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Adolescent-Onset Triple-Antibody Positive Juvenile Dermatomyositis Found in Hispanic Male Wrestler: A Case Report and Literature Review

Rajvee Sanghavi[1*], Patrycja Tesmer[1], Deepika Singh[1,2], Sukesh Sukumaran[1]

[1]Department of Pediatrics, Valley Children's Hospital, Madera, CA, USA
[2]School of Medicine, Stanford University, Stanford, CA, USA
Email: *rsanghavi1@valleychildrens.org, ptesmer@valleychildrens.org, dsingh2@valleychildrens.org, ssukumaran@valleychildrens.org

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Abstract

In this manuscript, we present a case report of a child with 16-year-old previously healthy Hispanic male who presented for progressive proximal muscle weakness, rash, and dysphagia. He was admitted to the acute care floor and diagnosed with juvenile dermatomyositis and found to be positive for anti-Mi-2 alpha, anti-Mi-2 beta, and anti-MDA-5 antibodies. He gradually improved with a combination of steroid, immunomodulatory treatment, and physical therapy. This case outlines the clinical course of a patient with this rare disorder as well as the importance of understanding the role of associated antibodies to manage potential long-term sequelae.

Keywords

Juvenile Dermatomyositis, Myositis-Associated Antibodies, Myositis-Specific Antibodies

1. Introduction

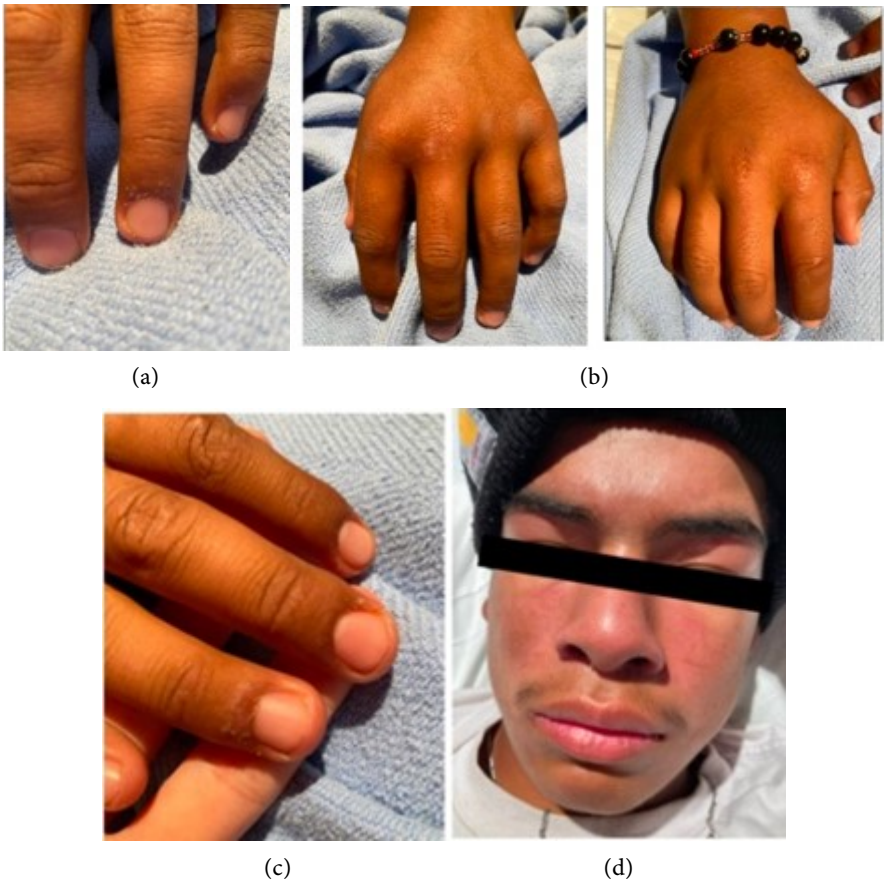
Juvenile dermatomyositis (JDM) is a rare condition of skin and muscle inflammation that can lead to exercise intolerance and disability. It has an incidence of 3.2 out of 1 million children in the United States per year [1]. Caucasian children are primarily affected among North Americans and females are twice as likely to be affected [1]. Although it is the most common idiopathic inflammatory myopathy in the pediatric population, adolescent onset is uncommon. Research has shown

that myositis specific autoantibodies (MSAs) have been identified in distinctive clinical subtypes of JDM and aid in understanding disease heterogeneity. Of these dozens of antibodies, Anti-Mi-2 is seen in classic JDM and is associated with severe muscle disease and rare organ involvement, responding well to standard treatment whereas anti MD-5 is more common in East Asian populations and associated with organ involvement and higher mortality [2] [3]. A review of the literature reveals that testing positive for more than one MSA is rare, although the literature in pediatric patients is sparse. We describe a case of triple-antibody positive JDM including Mi-2 Alpha, Mi-2 Beta and MDA-5 antibodies in a male adolescent with initial presentation of significantly elevated muscle enzymes.

2. Presentation

A 16-year-old previously healthy Hispanic male on the wrestling team initially presented for progressive proximal muscle weakness and pain for one month. He also complained of mild dysphagia and cough for 2 weeks. Of note, there was no known family history of myositis or autoimmune disease. On presentations he was febrile to 38.3˚C with severe proximal muscle weakness in both pectoral muscles, pelvic girdle, and quadriceps tenderness. He was unable to squat or comb himself. Physical examination revealed predominantly proximal muscle weakness of upper and lower extremities, small joints arthritis and skin findings on his face and hands. There was hypopigmentation to his metacarpophalangeal joints consistent with a Gottron-like rash. Nailfold capillaroscopy showed mild dilation and tortuosity and ragged cuticles. He also had a heliotrope rash and photosensitivity malar rash on face (**Figure 1**).

Laboratory findings revealed elevations in serum creatinine kinase (CK), lactate dehydrogenase (LDH), and ferritin, and transaminitis (**Table 1**). In addition, he also had elevations in ferritin. Urinalysis showed large blood with no RBCs suggestive of myoglobinuria. Rheumatoid arthritis markers RF, CCP IgG/IgA were normal and HLA-B27 was negative. Erythrocyte sedimentation rate was slightly elevated, and infectious work up detected the presence of EBV DNA (**Table 1**). A myositis specific antibody panel utilizing line immunoassay was obtained, and he was found to be positive for Mi-2 alpha, Mi-2 Beta, and MDA-5 19 (**Table 2**). Magnetic resonance imaging (MRI) of pelvis and thighs showed extensive diffuse STIR signal over lower back, pelvis, hips and bilateral thighs, consistent with systemic inflammatory myositis with no obvious muscle atrophy. Chest computed tomography (CT) showed no evidence of interstitial lung disease (ILD). Pulmonary function tests indicated normal predictive values of FEV1 and FVC. Echocardiogram was normal with no features of pulmonary hypertension. The Childhood Myositis Assessment Scale (CMAS) score was 11/52 upon admission. A diagnosis of JDM was made based on significantly elevated muscle enzymes, characteristic skin rashes, proximal muscle weakness and confirmatory MRI STIR findings.



(a) (b)

(c) (d)

Figure 1. Physical examination. (a) Left fourth digit; (b) Left and right upper extremities with gottron-like rash; (c) Ragged cuticles to right third; (d) Heliotrope rash and malar rash and fourth digits with nasal fold involvement.

Table 1. Initial workup.

Creatinine kinase (CK)	22,132 IU/L (normal range 33 - 145 U/L)
Lactic dehydrogenase (LDH)	**2256** U/L (normal range 130 - 250 U/L)
Ferritin	**1822** ng/mL (normal range 4.4 - 207 ng/mL)
Albumin	**2.7** g/dL (normal range 3.4 - 5.4 g/dL)
ALT	**442** U/L (normal range 9 - 24 U/L)
AST	**1253** (normal range 14 - 35 U/L)
GGT	normal
Aldolase	negative
Neopterin	**5.6** ng/mL (normal range < 2.5 ngmL)
Rheumatoid arthritis markers	
RF	negative
CCP IgG/IgA	normal
HLA-B27	negative
ESR	25 mm/HR-elevated

Continued

Infectious work up	
CMV PCR	unremarkable
Mycoplasma pneumoniae PCR	negative
Acute hepatitis panel PCR	unremarkable
Respiratory pathogen panel PCR	negative
EBV DNA	**detected**

Table 2. Myositis specific antibody panel.

Component	Result	Reference Range
Jo-1 Ab	<11	<11 SI
PL-7 Ab	<11	<11 SI
PL-12 Ab	<11	<11 SI
EJ Ab	<11	<11 SI
OJ Ab	<11	<11 SI
SRP Ab	<11	<11 SI
Mi-2 Alpha Ab	**97**	<11 SI
Mi-2 Beta Ab	**37**	<11 SI
MDA-5 Ab	**19**	<11 SI
TIF-1y Ab	<11	<11 SI
NXP-2 Ab	<11	<11 SI

Initially the patient was admitted to the acute care floor and parenteral hydration was quickly initiated due to concern for rhabdomyolysis given the presence of myoglobinuria. Due to severe clinical presentation with markedly elevated CK and muscle-derived transaminases, patient received a 3-day course of pulsed methylprednisolone at maximum dose of 1 g/day, followed by induction with IVIG at 2 g/kg at day four of hospitalization. Hydroxychloroquine 200 mg once daily was added and continued over 8 days for concern of overlap syndrome with mixed connective tissue disorder as he also had hypocomplementemia at level C3 80.9 mg/dL and C4 7.3 mg/dL. There was some improvement in synovitis and rash with minimal progress on CMAS score to 18/52. Given his refractory disease course, the treatment was intensified with addition of Rituximab 750 mg/m^2 on day 12, IVIG 2 g/kg every 2 weeks for a total 2 doses, and repeated pulsed dose of methylprednisolone 1g with a maintenance dose of prednisone 30 mg daily tapered over time. He was started on weekly Methotrexate 25 mg with Leucovorin 10 mg. During his hospital stay, he received additionally intense physical and occupational therapy and showed continued improvement in muscle strength. During his hospital course, the patient had an improvement in rash and Hydroxychloroquine was discontinued given its side effects in the muscle. He had slow

improvement in dysphagia and muscle weakness, with down trending transaminases as well as CK (Figure 2). He was discharged home with continuing improvement strength (CMAS score 37/52) and with referrals for continued physical and occupational therapy as well as close rheumatology follow up.

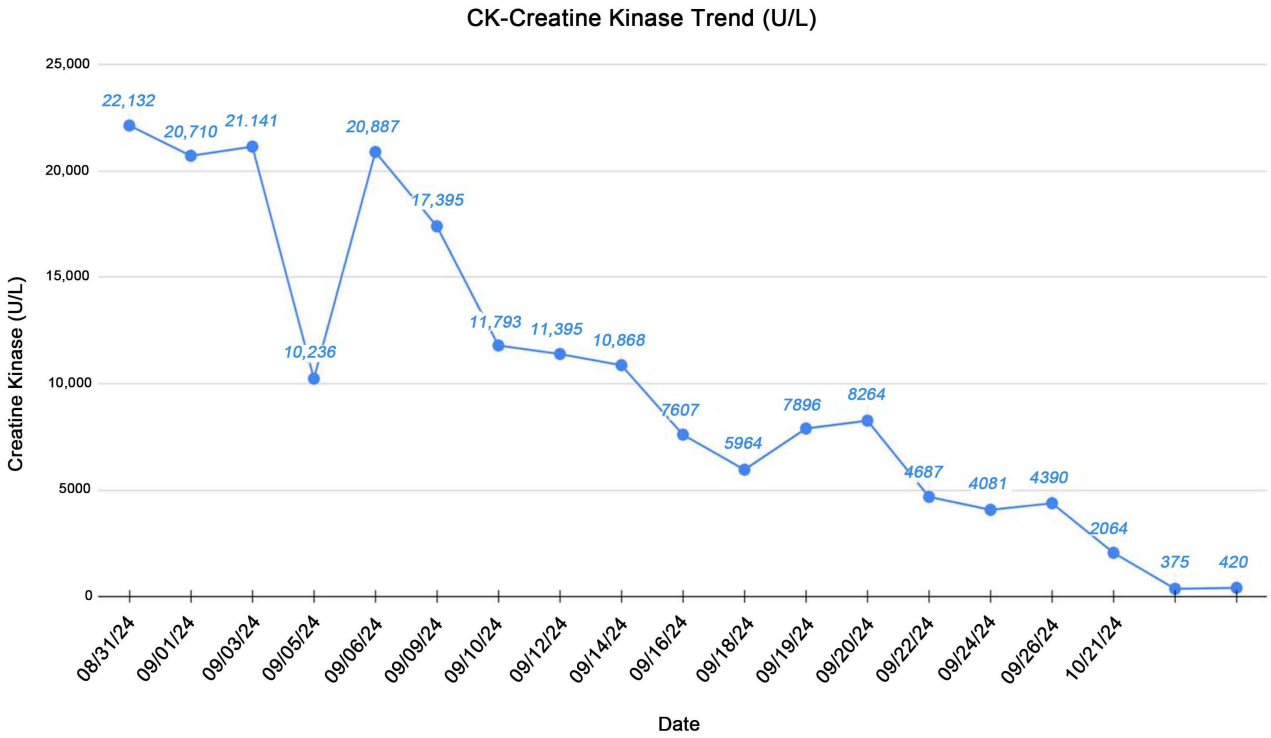


Figure 2. Creatine kinase trend.

3. Discussion

The exact cause of JDM is unknown, however a child's genetic or environmental factors may play a role in pathogenesis which can be multifactorial. Viral infections are known triggers of inducing JDM, and may have contributed to the loss of self-tolerance and onset of disease course in our patient who tested positive for EBV [4]. Ultraviolet (UV) radiation has also been linked to the development of JDM. Our patient resides in the Central Valley, California which typically has a moderate UV index, and he experienced onset of symptoms during periods of peak heat.

JDM is associated with circulating myositis-specific autoantibodies (MSAs) or myositis-associated antibodies (MAAS) which can be associated with certain phenotypes. They are believed to have a key role in the pathology of myositis. Anti-Mi-2 autoantibodies have been demonstrated in about 4% - 10% of JDM patients [5]. In the pediatric patients, anti-Mi-2 autoantibodies were associated with greater muscle weakness and dysphagia [5]. Affected patients typically present with significant skin and muscle involvement however respond well to conventional therapy and have a good prognosis [5]. MSAs to MDA5 (CADM140) have been identified in patients with clinically amyopathic dermatomyositis and

rapidly progressive lung interstitial lung disease (RP-ILD), higher IL-18, IL-6, and hyperferritinemia [5]. Children positive for ILD also have elevated neopterin which should prompt imaging to evaluate the lungs and pulmonary function testing **[5]**. Our patient's PFT and CT chest, however, showed no evidence of interstitial lung disease. One study by Sabbagh *et al.* reported coexistence of anti-Ro52 with anti-MDA5 antibody and prognostically strong association with ILD [6]. In another study by Kim *et al.*, the anti-MDA5 MSA group had less weakness with more joint symptoms (arthritis and arthralgia), skin ulcerations, and systemic features [7].

A review of the literature shows that such large elevation of muscle enzymes like our patient possessed with initial presentation of CK above 20,000 IU/L is also quite unique, with mean creatine kinase levels at presentation of 2245+/−3404 IU/L, and median level of 564 IU/L cited in one study [8]. Our patient may have also had a component of rhabdomyolysis given remarkable urinalysis; however, the lack of electrolytes derangements in the metabolic panel excluded this as the etiology of elevated creatine kinase. Interestingly, serum aldolase was double checked and negative. It is unclear if it could be related to error in fructose metabolism or other primary metabolic myopathy, hence genetic testing would be helpful. Although, EULAR/ACR diagnostic criteria for JDM do not include aldolase as one of the diagnostic serum muscle enzymes [9].

MSAs generally do not overlap and multiple antibodies can complicate clinical presentation and treatment [10]. There is an association between Anti-Mi-2 antibodies and classical dermatomyositis even when coexistent with anti-TIF1-alpha antibodies [10]. Our patient had severe muscle involvement suggesting Anti-Mi-2 antibody has significant influence on phenotype with cross positivity, however more longitudinal studies and research is needed. To our knowledge, this is the only case of juvenile dermatomyositis with triple positive antibodies. Although he presented acutely ill and failed initial therapy with systemic steroids, our patient responded well to his treatment, highlighting the role of combination therapy with anti-metabolites and biosimilars in order to achieve remission. He was also counseled on sun-protective behaviors. Long-term follow-up to investigate this patient's disease course will be crucial in evaluation of additional sequelae including developing ILD.

4. Conclusion

It is important to have a high index of suspicion and initiate treatment early in order to reduce long-term complications. This case has been described for its rarity and to emphasize the importance of early interventions. It also illustrates the importance of serum biomarkers which can track disease activity and help guide treatment. Knowledge of our patient's pathological biomarkers resulted in aggressive treatment, potentially preventing poor outcomes and ensuring targeted management. In addition, there has been paucity of research on JDM in the pediatric population that includes measurement of multiple positive JDM antibodies.

Patient Consent

We have obtained all appropriate patient consent forms. In the form, the patient's guardian has given his/her/their consent for his/her/their images and other clinical information to be reported in this journal. They understand that no personal identifiers will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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