.

19. Knowles A., *et al*. "Keloids and Hypertrophic Scars". *Dermatology Clinics* 41.3 (2023): 509-517.

20. Mayes MD., *et al*. "Prevalence, incidence, survival, and disease characteristics of systemic sclerosis in a large US population". *Arthritis Rheumatology* 48.8 (2003): 2246-2255.

21. Barzilai A., *et al*. "Keloid-like scleroderma". *American Journal of Dermatopathology* 25.4 (2003): 327-330.

22. Li Y., *et al*. "Nodular and diffuse spindle cell infiltration in keloidal scleroderma: a case report". *Frontiers in Medicine (Lausanne)* 10 (2023): 1291941.

23. Marcelus C., *et al*. "Questions raised by a case of adult-onset linear nodular scleroderma". *Dermatology Online Journal* 28.5 (2022).

24. Castelli E., *et al*. "Nodular morphea keloidal type: A rare case with paradigmatic histopathology significantly accompanied by a flawless surgical scar". *Journal of Cutaneous Pathology* 48.11 (2021): 1329-1334.

25. Hammami F., *et al*. "Atypical Keloidal Morphea". *Skinmed* 19.2 (2021): 132-133.

26. Dadkhahfar S., *et al*. "Development of keloidal morphea after treatment with cyclosporine in a case of recalcitrant generalized morphea". *Clinical Case Report* 8.5 (2020): 837-839.

27. Campione E., *et al*. "Nodular morphea in a patient with Steinert disease". *Italian Journal of Dermatology and Venereology* 154.2 (2019): 209-210.

28. Nakazato S., *et al*. "Nodular morphoea: a first case associated with linear morphoea". *European Journal of Dermatology* 26.1 (2016): 95-96.

29. Torchia D and Schachner LA. "Superimposed segmental morphea with keloidal features". *International Journal of Dermatology* 54.8 (2015): 944-945.

30. Salmon NE., *et al*. "Keloid-like morphoea". *Clinical and Experimental Dermatology* 39.1 (2014): 90-91.

31. El Khoury J., *et al*. "Indurated hyperpigmented plaques with overlying fibrotic nodules in an adolescent boy". *Pediatrics Dermatology* 29.1 (2012): 111-112.

32. Chiu HY and Tsai TF. "Images in clinical medicine. Keloidal morphea". *The New England Journal of Medicine* 364.1 (2011): 4 e28.

33. Kauer F., *et al*. "Nodular morphea". *Dermatology* 218.1 (2009): 63-66.

34. Jain K., *et al*. "Blaschko linear nodular morphea with dermal mucinosis". *Archives of Dermatology* 143.7 (2007): 953-955.

35. Yoshinaga E., *et al*. "Acrokeratoelastoidosis associated with nodular scleroderma". *European Journal of Dermatology* 13.5 (2003): 490-492.

36. Labandeira J., *et al*. "Polymorphic fibrosing reaction mimicking keloidal scleroderma but without associated classic scleroderma". *Dermatology* 207.2 (2003): 204-205.

37. Hsu S., *et al*. "Nodular morphea in a linear pattern". *International Journal of Dermatology* 38.7 (1999): 529-530.

38. Kubo M., *et al*. "Keloidlike morphea". *Acta Dermato-Venereologica* 77.1 (1997): 90-91.

39. Micalizzi C., *et al*. "Morphoea with nodular lesions". *British Journal of Dermatology* 131.2 (1994): 298-300.

40. BETTLEY FR. "Progressive symmetrical sclerodermia with sclerodermatous nodules". *Proceedings of the Royal Society of Medicine* 44.7 (1951): 573-575.

41. Kuzumi A., *et al*. "Extensive keloidal morphea in a patient with systemic sclerosis". *American Journal of Medical Sciences* 367.5 (2024): e58-e59.

42. Sanchez NG., *et al*. "Nodular (keloidal) scleroderma". *Rheumatology Clinics (Engl Ed)* 19.8 (2023): 463-464.

43. Chattopadhyay A., *et al*. "Keloidal Morphea: Clinical Picture". *Journal of Clinical Rheumatology* 26.6 (2020): e178-e179.

44. Srisuttiyakorn C and Aunhachoke K. "Scleroderma with Nodular Scleroderma". *Case Reports on Dermatology* 8.3 (2016): 303-310.

45. Lortscher DN., *et al*. "Nodular Scleroderma Revisited: Systemic Sclerosis Presenting as Annular Keloidal Sclerotic Plaques". *Journal Of Clinical And Aesthetic Dermatology* 9.6 (2016): 56-57.

46. Spierings J., *et al*. "Nodular Scleroderma". *Arthritis Rheumatology* 67.12 (2015): 3157.

47. Kokpol C., *et al*. "Nodular scleroderma in a patient with chronic hepatitis C virus infection: a coexistent or causal infection?" *Cutis* 96.2 (2015): E19-22.

48. Stadler B., *et al*. "Systemic sclerosis with keloidal nodules". *Anais Brasileiros de Dermatologia* 88.6 (2013): 75-77.

49. Moinzadeh P., *et al*. "Systemic sclerosis with multiple nodules: characterization of the extracellular matrix". *Archives of Dermatology* 305.7 (2013): 645-652.

50. Sen S., *et al*. "Keloids in scleroderma-keloidal scleroderma: a unique entity. Indian *Journal of Dermatology* 58.2 (2013): 153-154.

51. Heath CR., *et al*. "Nodular scleroderma presenting as multiple spontaneous keloidal scars". *Journal of the American Academy of Dermatology* 66.6 (2012) e245-246.

52. Le EN., *et al*. "Nodular/keloidal scleroderma: acquired collagenous nodules in systemic sclerosis". *Journal of Rheumatology* 39.3 (2012): 660-661.

53. Wriston CC., *et al*. "Nodular scleroderma: a report of 2 cases". *American Journal of Dermatopathology* 30.4 (2008): 385-388.

54. Melani L., *et al*. "A case of nodular scleroderma". *Journal of Dermatology* 32.12 (2005): 1028-1031.

55. Yamamoto T., *et al*. "Nodular scleroderma: increased expression of connective tissue growth factor". *Dermatology* 211.3 (2005): 218-223.

56. Santiago M., *et al*. "Keloidal scleroderma". *Clinical Rheumatology* 23.1 (2004): 50-51.

57. Mizutani H., *et al*. "Nodular scleroderma: focally increased tenascin expression differing from that in the surrounding scleroderma skin". *Journal of Dermatology* 22.4 (1995): 267-271.

58. Krell JM., *et al*. "Nodular scleroderma". *Journal of the American Academy of Dermatology* 32.2 (1995): 343-345.

59. Yamamoto T., *et al*. "Nodular scleroderma in a worker using a silica-containing abrasive". *Journal of Dermatology* 21.10 (1994): 751-754.

60. Sasaki T., *et al*. "Nodular scleroderma in systemic sclerosis under D-penicillamine therapy". *Journal of Dermatology* 19.12 (1992): 968-971.

61. Perez-Wilson J., *et al*. "Nodular (keloidal) scleroderma". *International Journal of Dermatology* 31.6 (1992): 422-423.

62. Akintewe TA and Alabi GO. "Scleroderma presenting with multiple keloids". *British Medical Journal (Clin Res Ed).* 291.6493 (1985): 448-449.

63. James WD., *et al*. "Nodular (keloidal) scleroderma". *Journal of the American Academy of Dermatology* 11.6 (1984): 1111-1114.

64. Cantwell AR Jr., *et al*. "Nodular scleroderma and pleomorphic acid-fast bacteria". *Archives of Dermatology* 116.11 (1980): 1283-1290.

65. Kennedy C and Leigh IM. "Systemic sclerosis with subcutaneous nodules". *British Journal of Dermatology* 101.1 (1979): 93-96.