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Juvenile Overlap Syndrome: Myth or Reality? About Two Cases and Literature Review

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Abstract

Juvenile overlap syndromes are rare and complex conditions characterized by the coexistence of clinical and immunological features of at least two distinct connective tissue diseases. Although well described in adults, these entities remain exceptional in pediatric populations, particularly in sub-Saharan Africa, where available data are scarce. We report two cases of juvenile overlap syndromes managed in a hospital setting: an 11-year-old girl with systemic lupus erythematosus-systemic sclerosis overlap, and an 8-year-old girl with dermatomyositis-systemic sclerosis overlap. The first case combined inflammatory polyarthritis, cutaneous lupus manifestations, diffuse skin sclerosis with Raynaud phenomenon, and a mixed immunological profile including positive anti-dsDNA and anti-Scl70 antibodies. The second case was characterized by proximal inflammatory myopathy, heliotrope rash, Gottron papules, diffuse skin sclerosis, complicated by early pulmonary fibrosis and pulmonary arterial hypertension. Management was based on tailored immunosuppressive therapy, including corticosteroids and disease-modifying agents (mycophenolate mofetil, hydroxychloroquine), with a favorable clinical outcome in the two cases. These observations highlight the diagnostic and therapeutic challenges of juvenile overlap syndromes in resource-limited settings and emphasize the need for multicenter African studies to better define their clinical, immunological, and prognostic profiles.

Keywords

Juvenile Overlap Syndrome, Lupus, Systemic Sclerosis, Dermatomyositis

1. Introduction

Systemic connective tissue disorders in children constitute a heterogeneous group of rare inflammatory autoimmune diseases characterized by multisystem involvement and the presence of specific or associated autoantibodies. Their clinical presentation is often polymorphic, making diagnosis difficult and leading to diagnostic uncertainty, particularly in settings with limited resources. Among the most frequently described entities are juvenile systemic lupus erythematosus, juvenile dermatomyositis and juvenile systemic scleroderma [1] [2]. The term overlap syndrome refers to the coexistence, in the same patient, of clinical and/or immunological criteria relevant to at least two well-defined connective tissue diseases, without any one being clearly predominant. In adults, these forms are well recognized, particularly in the combinations of lupus-scleroderma or dermatomyositis/polymyositis-scleroderma, sometimes included in the context of mixed connective tissue diseases in the presence of anti-U1RNP antibodies. However, overlap syndromes remain rare in children, where the literature is mostly limited to isolated observations or small series [2]. In sub-Saharan Africa, data on juvenile overlap syndromes are particularly scarce. Diagnostic constraints, limited access to specialized immunological investigations and the high prevalence of chronic infectious diseases complicate early recognition. We report here two cases of juvenile overlap syndrome: lupus-scleroderma overlap and dermatomyositis-scleroderma overlap, observed in a sub-Saharan context, and discuss their clinical, immunological, therapeutic and evolutionary aspects, including literature review.

1.1. Patients and Methods

We are reporting here two cases of juvenile overlap syndrome and we will conduct à review of the literature related to these cases. A narrative review of the literature was conducted to identify existing data on pediatric overlap syndrome. The bibliographic search was performed in PubMed/MEDLINE, Scopus, and Google Scholar databases, covering the past fifteen years. Keywords used, alone or in combination, included: pediatric overlap syndrome, connective tissue disease, children, juvenile, myositis, systemic lupus erythematosus, and systemic sclerosis. Included were original articles, reviews, case series, and case reports focusing on pediatric patients (age < 16 years) describing clinical presentations of overlap between systemic autoimmune diseases. Non-English or non-French articles, exclusively adult studies and publications without exploitable clinical data were excluded. Article selection was based on title and abstract, then confirmed after full-text reading when relevant.

1.2. Clinical Case No. 1: Overlap of Systemic Lupus Erythematosus and Scleroderma

This was an 11-year-old female patient with no significant past medical history who was referred for consultation due to chronic polyarthralgia that had been developing for several months, associated with intermittent episodes of fever. Her

parents reported unquantified weight loss and repeated episodes of mouth ulcers. Clinical examination revealed non-deforming polyarthritis affecting the hands, knees, elbows and ankles, without joint swelling. There was diffuse skin sclerosis with sclerodactyly affecting all fingers, digital ulcerations with depressed pulp scars, Raynaud's phenomenon, and telangiectasia of the toes (see **Figure 1**). The patient also presented with non-scarring alopecia, discoid lupus lesions, and mottled facial acromia with a cardboard-like appearance of the skin. Laboratory tests revealed marked inflammation (ESR 137 mm in the first hour, CRP 9.7 mg/L), moderate hypochromic and microcytic anaemia (Hb 9.2 g/dl), thrombocytopenia at 100,000/mm^3, with a normal white blood cell count. Urinalysis revealed isolated cylindruria with no alteration in renal function. Complement (C3 and C4) was normal and serum protein electrophoresis was unremarkable. Viral serology, blood culture and cytobacteriological examination of urine were negative. Immunological testing showed high titre antinuclear factors (1/1280, speckled pattern), positive native DNA antibodies (50 IU/ml), positive anti-Scl70 antibodies and positive anti-SSA antibodies. Rheumatoid factor and anti-CCP antibodies were negative. X-rays of the hands revealed calcinosis, while the chest CT scan was unremarkable. Following clinical and paraclinical evaluation, a diagnosis of lupus-scleroderma overlap syndrome was made. The patient was placed on a combination treatment of erythromycin (125 mg/day) for gastrointestinal motility, colchicine (0.5mg/day), mycophenolate mofetil (500 mg/day) and hydroxychloroquine (200 mg/day). Corticosteroid therapy was started at 16 mg/day and gradually tapered off. The patient's condition improved rapidly, with a reduction in joint pain and asthenia, complete apyrexia, but persistent sclerosis, a drop in ESR (41 mm/h), negative proteinuria without cylindruria, and normal liver and kidney function. She was able to return to school.

1.3. Clinical Case No. 2: Overlap of Juvenile Dermatomyositis and Scleroderma

This was an 8-year-old female patient referred for progressive walking difficulties, difficulty maintaining prolonged standing, and chronic inflammatory polyalgia associated with severe asthenia. The condition had been present for some time, with significant functional impact leading to exclusion from school. The only notable family history was systemic lupus erythematosus in the mother. Clinical examination revealed Raynaud's phenomenon, diffuse cutaneous sclerosis, moderate heliotrope rash on the upper eyelids, Gottron's papules on the metacarpophalangeal and proximal interphalangeal joints, and ulcerations of the toes (see **Figure 2**). There was bi-arthritis of the knees. Muscle examination revealed proximal muscle weakness predominantly in the quadriceps and deltoids (Gowers' sign). Laboratory tests showed a normal complete blood count, a discrepancy between ESR and CRP (ESR at 69 mm/h, CRP normal) and inflammatory serum protein electrophoresis with polyclonal hypergammaglobulinemia. Proteinuria was not significant. Muscle enzymes were significantly elevated (CPK, LDH, aldolase,

ASAT). Antinuclear factors were positive at 1/640, anti-Scl70 antibodies were positive (42 IU/L), while anti-native DNA antibodies were negative, as were anti-Sm antibodies. Viral serology was negative. Echocardiography revealed pulmonary arterial hypertension estimated at 42 mm Hg. Comparative X-rays of the hands and feet showed no calcinosis. A chest CT scan confirmed early pulmonary fibrosis. These findings led to a diagnosis of juvenile dermatomyositis-scleroderma overlap syndrome, complicated by early pulmonary involvement. The patient received photoprotection, physiotherapy, prednisolone at 2 mg per kg of body weight, and mycophenolate mofetil at 500 mg, which was preferred to methotrexate given the early pulmonary fibrosis. These treatments were combined with adjuvant corticosteroid therapy. The patient's condition improved, with a reduction in muscle fatigue and then its complete disappearance. Raynaud's phenomenon improved and the biological signs of cellular distress improved. The patient remains under observation.

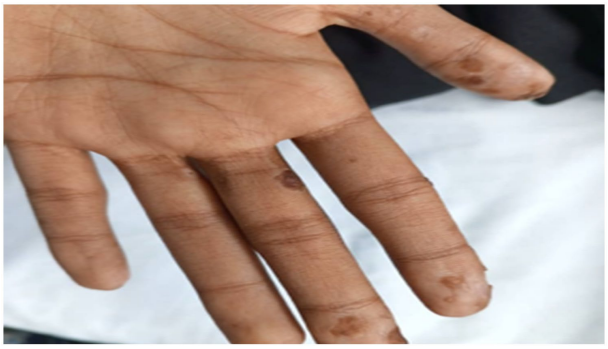

Figure 1. Scarring lesions of digital pulpitis and digital ulcerations.

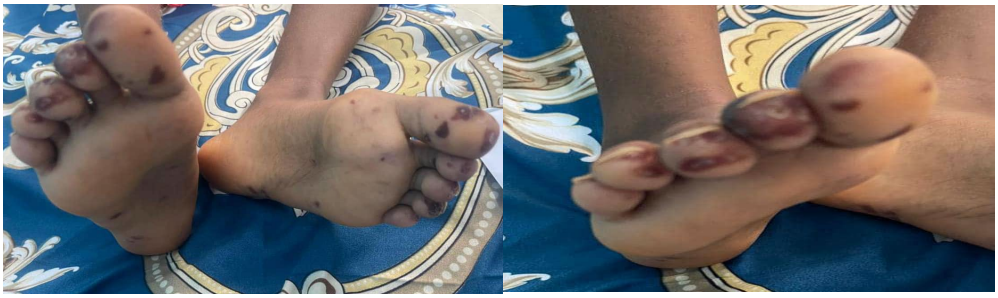

Figure 2. Ulcerated purpuric lesions of vasculitis of the toes.

2. Discussion

2.1. Rarity and Characteristics of Juvenile Overlap Syndrome

Overlap syndrome is not exclusive to children; several cases have been reported in adults, and the proportion of overlap syndrome in children remains low, with some authors reporting less than 10 per cent overlap of connective tissue disorders in children. The most common combinations are lupus-scleroderma and dermatomyositis-scleroderma [3]. In our two cases, we observe lupus-scleroderma overlap (case 1) and dermatomyositis-scleroderma overlap (case 2). These

clinical profiles, detailed above, illustrate the concept of true overlap, where the diagnostic criteria for both diseases are met [4] [5]. Juvenile scleroderma is difficult to diagnose in children, and its localized or diffuse nature remains a diagnostic enigma. It is a rare disease, and its association with other connective tissue diseases further complicates the clinical picture and prognosis. Pediatric systemic forms are characterized by diffuse or limited sclerotic skin involvement, often associated with Raynaud's phenomenon, digital ulcerations, and sometimes life-threatening pulmonary, cardiac or renal visceral involvement. In the context of overlap, these manifestations may be intertwined with lupus signs (hematological involvement, anti-native DNA autoantibodies, specific skin lesions) or signs of dermatomyositis (heliotrope rash, Gottron's papules, inflammatory myopathy), as was the case in one of our clinical cases presented above [6]. Early diagnosis of overlap syndrome in children is essential, as it prevents harmful complications such as pulmonary arterial hypertension or diffuse interstitial lung disease, which have a major impact on growth, quality of life and schooling. Deformities are not uncommon and seriously impair quality of life and slow down schooling. The role of certain autoantibodies (anti-Scl70, anti-SSA, anti-native DNA, high titre antinuclear factors) can guide the clinician towards a form of overlap and may help in the choice of appropriate immunosuppressive therapies [7].

2.2. Immunological Profile: Overlap Markers

Autoantibodies play a central role in the classification of connective tissue diseases. They enable classification and can be used for diagnostic purposes. In adults, certain serological profiles are classically associated with overlap syndromes, notably anti-U1RNP antibodies in mixed connective tissue diseases, or anti-PM/Scl antibodies in myositis-scleroderma overlaps. In children, these data are more limited. In our two observations, no patients presented with anti-U1RNP, but similar profiles have been reported in certain series, albeit limited ones [8]. In the first case, the presence of 1/1280 speckled antinuclear factors associated with positive native anti-DNA, positive anti-Scl70 and positive anti-SSA indicates a mixed serological profile, combining markers typical of lupus and scleroderma. Anti-Scl70 antibodies are classically associated with diffuse scleroderma with an increased risk of interstitial pneumonia, while native DNA antibodies are characteristic of systemic lupus erythematosus and often correlate with disease activity [9]. In the second case, ANF at 1/640 associated with positive anti-Scl70, in the absence of native anti-DNA and anti-Sm, in the presence of signs of muscle pain, are more consistent with a scleroderma profile with dermatomyositis overlap. The significant increase in muscle enzymes confirms muscle involvement. More specific antibodies for overlap myositis-scleroderma, such as anti-PM/Scl, were not sought due to technical unavailability, illustrating a common limitation in requesting immunological tests due to the precarious situation of families [10].

2.3. Organ Involvement and Prognostic Implications

Overlap syndromes involving scleroderma are often associated with an increased risk of visceral involvement, particularly pulmonary (diffuse interstitial pneumonia, pulmonary arterial hypertension), cardiac and renal. These complications may be present at onset in children or occur during the course of the disease, warranting close monitoring [11]. In our series, the patient in the second observation presented at diagnosis with early pulmonary fibrosis on chest CT scan and pulmonary arterial hypertension estimated at 42 mmHg on echocardiography. These complications, which are well described in adults with scleroderma, are rare but serious in pediatrics and constitute a poor prognostic factor if not treated early [12]. The young patient in the first observation presented with isolated cylindruria without impaired renal function, in a context of lupus-scleroderma. Even in the absence of renal failure, this condition requires strict monitoring of renal function, blood pressure and proteinuria, due to the potential risk of lupus nephritis or scleroderma renal crisis [13].

2.4. Therapeutic Aspects: Immunosuppression and Resource Constraints

The management of juvenile overlap syndromes is based on a combination of immunomodulatory and/or immunosuppressive drugs. Recommendations for juvenile lupus, juvenile dermatomyositis and juvenile scleroderma advocate the use of systemic corticosteroids combined with immunosuppressants (methotrexate, azathioprine, mycophenolate mofetil, cyclophosphamide) and, in certain situations, biotherapies (rituximab, agents targeting interleukin or B lymphocytes) [14]. In the first case, the patient received treatment combining erythromycin, colchicine, mycophenolate mofetil and hydroxychloroquine, with a rapid favorable outcome within two months, marked by the disappearance of joint pain, apyrexia and a return to school. The use of mycophenolate, which is increasingly reported in lupus renal disease and scleroderma interstitial lung disease, seems relevant here to control both the lupus and scleroderma aspects. Hydroxychloroquine remains a mainstay of treatment for systemic lupus and may also improve certain scleroderma skin manifestations [15] [16]. In the second case, the therapeutic objective was not only to control the muscle inflammation associated with dermatomyositis but also to slow the progression of scleroderma and pulmonary involvement. High-dose systemic corticosteroids were used in combination with an immunosuppressant such as mycophenolate. We did not consider it useful to use intravenous cyclophosphamide or rituximab, as these are reserved for severe or refractory forms. In countries with limited resources, the availability of biotherapies and certain immunosuppressants may be restricted, requiring therapeutic protocols to be adapted [15]-[18].

2.5. Functional Impact, Delayed Diagnosis and the African Context

Both patients had major functional repercussions at the time of diagnosis: educational delay, limitation of daily activities, significant asthenia and chronic pain.

This profile illustrates the overall impact of systemic connective tissue diseases in children, particularly when they are not recognized early. In many low- and middle-income countries, delayed diagnosis is exacerbated by limited access to specialists (rheumatologists, pediatric specialists), the cost of immunological and imaging tests, and low awareness among frontline staff of the manifestations of juvenile connective tissue disorders. The African context is also marked by the need to make a differential diagnosis with chronic infectious diseases (tuberculosis, HIV, recurrent bacterial infections) responsible for prolonged fever, weight loss and joint pain. In our cases, the exclusion of infectious aetiologias through negative viral serology, sterile blood cultures and laboratory tests pointing to a non-specific inflammatory syndrome provided an opportunity to rule out pathologies that could mimic these connective tissue disorders. The majority of published data comes from Europe and North America. African series remain exceptional, making it difficult to extrapolate international recommendations to our context. Diagnostic delays, the burden of chronic infectious diseases and socio-economic constraints are additional challenges.

2.6. Contributions and Limitations of These Observations

These observations contribute to the literature on juvenile overlap syndromes involving scleroderma, which are still poorly described in sub-Saharan Africa. They highlight the importance of a comprehensive clinical examination (skin, extremities, muscles, lungs, heart, kidneys), targeted immunological testing (FAN, anti-native DNA, anti-Scl70, other specific autoantibodies) and systematic additional investigations (chest CT scan, echocardiography, respiratory function tests where available). However, our work has limitations: the very small sample size, the absence of certain autoantibodies (anti-U1RNP, anti-PM/Scl, anti-centromere) due to financial constraints, and a relatively short follow-up period that does not allow for a full assessment of the long-term prognosis, particularly with regard to lung function and height and weight growth.

3. Conclusion

Juvenile overlap syndrome is not a myth is a reality. It is difficult to diagnose and complex to manage in adults, and even more so in children, where it can very quickly become life-threatening. These two cases highlight the need for multicenter studies involving a larger number of children with overlap syndromes in order to better define the clinical, immunological and evolutionary profile of these forms in Africa.

Ethical Considerations

The parents agreed to the publication of the clinical case in a scientific journal.

Conflicts of Interest

The authors declare no conflict of interest.

References

[1] Petty, R.E., Laxer, R.M., Lindsley, C.B. and Wedderburn, L.R. (2011) Textbook of Pediatric Rheumatology. 6th Edition, Elsevier Saunders.

[2] Ravelli, A. and Martini, A. (2007) Juvenile Idiopathic Inflammatory Myopathies. *Current Opinion in Rheumatology*, **19**, 578-584.

[3] Martini, A. (2011) Juvenile Idiopathic Inflammatory Myopathies. *Nature Reviews Rheumatology*, **7**, 210-219.

[4] Sharp, G.C., Irvin, W.S., Tan, E.M., Gould, R.G. and Holman, H.R. (1972) Mixed Connective Tissue Disease—An Apparently Distinct Rheumatic Disease Syndrome Associated with a Specific Antibody to an Extractable Nuclear Antigen (ENA). *The American Journal of Medicine*, **52**, 148-159. https://doi.org/10.1016/0002-9343(72)90064-2

[5] Steen, V.D. and Medsger, T.A. (1987) Outcome in Early Systemic Sclerosis: Analysis of 97 Patients with Disease Duration < 5 Years. *Annals of Internal Medicine*, **107**, 168-173.

[6] Zulian, F., Athreya, B.H., Laxer, R., Nelson, A.M., Feitosa de Oliveira, S.K., Punaro, M.G., *et al.* (2005) Juvenile Localized Scleroderma: Clinical and Epidemiological Features in 750 Children. an International Study. *Rheumatology*, **45**, 614-620. https://doi.org/10.1093/rheumatology/kei251

[7] Martini, G., Foeldvari, I., Russo, R., Cuttica, R., Eberhard, A., Ravelli, A., *et al.* (2006) Systemic Sclerosis in Childhood: Clinical and Immunologic Features of 153 Patients in an International Database. *Arthritis & Rheumatism*, **54**, 3971-3978. https://doi.org/10.1002/art.22207

[8] Bohan, A. and Peter, J.B. (1975) Polymyositis and Dermatomyositis. *New England Journal of Medicine*, **292**, 344-347. https://doi.org/10.1056/nejm197502132920706

[9] Lundberg, I.E., Tjärnlund, A., Bottai, M., Werth, V.P., Pilkington, C., Visser, M.d., *et al.* (2017) 2017 European League against Rheumatism/American College of Rheumatology Classification Criteria for Adult and Juvenile Idiopathic Inflammatory Myopathies and Their Major Subgroups. *Annals of the Rheumatic Diseases*, **76**, 1955-1964. https://doi.org/10.1136/annrheumdis-2017-211468

[10] Tansley, S.L. and McHugh, N.J. (2013) Myositis-Specific Autoantibodies in Juvenile Myositis. *Current Opinion in Rheumatology*, **25**, 772-777.

[11] Mimori, T. (2005) Clinical Significance of Anti-U1 RNP Antibodies. *Internal Medicine*, **44**, 6-13.

[12] Wedderburn, L.R. and Rider, L.G. (2017) Juvenile Dermatomyositis: Developments in Assessment and Treatment. *Best Practice & Research Clinical Rheumatology*, **31**, 511-526.

[13] Oddis, C.V., Rider, L.G., Reed, A.M., Ruperto, N., Brunner, H.I., Koneru, B., *et al.* (1999) International Consensus Guidelines for Trials of Therapies in the Idiopathic Inflammatory Myopathies. *The Journal of Rheumatology*, **26**, 789-795.

[14] Zulian, F. (2005) Scleroderma in Children. *Pediatric Clinics of North America*, **52**, 521-545. https://doi.org/10.1016/j.pcl.2005.02.001

[15] Foeldvari, I., Klotsche, J., Torok, K.S., *et al.* (2019) Consensus-Based Recommendations for the Management of Juvenile Systemic Sclerosis: SHARE Initiative. *Annals of the Rheumatic Diseases*, **78**, 1019-1024.

[16] Hachulla, E., Launay, D., Hatron, P.Y., *et al.* (2005) Systemic Sclerosis: Clinical and Prognostic Features. *Arthritis & Rheumatology*, **52**, 3143-3152.

[17] Aggarwal, R. and Oddis, C.V. (2015) Therapeutic Advances in Inflammatory Myopathies. *Arthritis & Rheumatology*, **67**, 2139-2149.

[18] Kostik, M.M., *et al.* (2017) Juvenile Connective Tissue Disorders: Clinical Patterns. *Pediatric Rheumatology*, **15**, Article No. 40.