Pediatric Rheumatology

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Monozygotic twins discordant for juvenile dermatomyositis: clinical, serological and gene expression studies

Lauren M. Pachman[1,2*], Amer Khojah[3], Gabrielle Morgan[1], Wilfredo Marin[1], Judith James[4], Sabah Kadri[2,5] and Kai Lee Yap[2,5]

Abstract

Background Juvenile Dermatomyositis (JDM) is a rare pediatric autoimmune disease involving a combination of environmental and genetic susceptibility factors. Monozygotic twins provide a unique opportunity to examine disease-specific gene expression as they share the same DNA. The goal of this study is to characterize gene expression differences between monozygotic twins discordant for JDM.

Methods Five pairs of monozygotic twins were included. Each twin set was discordant for JDM. Detailed clinical and laboratory assessments were performed at enrollment. Nailfold capillary end row loops (ERL) count was obtained for all study subjects. Serum levels of cytokines and chemokines were measured using the Meso Scale Discovery® technique. Three pairs of twins had their peripheral blood mononuclear cells (PBMCs) tested by RNASeq.

Results The JDM twin had significantly lower nailfold capillary ERL than the healthy control, and two non-JDM twins also had decreased ERL In addition, serum endoglin was significantly lower in both JDM and non-JDM twins than in the healthy control. RNASeq identified four genes differentially expressed between the JDM and non-JDM twins: DCD, KRT14, COL1A1, and COL3A1.

Conclusions JDM twins (and two of the non-JDM twins) had significantly lower nailfold capillary ERL and decreased serum endoglin levels compared to healthy controls. Further studies are needed to explore the role of the differentially expressed genes (DCD, KRT14, COL1A1, and COL3A1) in the pathophysiology of JDM.

Keywords Juvenile dermatomyositis, Monozygotic twins, Nailfold capillary, DCD, KRT14, COL1A1, COL3A1

*Correspondence:
Lauren M. Pachman
Pachman.lab@gmail.com; pachman@northwestern.edu
[1]Division of Pediatric Rheumatology, Ann & Robert H. Lurie Children's Hospital of Chicago, 225 East Chicago Avenue, Box 50, Chicago, IL 60611, USA
[2]Northwestern University Feinberg School of Medicine, Chicago, IL, USA
[3]Department of Pediatrics, College of Medicine, Umm Al-Qura University, Makkah, Saudi Arabia
[4]Arthritis & Clinical Immunology, Oklahoma Medical Research Foundation, Oklahoma City, OK, USA
[5]Department of Pathology and Laboratory Medicine, Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, IL, USA

Background

Autoimmune diseases, including Juvenile Dermatomyositis (JDM), are considered to involve a combination of environmental and genetic susceptibility factors [1, 2]. JDM is a pediatric autoimmune disease with an annual incidence of 3.2–4.1 cases per million children in the United States [3]. JDM is characterized by symmetrical muscle weakness and an erythematous rash in specific areas, such as the periorbital area and over the knuckles on the hands, the elbows, and the knees [1, 4]. In addition, children with JDM typically have a rash in the periungual area, which is associated with loss of the end row capillary loops [5, 6]. Although JDM has been classified as a vasculopathy [7, 8], evidence suggests it shares vasculitis characteristics [9, 10]. This association is further supported by an elevated von Willebrand Factor Antigen (vWF: Ag) in severe JDM [11] and increased circulating endothelial cells, which are associated with extra-muscular disease activity [12]. Myositis-specific antibody (MSA) is another important aspect of disease pathophysiology that has recently provided a valuable means of classifying children into disease subgroups, each with distinctive clinical and serologic characteristics [1]. A previous study has provided evidence for the dominant role of genetics in JDM by showing that around 50% of individuals with JDM have a family history of autoimmune diseases, such as systemic lupus erythematosus (SLE) and type 1 diabetes [4, 13]. Additionally, JDM children with a family history of SLE have higher levels of interferon-alpha (IFN-α) activity than those children without a background of SLE, highlighting the shared genetic susceptibility between JDM and SLE through the interferon pathway [13]. This is further corroborated by genome-wide association studies [14]. While traditional inflammatory markers, such as erythrocyte sedimentation rate (ESR), are elevated in approximately 30% of JDM patients, neopterin—produced by macrophages upon interferon stimulation—is elevated in the majority of treatment-naïve patients [15]. Additionally, strong correlations have been observed between CXCL10, CXCL11, and neopterin levels, suggesting that the interferon pathway plays a crucial role in JDM pathophysiology [15]. Monozygotic twins provide a unique opportunity to examine disease-specific gene expression as they share the same DNA [16, 17]. The goal of this study is to characterize clinical, serological and gene expression differences present in monozygotic twins discordant for JDM.

In this report, we conducted a thorough clinical and laboratory evaluation of 5 pairs of monozygotic twins discordant for JDM. Of note, in one twin pair, both children had developed the same MSA—Mi-2, but only one twin fulfilled the clinical diagnostic criteria for JDM. In addition, three pairs of twins had their peripheral blood mononuclear cells (PBMCs) tested by RNASeq.

Methods

Study subjects

To assess gene expression and clinical differences in monozygotic twins discordant for JDM were recruited for the study. All twins with JDM were diagnosed and followed by a pediatric rheumatologist experienced in JDM and recruited using advertisements and word of mouth. Discordancy for JDM was reported by the parent and confirmed by the pediatric rheumatologist. Five pairs of twins meeting these criteria, living in the USA, were enrolled in the study. After obtaining age-appropriate written informed consent (Ann & Robert H. Lurie Children's Hospital of Chicago IRB #2010–14117, 2001–11715, 2008–13457), the JDM child and their twin were interviewed and examined in person by a pediatric rheumatologist experienced in JDM (LMP) and admitted to the study. The twins' families were compensated with a $125 gift card. Eleven healthy control volunteers were enrolled in the study, also giving written age-appropriate informed consent (IRB #2001–11715), after screening to confirm the absence of medical illnesses. Each member of this control population was compensated with a $25 gift card after case history, physical examination, nailfold capillaroscopy and blood studies were obtained.

Clinical assessment

JDM children were evaluated by a pediatric rheumatologist to assess the state of their disease activity by using a total disease activity score (DAS-T), which is divided into skin (DAS-S) and muscle (DAS-M) domains. In addition, physical therapists obtained the Childhood Myositis Assessment Scale (CMAS) to evaluate muscle strength. The CMAS ranges from 0 to 52, with a score of 52 indicating full strength. However, for children younger than 4 years old, a score of 46 indicates full strength [4]. Nailfold capillaroscopy was performed using a Nikon Coolpix p6000 digital camera and Dermlite2 Pro HR attachment. Photos of eight digits, excluding thumbs were captured by a research nurse, and nailfold capillary end row loops (ERL) were counted for all eight digits and averaged per mm, by a trained clinical research assistant, blinded to case-control status, utilizing Photoshop [6, 18].

Laboratory assessment

To evaluate disease activity, various laboratory tests were conducted, which included measurement of muscle enzymes, erythrocyte sedimentation rate (ESR), vWF: Ag, and serum neopterin. The assessment of serum neopterin was carried out using a competitive enzyme-linked immuno-sorbent assay [15]. JDM participants underwent flow cytometry assessment to examine CD45, CD3, CD4, CD8, CD16, CD56, and CD19. All the antibodies used in the flow cytometry tests were produced by BD Biosciences, San Jose, CA. Additionally, MSAs were assessed

via immunoprecipitation and immunodiffusion at Oklahoma Medical Research Foundation [19]. Soluble Endoglin, TGF-β, Angiopoietin2, CXCL11, and CXCL10 were assessed by the Meso Scale Discovery® technique [20].

Sample preparation and RNA-sequencing

PBMCs were isolated from whole blood using Ficoll gradient density centrifugation and stored in liquid nitrogen until RNA extraction. Total RNA was obtained using the miRNeasy mini kit (Qiagen #217004) and quantified using a Qubit 3 with the Qubit RNA HS kit (Invitrogen #Q32852). Total RNA libraries were generated using a ribosomal depletion method (Takara SMARTer Stranded High-Input Mammalian Total RNA Sample Prep Kit; #634875). The raw data (FASTQ) was cleaned by trimming sequencing adapters and low-quality sequences using Trimmomatic v0.33 [21]. The cleaned data were aligned to the GRCh38 version of the human genome (primary contigs without alternative haplotypes) using Tophat v2.1.0 [22], and the number of reads for each annotated gene was counted using htseq-count in stranded mode v0.9.1. Finally, DESeq2 [23] was used to calculate differential expression after summing each biological sample's total reads per gene.

Statistical analysis

T-test was used to compare the means of ERL and Meso Scale Discovery® data results between the study groups. IBM SPSS Statistics and GraphPad Prism 9 software were used to conduct statistics and generate the figures.

Results

Summary of cases history

A summary of the clinical history and laboratory finding at the time of assessment for each case is provided below and in Table 1.

Table 1 JDM patient clinical and laboratory characteristics at the time of sample

	Reference Range	JDM Twin 1	JDM Twin 2	JDM Twin 3	JDM Twin 4	JDM Twin 5
Age at presentation		5.58	3.71	5.30	9.40	2.5
Sex		Male	Female	Male	Male	Female
Race		White	White	White	White	White
Duration of untreated disease (months)[a]		1.87	3.94	17.02	2.4	7.5
MSA		MJ (NXP2)+[b]	p155/140 (TIF1-γ)+[b]	Negative[b]	MJ (NXP2)+	p155/140 (TIF1-γ)+ & Mi-2 indeterminate
Age at assessment		9.30	7.31	13.63	9.85	5.69
Current medications[c]		OS, MTX	IVIG	none	OS, MTX	None
DAS-T		2.5	7	0	9	0
DAS-S		0	1	0	5	0
DAS-M		2.5	6	0	4	0
CMAS		49	47	52	ND	50
ERL (#/mm) [non-JDM twin ERL]	≥ 7	6.17 [7.73]	7.05 [7.72]	7.04 [6.00]	7.42 [8.04]	6.24 [6.5]
ESR (mm/h)	0–20	11	135	4	ND	17
Neopterin (nmol/L)	< 10	5.7	8	6.1	6.6	6
vWF: Ag (%)	48-234[d]	151	153	67	152	192
CK (IU/L)	29-268[e]	93	377	87	ND	40
LDH (IU/L)	188-403[f]	412	ND	275	286	321
AST (IU/L)	18–57	34	ND	25	26	33
Aldolase (U/L)	3.4–8.6	ND	3.9	6.4	9.1	4.1
Total T cells	1051–3031	2186	1629	1472	1668	
T helper cells (CD3 + CD4+)	548–1720	1133	872	846	1115	
T cytotoxic cells (CD3 + CD8+)	332–1307	992	692	583	466	
B cells (CD19+)	203–1139	458	106	428	986	
NK cells (CD16+/CD56+)	138–1027	461	237	205	244	

[a]duration of untreated disease refers to the period from the onset of symptoms to the initiation of medical therapy

[b]Myositis Associated Antibody: Ro indeterminate

[c]OS=oral steroid, MTX = methotrexate, IVIG = intravenous immunoglobulin

[d]all patients are blood type A

[e] reference range for CK by age: 6-9y; (age 6 m-5y = 81–279; 6-9y = 29–268;10-13y = 26–268)

[f] reference range for LDH by age: 3-6y; (age 7-11y = 188–358, ≥ 12y = 14–355)

Twin set 1 A five-year-old male with a history of horseshoe kidney and tethered cord presented with muscle pain and progressive muscle weakness over four weeks. He also had difficulty swallowing. Along with elevated muscle enzymes, an MRI and muscle biopsy showed evidence of myositis. He was started on oral prednisone and referred to a tertiary care center. Within three weeks of diagnosis, IV solumedrol pulse and weekly methotrexate were added to the treatment regimen. Skin rash was not observed until after treatment was initiated. The non-JDM twin brother also has a history of horseshoe kidney and tethered cord but did not have any JDM-related symptoms.

Twin set 2 A previously healthy 3-year-old female presented with a facial rash that eventually spread to joint-related skin and then to a more generalized appearance. A month later, muscle weakness was noted as trouble walking and swallowing. Two months later, she was diagnosed with JDM with a positive MRI and elevated muscle enzymes. Initial treatment included an IV solumedrol pulse as well as IVIG. Her twin sister did not have JDM-related symptoms.

Twin set 3 These male twins both presented with rashes over joints at age 5, initially diagnosed with eczema. Twin #1's rash cleared, while the other twin's rash persisted. Five months later, twin #2 was diagnosed with atopic dermatitis and his rash worsened in the summer months for both twins, and again, only twin #1's rash resolved. At age 6.7 years, twin #2 was diagnosed with JDM, with weakness noted around this time as well as abnormal nailfold capillaries. He also had both a positive MRI and skin biopsy. Twin #2 began treatment with alternate-day steroids, IVIG, methotrexate, and the eventual addition of hydroxychloroquine. Twin #1 has intermittent rashes that resolve, but no other JDM-related symptoms.

Twin set 4 A previously healthy 9.5-year-old male presented with back pain, x-ray negative for fractures. The following day, he developed a persistent, red-raised rash after sun exposure. Days later, he developed arm and leg pain, progressive muscle weakness, and difficulty swallowing. Within two months, a non-pruritic rash developed over joint-related areas. The diagnosis of JDM was made by MRI, elevated muscle enzymes, and positive skin biopsy. Muscle weakness was documented by a CMAS of 34 out of 52. Treatment was initiated with oral prednisone and weekly methotrexate. Twin's brother did not have JDM-related symptoms.

Twin set 5 A previously healthy three-year-old female presented with red cheeks with pimples after extensive sun exposure for eight weeks. Her twin sister did not have a rash. The primary care provider prescribed 1% hydrocortisone followed by 0.05% alclometasone dipropionate with little change in the rash. Muscle weakness was not reported by parents but was documented by the physician's physical exam and a CMAS of 23 on the physical therapist's assessment. JDM diagnosis was made after MRI, and treatment began with IV and oral prednisone and weekly methotrexate. Her twin sister had a positive anti-Mi-2 antibody and later developed abnormal ERLs and intermittent knee pain without arthritis. Whole genome sequencing (WGS) of the twins and their parents did not reveal any known pathological variants.

Nailfold capillary and cytokines assessment

The JDM twins had a significantly lower number of nailfold capillary ERL than the healthy control group (6.8 ± 0.6 /mm vs. 8.2 ± 0.7 /mm, $p = 0.002$). Surprisingly, the asymptomatic twin groups also had lower nailfold capillary ERL compared to healthy control (7.2 ± 0.9 /mm vs. 8.2 ± 0.7 /mm, $p = 0.033$), likely due to two non-JDM twins (twin numbers 3, 5) having decreased ERL, below the lower limit of normal (Fig. 1A). We next examined soluble endoglin and angiopoietin2. The serum endoglin was significantly lower in both JDM-twins and non-JDM twins than in the healthy control (Fig. 1B), but the angiopoietin2 level was similar in all three groups (Fig. 1C). To examine the reason for low serum endoglin, we evaluated serum TGF-β, which binds to endoglin. TGF-β was higher in the JDM twin than control (146.9 ± 19.9 pg/ml vs. 141.9 ± 4.9 pg/ml, $p = 0.005$) (Fig. 1D). Other cytokines, such as CXCL10 and CXCL11, did not differ significantly between the groups, possibly due to the small sample size and lack of disease activity in some of the test subjects (Fig. 1E, F). However, there was a positive correlation between serum CXCL10 and DAS-T with r^2 of 0.75 ($p = 0.05$).

RNA-sequencing

We conducted RNASeq from the PBMCs of 3 sets of JDM and non-JDM twin pairs (twin numbers 1, 3, 5) documented differential expression. Due to the limited number of samples, the variance across the patient samples leads to a lower resolution of the differentially expressed genes. Nevertheless, differential gene expression analysis revealed four genes that showed differential expression between JDM twins (case) with the non-JDM twins (control). These genes are DCD, KRT14, COL1A1, and COL3A1 (Fig. 2).

Discussion

In this study, we examined 5 sets of monozygotic twins discordant for JDM to explore potential disease-specific genetic dysregulation. Our results showed that JDM twins had higher mRNA expression of DCD, KRT14,

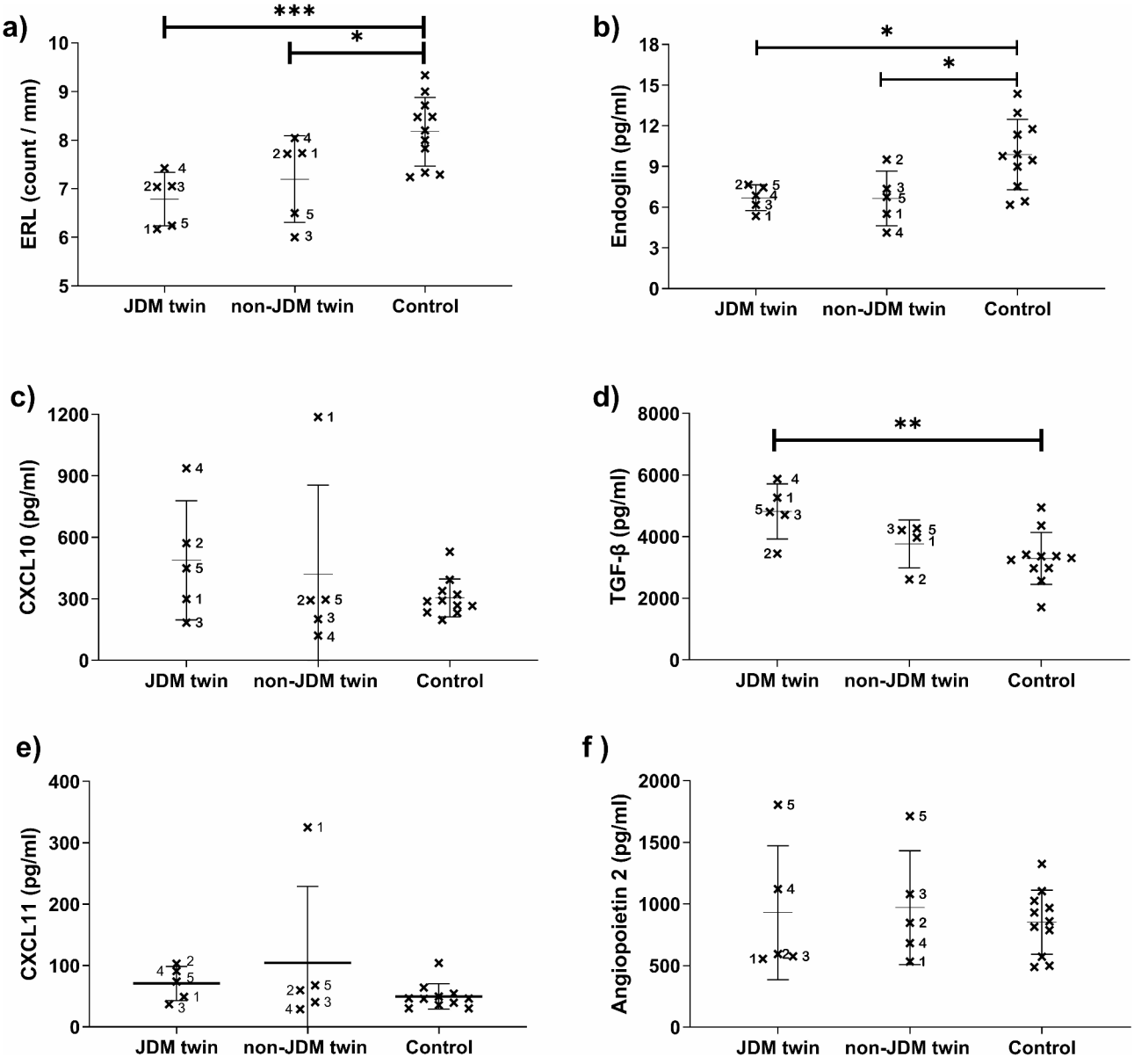

Fig. 1 Meso Scale measurement and nailfold capillary assessment. The JDM twin had significantly fewer nailfold capillary end row loops (ERL) than the healthy control, but to our surprised, two of the non-JDM twins had decreased ERL as well. The serum endoglin was significantly lower in both JDM-twins and non-JDM twins than in the healthy control. Serum TGF-β, which binds to endoglin, was higher in the JDM twin than control. Other cytokines did not differ significantly, which could be due to the small sample size

COL1A1, and COL3A1 than their non-JDM twin. These four genes play important roles in the structure and function of skin and connective tissues. DCD is a gene that codes for dermcidin, a protein primarily expressed in sweat glands, where it helps to protect the skin against infection by inhibiting the growth of certain bacteria and fungi [24]. DCD stimulated keratinocytes is shown to generate multiple cytokines and chemokines such as TNF-a and CXCL10 [25, 26], both of which are elevated in JDM [15, 27]. KRT14 is a gene that codes for keratin 14, an intermediate filament essential for the skin's structural integrity [28]. Pathogenic variants in KRT14 have been associated with epidermolysis bullosa simplex [28]. COL1A1 and COL3A1 code for collagen (type I alpha 1 and type 3 alpha 1), which are part of the structural component of the extracellular matrix in many tissues [29]. The differential expression of these genes in the twin PBMCs could suggest gene dysregulation on the WBC or the existence of other cells that express these markers, which are more typical of skin tissue. The utility of these markers for assessing disease activity is unclear and requires further investigation.

One interesting finding in our study was that one twin pair had concordant MSA—Mi-2, but only one twin met

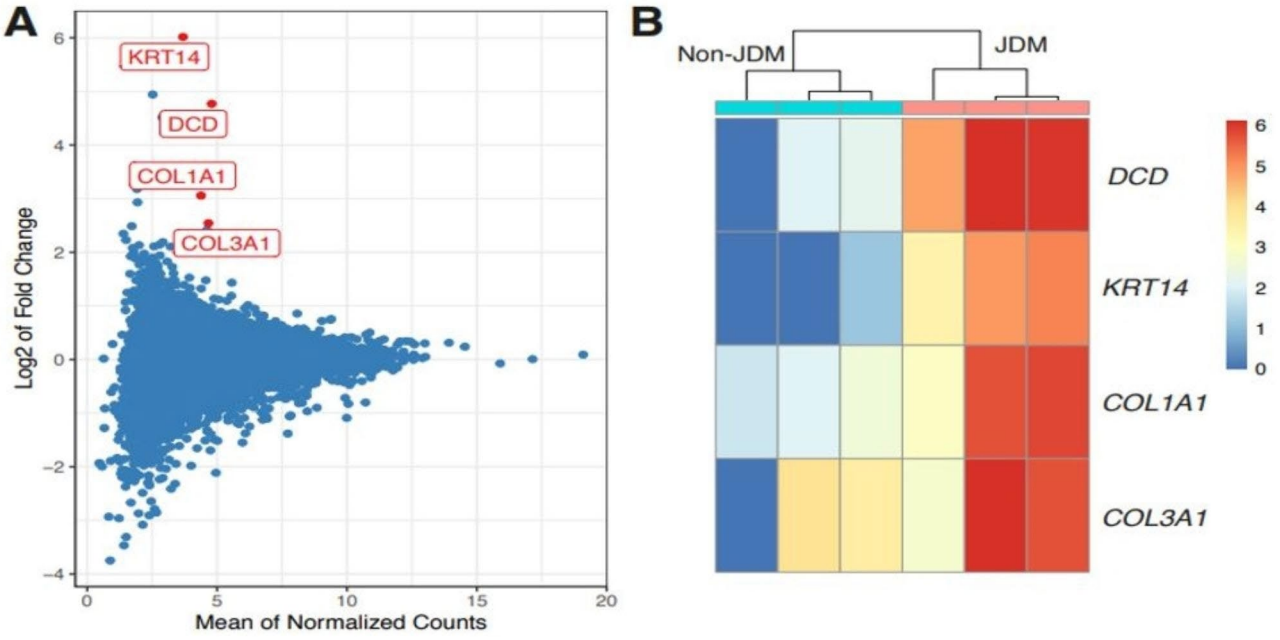

Fig. 2 Differential gene expression between the three sets of JDM and non-JDM twin pairs. (**A**) An MA plot showing the average normalized gene expression counts against the log2 of the fold change between the two groups. The four differentially expressed genes are highlighted in red. (**B**) Heat map of the differentially expressed genes across all six samples. The log-transformed normalized counts are plotted

the criteria for JDM. This finding suggests that other factors beyond MSA are necessary for the development of JDM. Alternatively, the asymptomatic twin could be in a preclinical phase of the disease, as seen in a lupus patient with ds-DNA antibodies and anti-smith antibodies testing positive 2–4 years before disease onset [30]. Furthermore, two non-JDM twins had abnormal ERL counts, despite not meeting the JDM diagnosis criteria. Although abnormal ERL counts typically take time to evolve [31], they could be an early feature in select cases. We also evaluated angiogenic factors known to be abnormal in JDM, such as endoglin and angiopoietin2 [20, 26]. Our results showed soluble endoglin was lower in the JDM twin, which corresponded with elevated TGF-β levels. Soluble endoglin, an antiangiogenic molecule that binds to TGF-β, was also lower in both JDM and non-JDM twins, compared to the control. This finding suggests that dysregulated angiogenic factors due to vascular damage, as manifested by the loss of nailfold ERL in both the JDM twin and their presumably healthy twin control.

This study has several limitations, including the small sample size and variation in the state of inflammatory disease activity which does not permit sufficient exploration of the varied mechanism of action of the identified genes. Recruitment relied on advertisements and word of mouth, potentially leading to the omission of some twins with JDM. Although the non-JDM twins were examined by a pediatric rheumatologist and had not been diagnosed with JDM at the time of enrollment, detailed laboratory testing for JDM was not performed on all non-JDM twins. ERL count was the only measure of nailfold capillary assessment used in this study; however, additional qualitative analyses, which could provide further insight into these changes, were not conducted. Additionally, the healthy controls enrolled were not monozygotic twin pairs, making it unclear whether decreased end row capillary loop counts are associated with monozygosity.

Conclusions

In conclusion, JDM twins– both affected and two of the apparently healthy twins–had a significant loss of ERL density and decreased serum endoglin levels compared to healthy controls. These findings suggest that the non-JDM twin may in fact be in a preclinical phase of an undefined inflammatory process. Further studies are needed to explore the role of the differentially expressed genes (DCD, KRT14, COL1A1, and COL3A1) in the pathophysiology of JDM.

Abbreviations

JDM	Juvenile dermatomyositis
ERL	End row loops
PBMCs	Peripheral blood mononuclear cells
RNASeq	RNA sequencing
MSA	Myositis-specific antibodies
SLE	Systemic lupus erythematosus
IFN-α	Interferon-alpha
MRI	Magnetic resonance imaging
DAS	Disease activity score
CMAS	Childhood myositis assessment scale
WGS	Whole genome sequencing
CXCL10	C-X-C motif chemokine ligand 10

vWF Ag	Von willebrand factor antigen
CK	Creatine phosphokinase
AST	Aspartate aminotransferase
LDH	Lactate dehydrogenase
ESR	Erythrocyte sedimentation rate
IVIG	Intravenous immune globulin
DCD	Dermcidin
KRT14	Keratin 14
COL1A1	Collagen type I alpha 1 chain
COL3A1	Collagen type III alpha 1 chain

Acknowledgements
The authors would like to thank the orthopedic department at Ann & Robert H. Lurie Children's Hospital of Chicago for providing muscle tissue from spinal surgery which was used as controls. We also acknowledge the clinical immunology laboratory at Ann & Robert H. Lurie Children's Hospital of Chicago for measuring the neopterin levels and flow cytometry of JDM patients. We thank the Genomics and Bioinformatics Facility of the Washington University RDRRC (P30-AR073752) for generating the raw data.

Author contributions
All authors have contributed to the manuscript. LMP: Conceptualization, NIH Funding Acquisition, Supervised Investigation, Project Administration, Resources, Supervised laboratory testing of patient samples; Writing– Original Draft, Writing– Review & Editing, Supervision. AK: Formal Analysis, Investigation, Visualization, Writing– Original Draft, Writing– Review & Editing. GM: Investigation, Data Curation, Writing– Original Draft, Writing– Review & Editing. WM: Investigation, Writing– Review & Editing. JJ: Investigation, Resources, Writing– Review & Editing. SK: Formal Analysis, Visualization, Writing– Review & Editing. KY: Formal Analysis, Visualization, Writing– Review & Editing.

Funding
This study is partly supported by grant from the National Institutes of Health (NIH) [NIH/NIAMS R21-AR066846 and R-21 AR077565] both to (LMP). Also, supported partly by The Vivian Allison and Daniel J. Pachman Fund, The DenUyl Family Fund, The Cure JM Foundation, and other much-appreciated donors. The REDCap database is supported by NUCATS and funded in part by a Clinical and Translational Science Award (CTSA) grant from the National Institutes of Health (NIH), [UL1TR001422]. Amer Khojah would like to thank the Deanship of Scientific Re-search at Umm Al-Qura University for supporting this work by Grant Code: (23UQU4300201DSR03).

Data availability
The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Institutional Review Board of Ann & Robert H. Lurie Children's Hospital of Chicago (IRB #2010–14117, 2001–11715, 2008–13457). Written informed consent was obtained by all participants.

Consent for publication
Written informed consent for study enrollment was obtained from all patients and controls.

Competing interests
The authors declare no competing interests.

Received: 23 December 2024 / Accepted: 15 March 2025
Published online: 26 March 2025

References

1. Pachman LM, Khojah AM. Advances in Juvenile Dermatomyositis: Myositis Specific Antibodies Aid in Understanding Disease Heterogeneity. J Pediatr. 2018;195:16–27.
2. Costin C, Morgan G, Khojah A, Klein-Gitelman M, Pachman LM. Lower NK Cell Numbers in Children with Untreated Juvenile Dermatomyositis During the COVID-19 Pandemic. Clin Immunol Commun. 2023;3:42-45.
3. Mendez EP, Lipton R, Ramsey-Goldman R, Roettcher P, Bowyer S, Dyer A, et al. US incidence of juvenile dermatomyositis, 1995–1998: results from the National Institute of Arthritis and Musculoskeletal and Skin Diseases Registry. Arthritis Rheum. 2003;49(3):300–5.
4. Pachman LM, Nolan BE, DeRanieri D, Khojah AM. Juvenile Dermatomyositis: New Clues to Diagnosis and Therapy. Curr Treatm Opt Rheumatol. 2021;7(1):39–62.
5. Khojah A, Liu V, Savani SI, Morgan G, Shore R, Bellm J, et al. Association of p155/140 Autoantibody With Loss of Nailfold Capillaries but not Generalized Lipodystrophy: A Study of Ninety-Six Children With Juvenile Dermatomyositis. Arthritis Care Res (Hoboken). 2022;74(7):1065–9.
6. Pachman LM, Morgan G, Klein-Gitelman MS, Ahsan N, Khojah A. Nailfold capillary density in 140 untreated children with juvenile dermatomyositis: an indicator of disease activity. Pediatr Rheumatol. 2023;21(1):118.
7. Papadopoulou C, McCann LJ. The Vasculopathy of Juvenile Dermatomyositis. Front Pead. 2018;6:284.
8. Gitiaux C, De Antonio M, Aouizerate J, Gherardi RK, Guilbert T, Barnerias C, et al. Vasculopathy-related clinical and pathological features are associated with severe juvenile dermatomyositis. Rheumatology (Oxford). 2016;55(3):470–9.
9. Conklin LS, Merkel PA, Pachman LM, Parikh H, Tawalbeh S, Damsker JM, et al. Serum biomarkers of glucocorticoid response and safety in anti-neutrophil cytoplasmic antibody-associated vasculitis and juvenile dermatomyositis. Steroids. 2018;140:159–66.
10. Duvvuri B, Pachman LM, Morgan G, Khojah AM, Klein-Gitelman M, Curran ML, et al. Neutrophil Extracellular Traps in Tissue and Periphery in Juvenile Dermatomyositis. Arthritis Rheumatol. 2020;72(2):348–58.
11. Gibbs E, Khojah A, Morgan G, Ehwerhemuepha L, Pachman LM. The von Willebrand Factor Antigen Reflects the Juvenile Dermatomyositis Disease Activity Score. Biomedicines. 2023;11(2):552.
12. Kishi T, Chipman J, Evereklian M, Nghiem K, Stetler-Stevenson M, Rick ME, et al. Endothelial Activation Markers as Disease Activity and Damage Measures in Juvenile Dermatomyositis. J Rheumatol. 2020;47(7):1011–8.
13. Niewold TB, Wu SC, Smith M, Morgan GA, Pachman LM. Familial aggregation of autoimmune disease in juvenile dermatomyositis. Pediatrics. 2011;127(5):e1239–46.
14. Miller FW, Cooper RG, Vencovský J, Rider LG, Danko K, Wedderburn LR, et al. Genome-wide association study of dermatomyositis reveals genetic overlap with other autoimmune disorders. Arthritis Rheum. 2013;65(12):3239–47.
15. Khojah A, Morgan G, Pachman LM. Clues to Disease Activity in Juvenile Dermatomyositis: Neopterin and Other Biomarkers. Diagnostics (Basel). 2021;12(1).
16. Bogdanos DP, Smyk DS, Rigopoulou EI, Mytilinaiou MG, Heneghan MA, Selmi C, et al. Twin studies in autoimmune disease: genetics, gender and environment. J Autoimmun. 2012;38(2–3):J156–69.
17. Gan L, O'Hanlon TP, Gordon AS, Rider LG, Miller FW, Burbelo PD. Twins discordant for myositis and systemic lupus erythematosus show markedly enriched autoantibodies in the affected twin supporting environmental influences in pathogenesis. BMC Musculoskelet Disord. 2014;15:67.
18. Khojah A, Morgan G, Klein-Gitelman MS, Pachman LM. Juvenile dermatomyositis: association between nail fold capillary end row loop–area under the curve–and disease damage indicators. Pediatr Rheumatol. 2023;21(1):137.
19. Targoff IN, Mamyrova G, Trieu EP, Perurena O, Koneru B, O'Hanlon TP, et al. A novel autoantibody to a 155-kd protein is associated with dermatomyositis. Arthritis Rheum. 2006;54(11):3682–9.
20. Tawalbeh SM, Marin W, Morgan GA, Dang UJ, Hathout Y, Pachman LM. Serum protein biomarkers for juvenile dermatomyositis: a pilot study. BMC Rheumatol. 2020;4:52.
21. Bolger AM, Lohse M, Usadel B. Trimmomatic: a flexible trimmer for Illumina sequence data. Bioinformatics. 2014;30(15):2114–20.
22. Kim D, Pertea G, Trapnell C, Pimentel H, Kelley R, Salzberg SL. TopHat2: accurate alignment of transcriptomes in the presence of insertions, deletions and gene fusions. Genome Biol. 2013;14(4):R36.
23. Love MI, Huber W, Anders S. Moderated estimation of fold change and dispersion for RNA-seq data with DESeq2. Genome Biol. 2014;15(12):550.
24. Schittek B, Hipfel R, Sauer B, Bauer J, Kalbacher H, Stevanovic S, et al. Dermcidin: a novel human antibiotic peptide secreted by sweat glands. Nat Immunol. 2001;2(12):1133–7.

25. Niyonsaba F, Suzuki A, Ushio H, Nagaoka I, Ogawa H, Okumura K. The human antimicrobial peptide dermcidin activates normal human keratinocytes. Br J Dermatol. 2009;160(2):243–9.
26. Wienke J, Pachman LM, Morgan GA, Yeo JG, Amoruso MC, Hans V, et al. Endothelial and Inflammation Biomarker Profiles at Diagnosis Reflecting Clinical Heterogeneity and Serving as a Prognostic Tool for Treatment Response in Two Independent Cohorts of Patients With Juvenile Dermatomyositis. Arthritis Rheumatol. 2020;72(7):1214–26.
27. Pachman LM, Fedczyna TO, Lechman TS, Lutz J. Juvenile dermatomyositis: the association of the TNF alpha-308A allele and disease chronicity. Curr Rheumatol Rep. 2001;3(5):379–86.
28. Khani P, Ghazi F, Zekri A, Nasri F, Behrangi E, Aghdam AM, et al. Keratins and epidermolysis bullosa simplex. J Cell Physiol. 2019;234(1):289–97.
29. Ricard-Blum S. The collagen family. Cold Spring Harb Perspect Biol. 2011;3(1):a004978.
30. Arbuckle MR, McClain MT, Rubertone MV, Scofield RH, Dennis GJ, James JA, et al. Development of Autoantibodies before the Clinical Onset of Systemic Lupus Erythematosus. N Engl J Med. 2003;349(16):1526–33.
31. Ostrowski RA, Sullivan CL, Seshadri R, Morgan GA, Pachman LM. Association of normal nailfold end row loop numbers with a shorter duration of untreated disease in children with juvenile dermatomyositis. Arthritis Rheum. 2010;62(5):1533–8.

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