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RESEARCH ARTICLE

Clinical Characteristics and Treatment Patterns in Pediatric Localized Scleroderma: A Referral-center Experience

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ABSTRACT

Objective: : Localized scleroderma is a rare disease that can cause significant morbidity. Due to its rarity, data are limited, and no standardized treatment exists for patients resistant to first-line therapies. This study aims to evaluate clinical and treatment features based on a referral pediatric rheumatology center's experience.

Materials and Methods: The medical files of 36 included pediatric localized scleroderma patients were retrospectively reviewed, and demographic, clinical, laboratory, treatment, and outcome data were recorded.

Results: Of the patients, 30 (83.3%) were female, the median age at diagnosis was 6.37 years (IQR: 4.04), and the median follow-up duration was 25.5 months (IQR: 56). The most common subtype was linear scleroderma (n=15, 41.67%), followed by circumscribed morphea (n=14, 38.89%). Among patients with linear scleroderma, 6 had craniofacial involvement. ANA positivity was observed in 38.9% of patients. Extracutaneous findings in the form of joint contractures were present in three patients. Systemic treatment was administered to 94% of patients, with methotrexate (MTX) used in 33 (91.67%) and corticosteroids in 26 (72.22%). MTX was effective in 58%, though some patients required additional or alternative therapies such as mycophenolate mofetil (n=14, 38.89%), intravenous immunoglobulin (n=9, 25.0%), or tocilizumab (n=2, 5.56%). Relapses occurred in 19%, and complete clinical response was achieved in 61%. Side effects were mostly mild and mainly related to MTX.

Conclusion: Pediatric localized scleroderma shows diverse clinical presentations and often requires systemic treatment, primarily MTX. While most patients respond well, a subset needs additional therapies. Early diagnosis and tailored treatment are essential to improve outcomes and reduce morbidity.

Keywords: Antirheumatic drugs, autoimmune diseases, localized scleroderma, rheumatology

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INTRODUCTION

Scleroderma comprises a group of chronic autoimmune connective tissue diseases characterized by sclerotic skin changes due to excessive collagen deposition and fibrosis.[1] It is generally divided into two main forms: systemic sclerosis (SSc), which affects internal organs along with skin involvement, and localized scleroderma (LS), also known as morphea, which is confined to the skin and sometimes underlying tissues. Among children, LS is the more frequently observed form and represents the vast majority of pediatric scleroderma cases.[2,3]

Localized scleroderma is considered a rare condition, though its true incidence may be underestimated. According to population-based data from the United States, its incidence is estimated to be around 0.4–2.7 per 100,000 individuals. It follows a bimodal distribution, with incidence peaks occurring between ages 2–14 and again in mid-adulthood. It is reported to be more common in females and among Caucasians.[4] In the pediatric population, linear morphea is the most prevalent subtype, whereas adults more commonly present with the plaque-type form.

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Although the precise pathogenesis of morphea is not fully understood, it is believed to involve an aberrant immune response triggered by environmental factors—such as trauma, infections, or certain medications—in individuals with a genetic predisposition. This dysregulation leads to T-cell activation and subsequent release of interferon-γ-associated cytokines, which initiate inflammatory and profibrotic cascades, ultimately causing excessive collagen deposition. Depending on the subtype, the disease may extend beyond the dermis to involve deeper tissues, including subcutaneous fat, fascia, muscle, and even bone.[4] Diagnosis is primarily based on characteristic cutaneous features, but in atypical cases or when differential diagnosis is needed, skin biopsy can offer valuable diagnostic information.[5]

Despite its rarity, morphea can result in significant morbidity, particularly when deeper tissues or functionally important areas are involved. The scarcity of large, multicenter studies—largely due to the low incidence of the disease—limits the development of standardized diagnostic and treatment approaches.[6] Although treatment options beyond first-line therapies have been described in the literature, especially for refractory cases, there is still no universally accepted therapeutic algorithm.[7] Therefore, real-life experiences remain valuable to better understand the clinical spectrum and management of this uncommon disease.

In this study, we aim to present the clinical characteristics, diagnostic approaches, and treatment patterns of pediatric localized scleroderma patients from a single center, contributing to the limited but growing body of evidence in the field.

MATERIALS and METHODS

This retrospective study included pediatric patients aged 0–18 years diagnosed with localized scleroderma who were followed up at the Pediatric Rheumatology Clinic of Istanbul University Faculty of Medicine. A total of 45 patient records were initially reviewed. Patients with clinical features suggestive of systemic sclerosis or with diagnoses such as lichen sclerosis, as well as those with incomplete data or lost to follow-up, were excluded. Consequently, 36 patients were included in the final analysis.

Demographic data (age at symptom onset, age at diagnosis, sex), family history, clinical features (localized scleroderma subtype, involved regions, extracutaneous findings), laboratory parameters including autoantibodies, and treatment-related information (first-line therapies, subsequent treatments if applicable, and treatment responses) were retrospectively collected from patient records. Antinuclear antibody (ANA) positivity was defined as a titer of 1:80 or higher.

Disease activity assessment was based on clinical examination, including evaluation of erythema, induration, and lesion size. Clinical improvement was defined as a reduction in erythema and induration, stabilization or regression in lesion size, and absence of new lesion formation, as documented in follow-up records.[8] Complete clinical response was defined as the absence of erythema and induration, no new lesion formation, and no progression of existing lesions. Relapse was defined as the reappearance of disease activity after a period of clinical improvement, characterized by new or expanding lesions, or recurrence of erythema and induration in previously inactive areas.

Statistical Analysis

Data were collected and organized using Microsoft Excel (Microsoft Corporation, Redmond, WA) and analyzed with SPSS version 17.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were used to summarize the data. Categorical variables are presented as counts and percentages, while continuous variables are expressed as means with standard deviations or medians with interquartile ranges, as appropriate. The normality of continuous variables was assessed using the Shapiro-Wilk test.

Ethics

Ethical approval was granted by the Istanbul University Faculty of Medicine Clinical Research Ethics Committee (Approval number: 2025-3429010). The study was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all patients and/or their legal guardians.

RESULTS

A total of 36 patients with localized scleroderma were included in the study. The median time from symptom onset to diagnosis was 5 months (IQR: 30.5). The median follow-up duration of the cohort was 25.5 months (IQR: 56). The demographic features, disease subtypes, and laboratory findings of the patients at diagnosis are summarized in Table 1.

Patients were referred to pediatric rheumatology primarily by dermatology (n=25, 69.44%), followed by general pediatrics (n=10, 27.78%) and neurology (n=1, 2.78%), which were also the specialties of initial presentation. Skin biopsy was performed at diagnosis in 17 (47.22%) patients.

Comorbidities were identified in three patients: type 1 diabetes mellitus in one, recurrent lower respiratory tract infections in another, and both congenital heart disease and hepatic hemangioma in a third patient. No patients had a family history of localized scleroderma. However, four patients (11.11%) reported a family history of rheumatic diseases—two with rheumatoid arthritis and two with psoriasis.

Table 1. Demographic, clinical, and laboratory characteristics of the cohort at the time of diagnosis

Demographic data	
Female, n (%)	30 (83.33)
Age at diagnosis (years), median (IQR)	6.37 (4.04)
Time from symptom onset to diagnosis (months), median (IQR)	5 (30.5)
Follow-up duration (months), median (IQR)	25.5 (56)
Subtypes, n (%)	
Linear (total)	15 (41.67)
Craniofacial	6 (16.67)
Trunk and extremities	9 (25)
Circumscribed	14 (38.89)
Generalized	1 (2.78)
Mixed	6 (16.67)
Laboratory evaluation at diagnosis	
White blood cell count (/µL), median (IQR)	7650 (2540)
Hemoglobin (g/dl), median (IQR)	12.2 (1.4)
Platelet count (×10³/µL)	325 (74)
CRP (mg/L), median (IQR)	0.7 (2.45)
ESR (mm/h), median (IQR)	6 (13)
ANA positivity, n (%)	14 (38.9)
Other autoantibodies (anti-Scl70), n (%)	1 (2.78)

IQR: Interquartile range; CRP: C-reactive protein; ESR: Erythrocyte sedimentation rate; ANA: Antinuclear antibodies

The most common subtype was linear scleroderma (n=15, 41.67%), followed by circumscribed morphea (n=14, 38.89%), mixed-type (n=6, 16.67%), and generalized morphea (n=1, 2.78%). Among the 15 patients with linear scleroderma, 6 presented with craniofacial involvement, including 3 with *en coup de sabre* and 3 with Parry-Romberg syndrome (PRS). All 6 patients classified as mixed-type exhibited features of both linear and circumscribed morphea. Notably, one patient within the mixed-type group had PRS accompanied by circumscribed morphea on the trunk. Representative images of different subtypes of localized scleroderma are presented in Figure 1, and the distribution of lesions by different localized scleroderma subtypes is summarized in Table 2.

At the time of diagnosis, autoantibody positivity was evaluated, and ANA were found to be positive in 14 patients (38.9%). One patient with linear scleroderma tested positive for anti-Scl-70 antibodies; however, during 73 months of follow-up, this patient did not develop systemic sclerosis or systemic organ involvement.

Extracutaneous involvement in the form of joint contractures was documented in 3 patients (8.33%). In two of these, joint limitation occurred in the same anatomical region as the skin lesion, while in one, the affected joint was unrelated to the lesion site. Among the three patients with extracutaneous involvement, age at diagnosis was 5.9, 7.2, and 7.3 years. Time from symptom onset to diagnosis varied considerably,

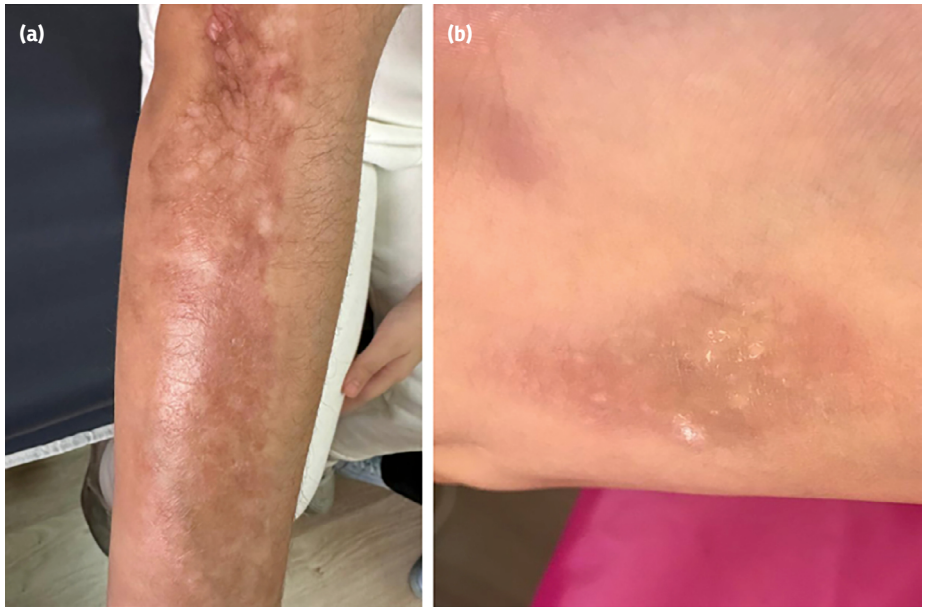

Figure 1. Examples of different subtypes of localized scleroderma. **(a)** Linear scleroderma on the forearm. **(b)** Circumscribed morphea on the dorsum of the foot

Table 2. Localization of the lesions according to scleroderma subtypes

	n	%	Head and neck	Trunk	Upper extremity	Lower extremity	Gluteal region
Circumscribed	14	38.89	5	1	4	7	1
Linear scleroderma (trunk and extremities)	9	25.0	–	4	6	5	0
Linear scleroderma (craniofacial)	6	16.67	6	–	–	–	–
Mixed	6	16.67	1	2	4	5	1
Generalized	1	2.78	–	–	–	–	–

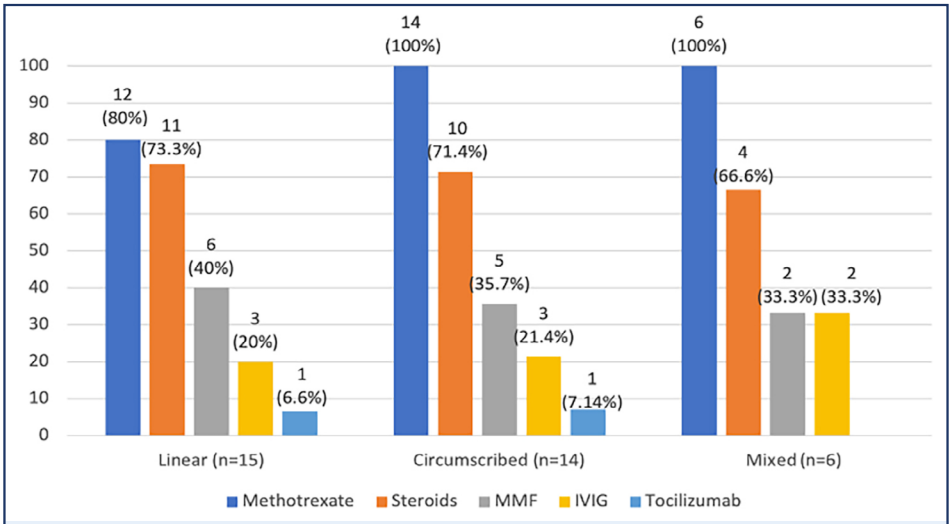

Figure 2. Treatment distribution by scleroderma subtypes. The percentages of patients receiving various treatments are shown according to scleroderma subtype

The generalized form of scleroderma included only one patient who received steroids, methotrexate, MMF, and IVIG; therefore, this subtype is not shown in the figure due to the limited sample size. MMF: Mycophenolate mofetil; IVIG: Intravenous immunoglobulin

with two patients diagnosed within 5 months of symptom onset, while one patient experienced a longer interval of 62 months, reflecting a delayed recognition of disease.

All patients with craniofacial scleroderma underwent at least one cranial MRI scan. No neurological or ocular involvement was detected, although mild signal increase in the right internal capsule suggestive of gliotic changes was observed in one patient on neuroimaging.

Systemic treatment was initiated in 34 out of 36 patients (94.44%). Treatment regimens included methotrexate (MTX) in 33 patients (91.67%), corticosteroids in 26 (72.22%), mycophenolate mofetil (MMF) in 14 (38.89%), intravenous immunoglobulin (IVIG) in 9 (25.00%), and tocilizumab in 2 (5.56%). MTX was administered to all patients at a dose of 10–15 mg/m² per week, with a median treatment duration of 12 months (IQR: 18 months) among patients who completed therapy or were still on treatment. MMF was given to all patients at 500–1000 mg/m² per day, with a median duration of 25 months (IQR: 36 months). IVIG was administered at 1 g/kg per dose, given once monthly; among the 9 patients receiving IVIG, 6 received 6 doses, 1 received 9 doses, 1 received 11 doses, and 1 patient discontinued after 4 doses due to an adverse event. Tocilizumab was administered subcutaneously at 162 mg every 2 weeks in 2 patients, with treatment durations of 3 years in one patient and 4 years in the other. Most patients were followed by dermatology and had received topical treatment prior to referral; however, detailed information on the specific agents used was not available.

As initial disease-modifying antirheumatic drugs therapy, MTX was started in 33 patients; MMF was used as the first-line agent in one patient. Among the 33 patients who received MTX, sufficient improvement was observed in 19 (57.58%). In five patients (15.15%), MTX was discontinued due to adverse

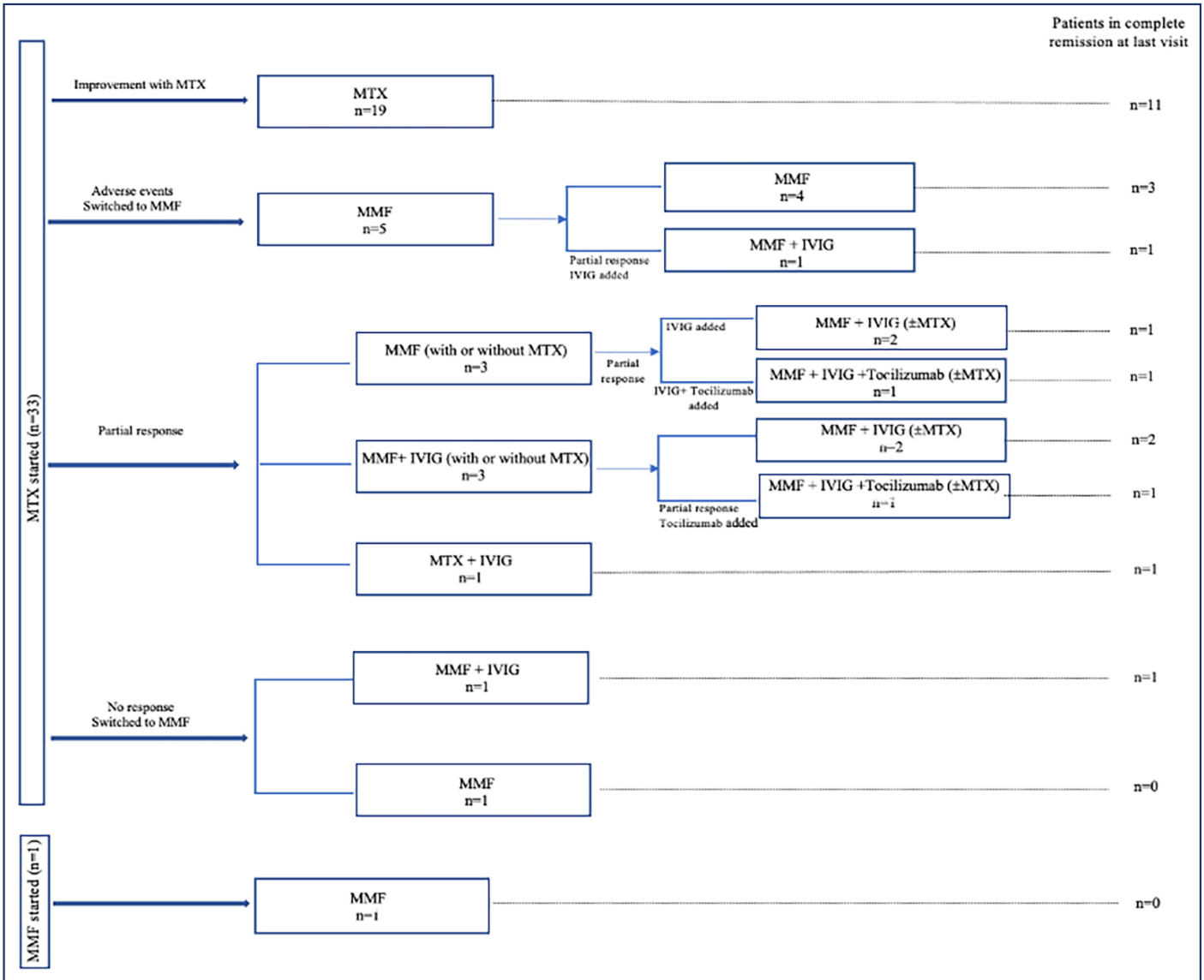

Figure 3. Systemic treatments in pediatric localized scleroderma patients

The figure illustrates the types of systemic therapies used, treatment switches, reasons for switching or discontinuation, and the number of patients achieving remission at the last follow-up for each therapy. MMF: Mycophenolate mofetil; MTX: Methotrexate; IVIG: Intravenous immunoglobulin

effects and switched to MMF. In six patients (18.18%), although MTX led to partial reduction in disease activity, MMF was either added or used as a replacement due to inadequate improvement. In two patients (6.06%), no response to MTX was observed, and treatment was switched to MMF. In one patient, MTX resulted in partial improvement, but due to extensive lesion distribution, IVIG was added to the treatment regimen.

Among the 14 patients who received MMF, four (28.57%) were started on IVIG simultaneously. In an additional four patients (28.57%), IVIG was added after an inadequate response to MMF alone. Sufficient response to MMF was achieved in the other six patients.

In two patients who showed insufficient response to corticosteroids, MTX, MMF, and IVIG, tocilizumab was used and resulted in clinical improvement.

Treatment distribution according to different localized scleroderma subtypes is illustrated in Figure 2. Treatments of patients receiving systemic therapy, treatment switches and their reasons, as well as the number of patients in remission at the last visit, are shown in Figure 3.

Relapses occurred in seven patients (19.44%), accounting for a total of nine episodes. Five occurred during MTX therapy, two during MMF, and one after cessation of all treatment. Complete clinical response, defined as complete resolution of disease activity, was observed in 22 patients (61.11%).

MTX-related side effects were reported in 7 patients (21.21%), primarily gastrointestinal symptoms such as vomiting. In five cases, treatment modification was required due to adverse effects. IVIG-related headache was reported in one patient. No significant side effects were associated with MMF or tocilizumab in this cohort.

DISCUSSION

This study presents data from a single tertiary referral center for pediatric rheumatology in Türkiye, focusing on patients with localized scleroderma. Given the rarity of this condition, cohort studies such as ours provide valuable insights into the clinical characteristics and subtype distribution in different populations.

In our cohort, skin biopsy was performed in 47.22% of patients. These observations align with the view that biopsy is not mandatory for diagnosis and is generally considered in selected cases.[5,7] The most frequently observed subtype was linear scleroderma, which is consistent with previous literature. However, the proportions of linear scleroderma and circumscribed morphea were relatively close. This is in contrast to many previously published cohorts, where linear scleroderma has been reported as more clearly predominant.[9–12] This discrepancy may reflect differences in patient populations, geographic and genetic factors, or referral patterns specific to different centers. It also highlights the heterogeneity in subtype distribution across different cohorts and underlines the importance of local data in understanding the full spectrum of the disease. In addition, we acknowledge the wide interquartile range for time to diagnosis in our cohort. This variability may reflect referral delays and initial misdiagnoses, which are common challenges in clinical practice and contribute to the observed heterogeneity.

Another notable difference observed in our study compared to the literature was the relatively low frequency of extracutaneous manifestations in our cohort. While the reported rates of extracutaneous involvement in localized scleroderma vary across studies, the U.S.-based National Registry for Childhood-Onset Scleroderma has reported such findings in up to 70% of patients.[10] In our cohort, musculoskeletal involvement was the most frequently observed extracutaneous manifestation, which is consistent with the literature.[11,13,14]

Neurological involvement is a well-recognized extracutaneous feature, particularly in patients with craniofacial scleroderma. It is recommended that all patients with *en coup de sabre* (ECDS) or PRS undergo neuroimaging, regardless of neurological symptoms.[7] In our study, all patients with ECDS or PRS underwent cranial imaging, but abnormalities were detected in only one case. This contrasts with findings from a previous study evaluating cranial involvement in juvenile localized scleroderma, where neuroimaging abnormalities were reported in 7 out of 14 patients with craniofacial involvement.[15] One possible explanation for the lower detection rate in our cohort could be the relatively short interval between symptom onset and diagnosis, allowing for earlier intervention. The abnormality observed in our patient was reported as gliotic changes. Although neurological involvement is known to occur more frequently in patients with facial involvement, no disease-specific pattern of neurological symptoms or imaging findings has yet been established in localized scleroderma.[16]

According to the SHARE (Single Hub and Access point for pediatric Rheumatology in Europe) recommendations, the first-line treatment for juvenile localized scleroderma consists of corticosteroids and MTX. In refractory cases, switching to or adding MMF may be considered.[7] For patients unresponsive to these therapies, alternative treatment options exist, but there are no standardized recommendations for this subgroup, leading to variability in therapeutic approaches reported in the literature.

In our cohort, systemic treatment was used in the majority of patients. This proportion appears higher than those reported in previous studies.[10,13,17] However, it is important to highlight that our center is a referral institution, where patients with more severe disease or those unresponsive to topical therapies are more likely to be evaluated. In our cohort, the most frequently used systemic treatments were corticosteroids and MTX, in line with existing studies.[11–14,18] The efficacy of MTX in localized scleroderma has been demonstrated in previous studies, and in our cohort, the majority of patients showed clinical improvement with MTX treatment.[19,20] Other agents used included tocilizumab and IVIG. A notable finding in our study was the relatively high use of IVIG, administered in approximately 25% of patients. Importantly, favorable responses to IVIG were observed in these cases. IVIG is commonly used in connective tissue diseases when first-line therapies fail and has also been employed in localized scleroderma, although data supporting its use in this condition remain limited.[21–24] Our findings contribute to the growing body of evidence suggesting a potential role for IVIG in selected patients with resistant disease.

CONCLUSION

This study provides valuable insight into the clinical features, subtype distribution, extracutaneous manifestations, and treatment patterns of juvenile localized scleroderma in a single-center cohort from Türkiye. As a rare disease, localized scleroderma remains understudied, and regional cohort data such as ours help fill important gaps in the literature. However, several limitations should be acknowledged, including the retrospective design, the relatively small sample size, and the wide variation in follow-up time, which may influence interpretation of outcomes and relapse rates. Despite these limitations, our results are largely consistent with existing literature and also offer new observations, such as the relatively high frequency of circumscribed morphea and the prominent use of IVIG. Further prospective, multicenter studies are needed to better define the natural history of the disease and to guide treatment strategies, particularly in patients with refractory or atypical presentations.

Disclosures

Ethics Committee Approval: The study was approved by the Istanbul University Faculty of Medicine Clinical Research Ethics Committee (No: 2025-3429010, Date: 26/06/2025).

Informed Consent: Written informed consent was obtained from all patients and/or their legal guardians.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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