Localized scleroderma and related comorbidities: a single centre cohort study

Running head: Localized scleroderma in Finland

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Ethics statement: The permission for this study was obtained from the hospital district of Southwest Finland (T287/2021-1). This study was a non-interventional retrospective study without direct patient contact and according to Finnish legislation, no patient consent or ethical committee approval was needed.

Patient consent: Not applicable.

What is already known about this topic?

- Morphea is a rare autoimmune skin disease with varying severity.
- Treatment options vary and may include topical or oral medications, as well as phototherapy depending on the specific subtype of disease.
- Concomitant autoimmune diseases are common.

What does this study add?

- Our results indicate that thyroid autoimmune diseases are the most common concomitant autoimmune diseases
- We found no evidence of an increased risk of malignancies in patients with morphea.
- A significant number of patients required multiple treatment approaches.
- The incidence of morphea remained stable throughout the study period.

Abstract

Background Localized scleroderma, or morphea is a rare autoimmune disease that affects the skin and underlying tissue. It is more common in females than males. The incidence has two peaks, one in childhood and another in middle-age. Concomitant autoimmune diseases are frequently observed, whereas systemic sclerosis occurs rarely simultaneously.

Objectives This study aimed to assess the clinical features, comorbidities, and treatments of localized scleroderma in Southwest Finland.

Methods Patients diagnosed with localized scleroderma (ICD-10 code L94) treated between January 1, 2005 and November 30, 2020, were identified from the hospital discharge register of Turku University Hospital. Diagnoses were classified into five main types and their subtypes based on the European Dermatology Forum (EDF) criteria. Basic demographic data, associated comorbidities, treatments used, and their efficacy were collected.

Results A total of 155 patients with morphea were included, with 125 females (80.6%) and 30 males (19.4%). The most common subtype was limited, plaque-type morphea (n=71, 45.8% of all patients), followed by the generalized type (n=57, 36.8%). Fifty-nine concomitant autoimmune diseases were identified in 45 patients (29.0%), most frequently autoimmune thyroid diseases (n=23, 14.8%). Simultaneous systemic sclerosis was rare (n=3, 1.9%). The most common malignancy was breast cancer (n=11, 7.1%). Extracutaneous manifestations were more common in pediatric-onset patients (18.5%) than in adult-onset patients (1.7%). The most commonly used systemic treatment was methotrexate (n=25, 16.1%) which was beneficial for 64% of treated patients. Phototherapy was administered to 63 patients (40.6%) and it was beneficial for 49 patients (77.8%).

Conclusions Patients with morphea at our centre often required systemic immunomodulatory treatment or phototherapy. The incidence of the generalized subtype and the occurrence of concomitant autoimmune diseases, particularly thyroid autoimmune diseases, were relatively high. No evidence of an increased risk of malignancy was observed among these patients.

Introduction

Localized scleroderma, or morphea, is an autoimmune condition that affects the skin and underlying tissues. Estimated incidence rates range from 0.4 to 2.7 per 100,000 inhabitants.[1-3] The disease is more prevalent in females than in males, with a female-to-male ratio of 6:1.[4] Incidence peaks occur in childhood and middle age.[3,5,6] Patients with pediatric-onset disease have a higher risk of recurrence.[5] Concomitant autoimmune diseases are common.[3,7] Differential diagnoses include especially extragenital lichen sclerosus (LS)[8] and radiation dermatitis.

Extracutaneous manifestations are common in pediatric-onset morphea. In a large study of 750 children with localized scleroderma, extracutaneous involvement was observed in 22.4% of cases.[9] Of these patients, 18.4% presented with a single manifestation, while 4.0% exhibited multiple manifestations. Articular involvement, such as arthritis, occurred in 47.2% of patients with extracutaneous manifestations.[9]

In 2017, the European Dermatology Forum (EDF) proposed, and subsequently updated in 2024, a classification system for localized scleroderma[2] based on German guidelines published in 2016.[10] According to EDF guidelines eosinophilic fasciitis is considered a separate entity. The five main categories of morphea are limited, generalized, linear, deep and mixed type.[2]

The aim of our study was to assess the clinical features and associated comorbidities of localized scleroderma and the efficacy of the various treatments in Southwest Finland.

Patients and methods

Patients

Adult and pediatric patients with a diagnostic ICD-10 code L94 for localized scleroderma, appearing at least once in their medical records between January 1, 2005 and November 30, 2020, were identified from the hospital discharge register of Turku University Hospital, a tertiary care centre serving the approximately 480,000 inhabitants of Southwest Finland. The annual population data were obtained from Statistics Finland.[11] The incidence was calculated based on the annual number of patients in relation to the population within the hospital's catchment area. Most visits took place at dermatology or pediatric outpatient clinics. Patient records were reviewed retrospectively by two authors (NH and SK). Cases involving other connective tissue disorders, incorrect diagnoses, or typographical errors were excluded.

Using the EDF classification criteria, diagnoses were categorized into five main types and their subtypes. Incidence rates were calculated for four-year intervals from 2005 to 2020. Data on extracutaneous manifestations were collected, along with basic demographic data such as age at disease onset, gender distribution, and systemic sclerosis (SSc)-related symptoms (e.g. Raynaud´s phenomenon). Information on skin biopsy results, autoantibody profiles, *Borrelia burgdorferi* antibody status, comorbidities, and treatments was also collected. A titer cut-off value of 320 was used to determine ANA–antibody positivity. Treatment efficacy was evaluated by reviewing electronic health records, based on clinicians' judgement. All study data were collected and managed using REDCap electronic data capture tools hosted at the University of Turku.[12,13]

Statistics

Statistical analyses are described in Supplementary material (Appendix S1).

Ethical considerations and study permissions

This was a non-interventional retrospective study without direct patient contact. According to Finnish legislation, no patient consent or ethical committee approval was needed. Permission for the study was obtained from the hospital district of Southwest Finland (permission number: T287/2021-1).

Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work the authors used ChatGPT-4o in order to revise the language during the final editing the manuscript. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

Results

Demographics

A total of 155 patients with a diagnosis of morphea were included in the study. Figure 1 presents the distribution of the main disease types and their subtypes. The majority of patients, n=125, (80.6%) were female, resulting in female-to-male ratio of 4.2:1. The female predominance was more pronounced among adult-onset patients compared to pediatric-onset patients, with female-to-male ratios of 4.5:1 and 3.3:1, respectively. The frequency of different subtypes differed between pediatric-onset and adult-onset patients ($\chi^2(3) = 50.85$, $p<0.0001$. However, no individual subtype was statistically significantly more common in either group (Table S1).

The median age at diagnosis was 50.0 years [IQR 19.0, 64.0]. For pediatric patients, the median age at diagnosis was 9.0 years [IQR 5.0, 14.0], whereas for adults it was 56.5 years [IQR 37.0, 67.0]. The distribution of age at disease onset and gender is shown in Figure 2. Most patients (n=117, 75.5%) had

adult-onset morphea, while 38 (24.5%) had pediatric-onset. For six patients, the age at diagnosis was unavailable; of these three diagnoses were made during childhood.

Histopathological findings from skin biopsies were available for 139 subjects, with diagnoses based on current international criteria for morphea. In sixteen patients without histological confirmation, biopsies were not performed in twelve due to a clinically evident diagnosis: six had generalised morphea, three limited, and three linear. Diagnosis was made by a dermatologist in six cases, a rheumatologist in one, and was undocumented in five. For four patients diagnosed at another hospital, biopsy status was unknown; two had linear and two had generalised morphea.

During the years 2005-2020, the annual incidence of morphea varied from 0.43 and 2.32 per 100,000 inhabitants with a mean annual incidence of 1.62 per 100,000 inhabitants (SD=4.8). When the mean annual incidence rates were grouped into four-year periods 2005-2008, 2009-2012, 2013-2016 and 2017-2020, the incidence rates were 1.53, 1.39, 1.79 and 1.77 per 100,000 inhabitants, respectively. No statistically significance differences were observed between these periods, and no increasing trend in incidence was identified.

Autoimmune diseases

Fifty-nine concomitant autoimmune diseases were diagnosed in 45 patients, representing 29.0% of all patients (Table 1). Autoimmune thyroid diseases were particularly common, with 23 cases. These were mainly diagnosed prior to the diagnosis of morphea (83%), whereas other autoimmune diseases could be diagnosed at any time (Table S2). Lichen sclerosus (LS) was the second most frequent concomitant autoimmune disease, with ten cases (Table S3). All patients had genital LS, and two also presented with extragenital involvement. Both of these patients had limited morphea. In all cases, the diagnoses of morphea and LS were confirmed by skin biopsy. Nine cases of rheumatoid arthritis (RA) were

observed, all in females. Among these, four patients had seronegative RA and three had seropositive RA. Two patients with a prior diagnosis of RA from decades earlier lacked immunological data. Patients with concomitant autoimmune diseases were predominantly those with adult-onset of morphea, although three pediatric-onset morphea cases were also noted. The difference between concomitant autoimmune diseases in adult-onset versus pediatric-onset patients was statistically significant ($\chi^2(1) = 5.38$, $p=0.0204$). Among the pediatric-onset patients, one was diagnosed with autoimmune hepatitis in childhood (at age 13), while two others were diagnosed with autoimmune conditions (SLE and Sjögrens syndrome) in adulthood. Among patients with concomitant autoimmune diseases, 43 were female and two were male, a difference that was statistically significant ($\chi^2(1) = 8.90$, $p=0.0028$). Three patients (1.9%) had limited cutaneous systemic sclerosis (lcSSc) (Appendix S2). Two of these patients had SSc diagnosed prior to developing morphea, and one was diagnosed afterward. Two of the three patients with both conditions exhibited Raynaud´s phenomenon and abnormalities in nailfold capillaroscopy. Overall, 19 patients (12.3%) experienced Raynaud´s phenomenon. Nailfold capillaroscopy (S3) was performed for 17 patients, of whom seven had Raynaud´s phenomenon. Abnormalities were detected in three patients, all of whom had Raynaud´s phenomenon. The morphea types associated with concomitant autoimmune disease included 27 plaque-type (38% of all plaque-type patients), 16 generalized type (27.6%), one guttata type (100%) and one en coup de sabre (14.3%). The difference between these groups was statistically significant ($\chi^2(3) = 10.11$, $p=0.0176$).

Autoantibodies and *Borrelia burgdorferi*

Autoantibodies were analysed in 140 patients, of whom 86 (61.4%) tested negative for autoantibodies. Antinuclear antibodies (ANA) were detected in 44 patients (29.5% of those tested). The majority of ANA-positive patients (66.7%) exhibited low titres (640 or below). ANA-positivity was more common in children than in adults, with rates of 48.2% versus 25.4% ($\chi^2(1) = 5.49$, $p=0.0191$). Only two patients

tested positive for anti-histone antibodies (AHA) or anti-DNA antibodies. Five patients were positive for anti-SSA/Ro, two for rheumatoid factor (RF) or anti-RNP, and one for ANCA, anti-centromere, anti-SSB, anti-Ku 72/86, or anti-PM-Scl 75– antibodies with some patients having multiple autoantibodies. ANA were more frequent in pediatric-onset patients (48.2%) than in adults (25.4%) ($\chi^2(1) = 5.4927$, p=0.0191). There were no statistically significant differences in the occurrence of any of these autoantibodies based on disease subtype, gender or the presence of concomitant thyroid autoimmune disease or LS.

Antibodies for *Borrelia burgdorferi* were analysed in 103 patients, with only three (2.9%) testing positive with low titers. In two patients, skin biopsies examined by PCR to detect *Borrelia burgdorferi* ruled out a local cutaneous infection as the cause of skin symptoms. One patient, who had a high titer of *Borrelia burgdorferi* antibodies, was treated with antibiotics for erythema migrans prior to the skin biopsy and the PCR test was negative. All three patients were treated with antibiotics, but none experienced improvement in morphea lesions.

Malignancies

Twenty-seven cases of malignancy were identified in 23 patients, representing 14.8% of the total patient cohort (Table 2). The median age at cancer diagnosis was 62 years and 1 month [IQR 58.3, 70.9]. Four patients were male (13.8% of all male patients) and 19 were female (15.4% of all female patients); this difference was not statistically significant. Only one case of malignancy, occurred in a pediatric-onset morphea patient, a metastatic adenocarcinoma, likely originating from the pancreas, diagnosed at age 58. The remaining 26 malignancies were diagnosed in patients with adult-onset morphea; this difference was also not statistically significant. Concomitant LS was associated with an increased risk of malignancy (LR $\chi^2(1) = 4.13$, p=0.042), as four of the ten patients with LS also had

malignancies. The observed cancers included breast cancer, colorectal cancer, cholangiocarcinoma and gastrointestinal stromal tumors (GIST), diagnosed between ages 61 and 85.

Breast cancer was the most common malignancy, with eleven cases. The median age at breast cancer diagnosis was 62 years [IQR 54.3, 67.6]. All breast cancer patients were female, with seven having plaque-type of morphea and four generalized morphea. Seven of the breast cancer diagnoses were made within four years of the morphea diagnosis. Breast cancer was most often diagnosed prior to the diagnosis of morphea, whereas other malignancies were mainly diagnosed after the diagnosis of morphea (Table S2).

Extracutaneous manifestations

Extracutaneous manifestations (Table S4) were observed in six patients with musculoskeletal involvement, including three with linear scleroderma (two with en coup de sabre and one of extremity subtype), one with plaque-type morphea, one with generalized morphea, and one with deep morphea. Magnetic resonance imaging (MRI) of the head was performed in five of the seven patients with en coup de sabre. Of these, two MRIs revealed soft tissue changes only, one showed inflammation in the fascia, and two exhibited bony lesions. No patients exhibited brain tissue abnormalities. For one patient, diagnosed in the 1970s, MRI was not available, but the patient had undergone facial plastic surgery during childhood. Extracutaneous manifestations were more common in pediatric-onset patients (18.5%) than in adult-onset patients (1.7%) ($\chi^2(1) = 13.67$, $p=0.0002$).

Treatments

Topical therapy was the most commonly used treatment, applied to 136 patients (87.7% of all patients) (Table 3). High-potency topical glucocorticoids were the most frequently used (122 patients, 78.7%). Additionally, 57 patients (36.8%) received topical calcineurin-inhibitors, 11 patients (7.1%) used

calcipotriol, and four patients (2.6%) used calcitriol. Systemic immunomodulatory treatment was administered to 41 (26.5%), with methotrexate being the most common agent, used in 25 patients (16.1%) (Table 4). The median methotrexate dose was 10 mg once weekly for adult patients and 15 mg for paediatric patients. Other systemic agents included hydroxychloroquine (17 patients, 11.0%), systemic glucocorticoids (4 patients, 2.6%), leflunomide (1 patient, 0.6%), pentoxiphylline (1 patient, 0.6%) and a combination of methotrexate and hydroxychloroquine (2 patients, 1.3%). One patient with disabling pansclerotic morphea received multiple immunomodulatory agents. Systemic treatment was most commonly used in patients with linear and deep morphea subtypes ($\chi^2(3) = 17.60$, p=0.0005). The types of treatments initiated did not differ between pediatric-onset and adult-onset patients (Table S1).

Of the 63 patients treated with phototherapy (40.6% of all patients), 25 (39.7%) also received systemic immunomodulatory agents, but these treatments were administered at different times and not concurrently. The most commonly used phototherapy modality was UVA1 (54 patients, 85.7%), followed by psoralen plus UVA (PUVA) in five patients (7.9%) and UV311 phototherapy in four patients (6.3%). Phototherapy was most frequently used in patients with the generalized subtype ($\chi^2(3) = 20.21$, p=0.0002).

Discussion

Patients with morphea at our centre required systemic immunomodulatory treatment or phototherapy and had a higher proportion of generalized morphea than previously reported.[4,14] This may be because patients with milder forms of the disease were not referred to tertiary care centre in Southwest Finland. The incidence, age at disease onset, and gender distribution observed in our study were comparable to previous reports.[1–3,7] The female preponderance was particularly pronounced in adult-onset cases, with

the peak incidence occurring between ages 60 and 64. Extracutaneous manifestations occurred in 18.5% of pediatric-onset cases, consistent with previous reports (22.4%)[9], but were rare in adult-onset disease (1.7%).

The annual incidence of morphea remained stable over the 16-year follow-up period in our cohort. In contrast, studies from the United States have reported an increasing trend, with the most recent incidence reaching 10 cases per 100,000 inhabitants.[1,15]

The occurrence of concomitant autoimmune diseases was relatively high, with 29% of subjects having one or more autoimmune conditions concurrently. Autoimmune thyroid diseases, LS and RA were particularly common. Comorbidity was more prevalent among adult patients, with 32.8% of those with adult-onset disease having at least one autoimmune condition, compared to only 13.3% among pediatric-onset patients. In a hospital-based Finnish study with 455 female patients with LS and an age and sex matched population, the relative risk (RR) for concomitant morphea was 60.0.[16]

In a large U.S. study, 29% of adults had concomitant autoimmune diseases, which is comparable to our findings. However, autoimmune diseases were more common among pediatric-onset patients in our study than the 3% reported in the U.S. study. Additionally, most autoimmune diseases in our cohort occurred in the adulthood in pediatric-onset patients in contrast to the U.S. study. The most frequently observed autoimmune diseases in the U.S. study were psoriasis and alopecia areata, with no reported cases of concurrent SSc and only one patient with autoimmune thyroiditis.[7]

The concurrent occurrence of SSc and morphea is rare,[17] with reported rates ranging from 2.4% to 7.4%.[18] In our study, two of the three patients with both diseases exhibited Raynaud´s phenomenon and nailfold capillaroscopy abnormalities, a combination previously reported.[18] Only one patient tested

positive for ANA, and none had SSc-specific autoantibodies. The pathogenesis of morphea and SSc involve different mechanisms[19], and although both affect the skin, they are considered distinct diseases.

ANA were detected less frequently in our morphea patients compared to SSc, where 85% to 99% of patients test positive for ANA.[20] Previously, up to 50% of morphea patients have been found to harbor three main autoantibodies: ANA, AHA or anti-ssDNA, in.[21] The occurrence of other autoantibodies is typically below 10% each. In our study, only 29% of patients were ANA-positive, and the occurrence of other antibodies was even rarer.

Borrelia burgdorferi antibodies or PCR testing of skin biopsies were conducted in 66.5% of patients, with only 3.9% yielding positive results. The high rate of antibody testing reflects our centre's location in an endemic area for the disease.[22,23] However, the occurrence of positive findings remained low. Routine testing for *Borrelia* is not recommended.[2,3]

Breast cancer was the most common malignancy, accounting for 11 cases (40.7% of all cancers and 57.9% of all female cancers). The median age at breast cancer diagnosis was 62 years, consistent with the age at diagnosis reported in the general population according to the Finnish Cancer Registry.[24] Most morphea cases among these patients were diagnosed within four years of breast cancer diagnosis, with morphea being distinguished from radiation-induced morphea. A recent study identified breast cancer as the most common malignancy preceding morphea diagnosis, occurring in 10 of 12 cases.[25] Notably, no cases of malignant melanoma were observed in our study, despite evidence suggesting an increased risk in patients with morphea.[26] The number of malignancies was higher in patients with both morphea and LS; however, we lacked data solely on patients with LS. Therefore, it remains unclear whether the elevated cancer risk is attributable to LS alone. Finnish studies have indicated an increased risk of urogenital cancers in patients with LS.[27,28] Since our study did not include data on the background population, we could not assess the relative risk of malignancies within our study cohort.

In several cases, data on the efficacy of topical treatments were unavailable, as these patients were usually not followed at our centre. Topical glucocorticoids and calcineurin inhibitors were commonly used. However, in this study, we only assessed the efficacy of systemic immunomodulatory treatments and phototherapy. Methotrexate was the most frequently used systemic agent and appeared to have the best efficacy. Previous studies have indicated that methotrexate is effective compared to systemic glucocorticoids in children and generally well tolerated.[3] None of the patients received mycophenolate mofetil, which has been reported to be beneficial in a small series.[29] Unlike previous studies,[30] the efficacy of hydroxychloroquine in our cohort was modest. Phototherapy, particularly UVA1 phototherapy, appeared to be effective.

The strength of our study is that all patient records were reviewed by clinicians rather than relying solely on ICD codes. Our hospital serves as a tertiary care centre in the region, providing specialized level treatment and diagnostic tools, including skin biopsies and autoantibody analyses. Furthermore, we have comprehensive data on comorbidities, as all malignancies in these patients were treated within our hospital.

Our study data were collected retrospectively, and some records were unclear or incomplete. Patients treated solely with topical therapies were not followed at our centre, resulting in a lack of data on their treatment efficacy. Due to inaccuracies in the records, the exact durations of systemic therapies and phototherapy could not be accurately determined. It is possible, that not all patients with limited morphea were referred to our centre. Treatment efficacy assessments were based on clinicians' judgement. Additionally, we could not evaluate the risk of concomitant autoimmune diseases or malignancies in patients with morphea, as we lacked data on the background population. Also, patient-reported outcome measures were not available.

Conclusions

Our results provide real-world data on morphea patients from a single European centre. Patients frequently required multiple treatments, and the occurrence of concomitant autoimmune diseases, particularly thyroid diseases, was relatively high. No evidence of an increased risk of malignancy was observed.

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Figure legends

Figure 1. The flowchart of different subtypes of morphea by confirmed cases. Atr = atrophoderma.

Figure 2. The distribution of age at the disease onset for the whole study population and for females and males separately. The age was categorized for the five-year intervals for the figure.

Table 1 Autoimmune diseases occurring simultaneously in 155 patients with localized scleroderma

Autoimmune disease	Number of cases (male/female)	% of all patients (n=155)
Thyroid diseases	23 (0/23)	14.8
Autoimmune thyroiditis	21 (0/21)	13.5
Graves disease	2 (0/2)	1.3
Autoimmune skin diseases	17 (1/16)	10.3
Lichen sclerosus	10 (0/10)	6.5
Psoriasis	2 (1/1)	1.3
Vitiligo	2 (0/2)	1.3
Lichen planus	2 (0/2)	1.3
Frontal fibrosing alopecia	1 (0/1)	0.6
Rheumatic diseases	16 (1/15)	10.3
Rheumatoid arthritis	9 (0/9)	5.8
Systemic sclerosis	3 (0/3)	1.9
SLE	1 (0/1)	0.6
UCTD	1 (0/1)	0.6
Sjögrens syndrome	1 (0/1)	0.6
Ankylosing spondylitis	1 (1/0)	0.6
Coeliac disease	1 (0/1)	0.6
Autoimmune hepatitis	1 (0/1)	0.6
Inflammatory bowel disease	1 (0/1)	0.6

SLE; systemic lupus erythematosus, UCTD; undifferentiated connective tissue disease

Table 2 Malignancies occurring simultaneously in 155 patients with localized scleroderma

Cancer	Number of cases (male/female)	% of all patients (n=155)
Breast cancer	11 (0/11)	7.1
Lung cancer	2 (1/1)	1.2
Gynecological cancer	2 (0/2)	1.2
Basal cell carcinoma	2 (0/2)	1.2
Myeloma	1 (0/1)	0.64
Bladder cancer	1 (1/0)	0.64
GIST tumor	1 (0/1)	0.64
Lymphoma	1 (1/0)	0.64
Hypernephroma	1 (1/0)	0.64
Thyroid cancer	1 (1/0)	0.64
Biliary tract cancer	1 (0/1)	0.64
Colorectal cancer	1 (0/1)	0.64
Squamous cell carcinoma of the skin	1 (1/0)	0.64
Origin not known	1 (0/1)	0.64

Table 3. Different treatments and their combinations by the subtype of morphea, n (% of different subtypes). The data was not available for 12 patients

	Systemic	Topical	Phototherapy	Systemic and topical	Systemic and phototherapy	Topical and phototherapy	Systemic, topical and phototherapy
Limited n=66	1 (1.5)	44 (66.7)	1 (1.5)	5 (7.6)	0 (0)	11 (16.7)	4 (6.0)
Generalized n=56	0 (0)	16 (28.6)	0 (0)	5 (8.9)	2 (3.6)	21 (37.5)	12 (21.4)
Linear n=18	2 (11.1)	2 (11.1)	0 (0)	3 (23.1)	0 (0)	5 (27.8)	6 (33.3)
Deep n=3	0 (0)	1 (33.3)	0 (0)	1 (33.3)	1 (33.3)	0 (0)	0 (0)

Table 4 Efficacy of systemic treatments and phototherapy, n=113 (%)

Treatment	Improved	Stable	Progressive	Intolerant	Missing data
Any treatment	45 (39.8)	31 (27.4)	22 (19.5)	12 (10.6)	26 (23.0)
Any systemic n=50	13 (26)	14 (28)	8 (16)	4 (8)	11 (22)
Methotrexate n=25	7 (28)	9 (36)	2 (8)	2 (8)	5 (20)
Glucocorticoids n=4	1 (25)	1 (25)	1 (25)	-	1 (25)
Hydroxychloroquine n=17	2 (11.8)	3 (17.6)	5 (29.4)	2 (11.8)	5 (29.4)
Methotrexate+hydroxychloroquine n=2	2 (100)	-	-	-	-
Leflunomide n=1	1 (100)	-	-	-	-
Pentoxiphylline n=1	-	1 (100)	-	-	-
Phototherapy n=63	32 (50.8)	17 (27)	6 (9.5)	4 (6.3)	4 (6.3)

Efficacy of treatment was assessed by clinicians' judgement.

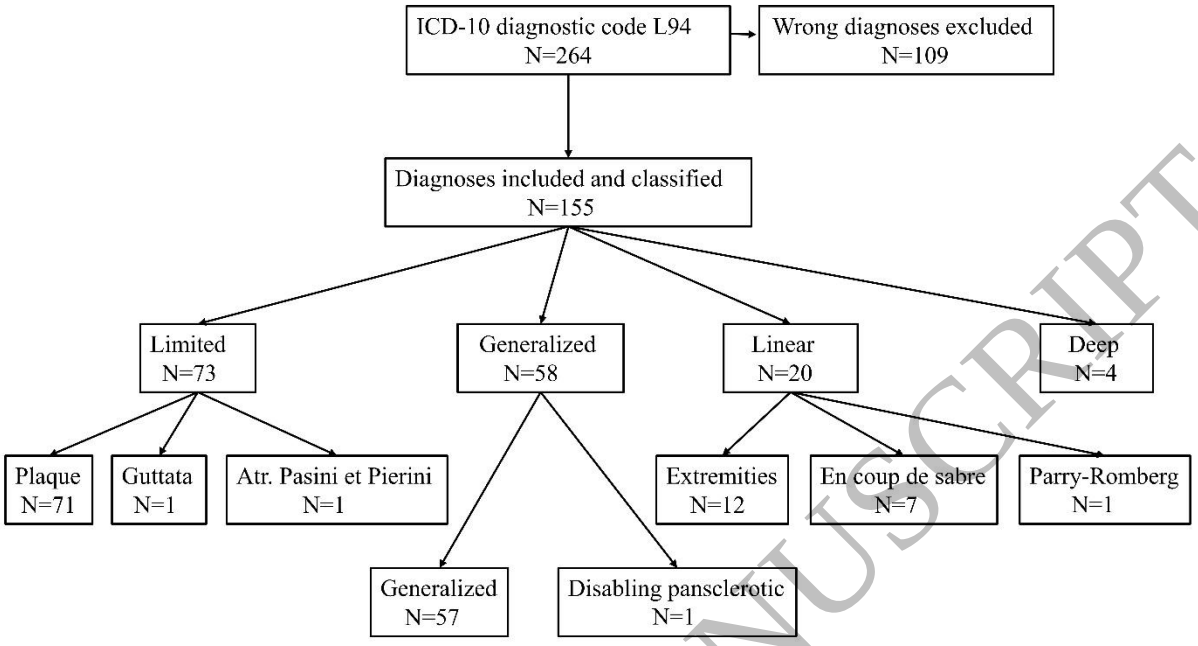

Figure 1
170x96 mm (x DPI)

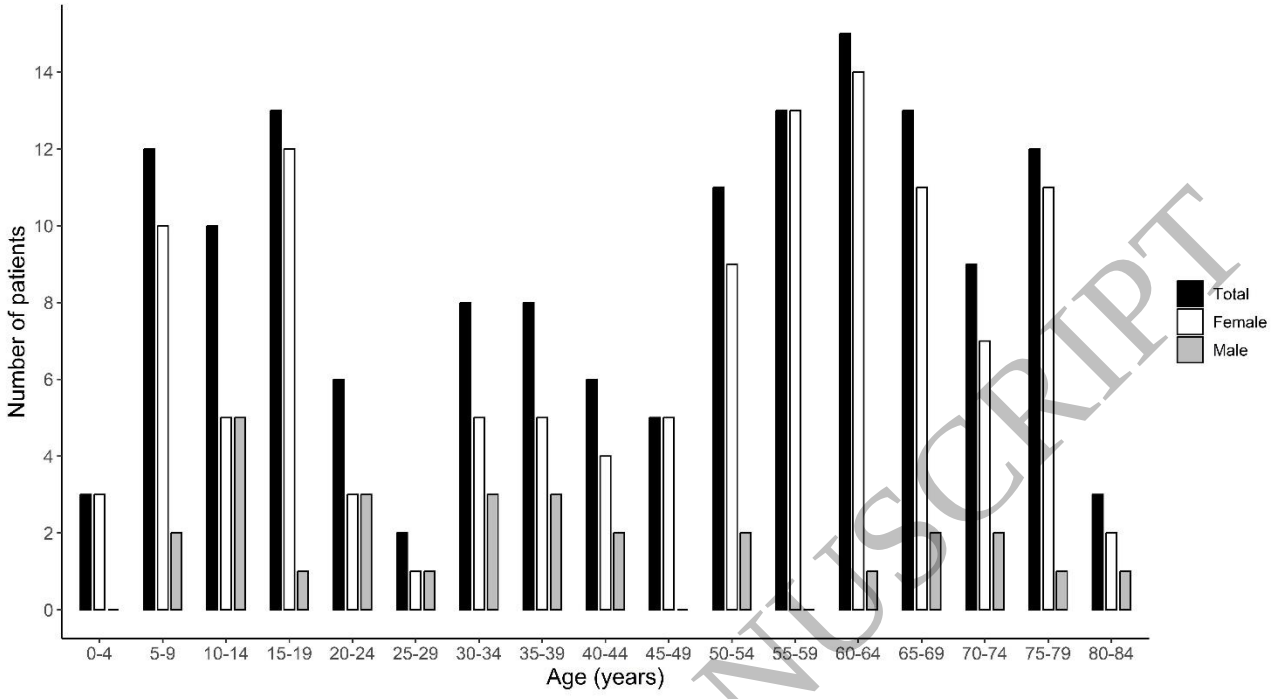

Figure 2
170x93 mm (x DPI)