Results: Out of 31 children, 54.8% (17) were Caucasian, followed by North African (25.8%, n=7), and other minority groups. Male to female ratio was 14/17. All 31 patients had IgG1 isotype, and 14 had more than one isotype of anti-TIF1γ antibody. Although IgG2 isotype of anti-TIF1γ has been shown to be a biomarker for malignancy and mortality in adult DM, there were no reports of malignancy in this paediatric cohort. In our JDM cohort, the rate of IgG2-positive was 25.8% (8/31) which is lower than observed in adult DM of 55% [2]. Two cases in this JDM cohort died: both were positive for IgG4, but both were negative for IgG2. Interestingly, there were significant differences regarding IgG2 isotype of anti-TIF1γ antibody presence between ethnic groups (p = 0.008). Specifically, although Caucasian patients were the majority, only 1 out of 8 IgG2 positive cases was Caucasian. Between Caucasian and non-Caucasian groups, significant differences were observed when comparing the groups’ means (p = 0.02) and variances (p = 0.01). Notably, 4/8 IgG2 positive were found in North African population, making up 44.4% (4/9) of this ethnic group. We also showed that anti-TIF1γ isotypes can change over time. Specifically, of 6 patients tested for anti-TIF1γ isotypes at a second time point, 4 cases had changes in serological levels of anti-TIF1γ isotypes: 2 had lower titer levels, 1 lost positive status for IgG2 and IgG3, and 1 gained positive status for IgG4.

Conclusion: Our study indicates that there may be a relationship between anti-TIF1γ IgG2 isotype and ethnicity. Importantly, although IgG2 is a biomarker for cancer in adult DM, it is not associated with severe onset or manifestations such as mortality or malignancy in JDM patients.

REFERENCES:

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**PROTEASOME ACTIVITY TEST AS A POTENTIAL CLINICAL TOOL FOR THE DIAGNOSIS OF CHRONIC ATYPICAL NEUTROPHILIC DERMATOSIS WITH LIPODYSTROPHY AND ELEVATED TEMPERATURE (CANDLE) SYNDROME AND RELATED PROTEASOME DISORDERS**

**Keywords:** Diagnostic tests, Rare/orphan diseases, Genetics/epigenetics

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**Background:** Chronic atypical neutrophilic dermatosis with lipodystrophy and elevated temperature (CANDLE) syndrome, is an interferonopathy caused by proteasomal dysfunction. Chronic characteristics include early onset inflammation, nodular rashes, hepatosplenomegaly, myositis, panaritium, lipodystrophy and basal ganglion calcifications. CANDLE and associated syndromes are grouped into the proteasome-associated autoinflammatory syndromes (PRAAS). Our patient presented at age of 3 months with features strongly suggestive of PRAAS. Genetic testing revealed a novel proteasome variant classified as a variant of unknown significance (VUS). Genetic testing revealed a novel proteasome variant classified as a variant of unknown significance (VUS).

**Objectives:** Functional testing of the proteasome was undertaken in order to support the suspicion of PRAAS. Our aims are to describe the potential role of this test for aiding in the diagnosis of PRAAS.

**Methods:** First, interferon signature was obtained and whole exome sequencing was analyzed for the patient and her parents. Next, samples of whole blood were taken from the patient, parents and 3 healthy controls. PBMC were lysed using activity preserving methods (active extraction). Samples were normalized using BCA enzymatic assay. Activity of the proteasomal subunits was measured using peptides specific to different subunits (caspase, chymotrypsin and trypsin activity).

**Results:** Interferon signature was abnormally high, suggestive of an interferonopathy. Whole exome sequencing revealed a novel heterozygous variant in a PSMB4, the gene that encodes for Μ, a structural non-catalytic subunit of the proteasome classified as a variant of unknown significance (VUS). A pilot analysis of proteasome activity showed a 50% reduction in the catalytic activity of proteasome subunit Μ, indicating severe impairment of proteasomal activity, with compensatory hyper-activation of the immunoproteasome subunit Μ (Figure 1). Presence of both subunits of Μ and hyper activation of Μ suggested a proteasomal assembly dysfunction. Using the above findings, the patient commenced JAK inhibitor (baricitinib) with remarkable clinical improvement (Figure 2).

**Conclusion:** Proteasome activity testing may serve as a useful tool for the diagnosis of CANDLE/PRAAS in suspicious cases. Since JAK inhibitors may provide an adequate therapeutic response, it is of great importance to timely diagnose this disease in cases where the genetic results are equivocal.

**REFERENCES:**

**Figure 1.** Reduced Μ1 proteasomal subunit activity as measured by caspase reaction, compared to healthy controls.

**Figure 2.** The patient, before (A) and 2 weeks after (B) starting the treatment with JAK inhibitor (baricitinib)

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**TOWARDS THE DEVELOPMENT OF COMPOSITE PARENT-CENTERED DISEASE ACTIVITY SCORES FOR JUVENILE DERMATOMYOSITIS**

**Keywords:** Outcome measures, Myositis, Patient reported outcomes

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**Background:** In recent years, increasing attention has been paid to the development of parent- and child-centered composite disease activity scores for the assessment of health status of children with rheumatic diseases.