ATYPICAL KAWASAKI DISEASE SHOCK SYNDROME
A CASE OF ADENOSINE DEAMINASE 2 DEFICIENCY

Background: Kawasaki disease (KD) is an acute, self-limited vasculitis of unknown etiology with peak incidence at 9-12 months of age. The term Kawasaki Disease Shock Syndrome (KDSS) was introduced in 2009 after reports of hemodynamic instability during the acute phase of the illness. The term was defined as 'a patient with nonspecific inflammatory syndrome associated with signs of vasodilatation syndrome, extremity edema and non-specific rash in a severely-ill adolescent with no response to broad spectrum antibiotics and negative cultures, the possibility of KD was raised. Due to ongoing fevers and inflammation after 36h of first IVIG, he received a second IVIG dose 2g/Kg, methylprednisolone IV pulses for 3 days and aspirin, with rapid clinical and laboratorial improvement. Within 24h the patient was off inotropic support, 48h off mechanical ventilation and 3 days later he was discharged from the ICU. His general condition continued to improve gradually, with increased platelet counts, normalization of liver function and CRP. In this phase, skin desquamation (buttocks/perineal region) was noted. At follow-up, throracoabdominal angiography showed patent CCA and SMA aneurysms. The patient was weaned off corticosteroids and aspirin without recurrence of symptoms.

Conclusion: In this case, despite the atypical age and lack of some classical signs/symptoms, broad-spectrum antibiotic refractoriness and the described clinical presentation raised the hypothesis of KSSD. Diagnosis can be difficult, especially if shock occurs in incomplete forms of KD, but must be suspected early and treatment promptly started in order to ensure a good prognosis. Clinicians should be aware that thrombocytopenia and hepatitis are risk factors for refractory severe KD. MAS must always be excluded in cases of hemodynamic instability.

REFERENCES

Disclosure of Interests:None declared

A CASE OF ADENOSINE DEAMINASE 2 DEFICIENCY
(DADA2) WITH AN UNCOMMON CLINICAL PRESENTATION AND RESPONSE TO IV IG

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Background: DADA2 is an autoinflammatory disease with autosomal recessive inheritance characterized by a heterogenous clinical phenotype ranging from multisystemic inflammation (fever, polyarteritis nodosa, cerebral stroke, livedo reticularis etc.) to immune-dysregulation and immunodeficiency.

Objectives: To extend the clinical spectrum of DADA2 reporting a case of isolated nonspecific systemic inflammatory syndrome associated with signs of immune-dysregulation in a patient with a novel ADA2 mutation.

Methods: In a patient with nonspecific inflammatory phenotype associated to susceptibility to viral infections, Next Generation Sequencing (NGS) panel was performed; mutations detected were confirmed by Sanger analysis. ADA2 enzymatic activity was analyzed in a monocyte isolated from the patient and incubated with adenosine and an ADA1 inhibitor. Immunologic assessment demonstrated impaired immunological response to viruses (CMV related hepatitis, measles after vaccination) were reported. After few months a patient developed clinical and laboratory findings of HLH (Hemophagocytic Lymphohistiocytosis), confirmed on bone marrow samples; treatment with intravenous (IV) high dose (HD) steroids was started, with prompt response. During steroids tapering fever and systemic inflammation reappeared; anti-IL1 treatment (anakinra) was not effective. Immunologic assessment demonstrated mild hypogammaglobulinemia and moderate NK deficiency or lymphocyte subsets. HD IV Immunoglobulins (IG) (2 g/kg every month) allowed to achieve a complete control of the clinical picture; the frequency of administration was progressively reduced to every 4 months due to persistent wellbeing. At the age of 9, after switching IG to the
substitutional dosage, the patient experienced Herpes Zoster virus reactivation (requiring prolonged antiviral treatment), followed by the reappearance of the inflammatory phenotype complicated by HLH with neurological involvement (irritability and lethargy), responsive to HD steroids and IG. A later cerebral MRI evidenced a small gliotic area in left Centrum Ovale. After steroids suspension, monthly HD IV IG administrations maintained clinical remission. Further immunological studies confirmed a reduction of NK cells with normal function. Hereditary HLH, Autoimmune Lymphoproliferative Syndrome (ALPS) and main primary immunodeficiencies were ruled out. Given the clinical picture, a large NGS diagnostic panel (courtesy by K. Botzug, Vienna) for autoinflammatory diseases and immunodeficiencies was performed revealing the homozygous LEU141P RO AD2 mutation, confirmed by Sanger analysis. Being this mutation novel, an AD2 enzymatic activity test was performed revealing a complete loss of AD2 activity. The parents refused anti-TNF treatment and the patient is still on monthly HD IG with a complete wellbeing after 3 years of follow-up.

Conclusion: The current report enlarges the clinical spectrum associated with DADA2 to a persistent unspecific inflammatory syndrome, complicated by HLH. This case further emphasizes the possibility that NGS could unravel unusual phenotypes of already known inflammatory syndromes. Even if further reports are required, the response to HD IG observed in the present case it is of interest. Even if anti-TNF is the treatment of choice HD IG could be a possible treatment in DADA2, especially during the acute phase.

REFERENCES


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INITIAL BIOLOGICAL THERAPY RESPONSE IN PATIENT’S WITH SUSPECTED AUTOINFLAMMATORY DISEASE

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Background: The choice of the initial biological therapy for patients with suspected autoinflammatory diseases and not conclusive genetic test remains challenging.

Objectives: To assess the clinical response to the initial biological therapy in pediatric patients with suspected autoinflammatory disease with no genetic diagnosis.

Methods: We retrospectively reviewed the clinical charts of patients followed in our clinic who started empirical biological therapy after being diagnosed with suspected autoinflammatory disease (sAID) due to the intensity of their symptoms and no response to colchicine or FAMEs. Next generation sequencing using an immune deficiency/dysregulation (115 genes) and autoinflammatory panel (12 genes) was negative/inconclusive in all patients.

<table>
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<th>Mean</th>
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<th>Median</th>
<th>IQR</th>
<th>Min</th>
<th>Max</th>
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<td>Data in 5 patients: 1 patient 3.7, 2 patients &gt; 4</td>
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Results: We identified 9 patients/6/9 were male, median age at fever onset 1:33 years old IQR (0.46-4), age at diagnosis of sAID 3.8 years old IQ(1.75-7). Clinical presentation included fever/9/9, abdominal pain and arthromyalgia/7/9, aphthous/6/9, headache, rash and adenopathy/5/9, delayed growth/4/9, tonsillitis and pericarditis/3/9 as well as diarrhea and pleuritis/2/9. One patient presented with stroke, cutaneous lesions, vasculopathy and haemolytic uraemic syndrome and 1 patient with amyloidosis and secondary hepatosplenomegaly. None of the children suffered from uveitis or meningitis. The flares lasted a median of 14 days/IQR 8-20). Two patients had persistent symptoms. Their mean/median lab val- ues are shown at table. 4/9 patients had homozygous mutations with uncertain significance, heterozygous mutations or polymorphism but their symptoms or familiar study was not suggestive of the corresponding AID. One patient had an heterozygous mutation in MEFV (p.P369L,p.R408Q) and also a CECR1 heterozygous mutation with uncertain significance, one patient had p.R92Q heterozygous mutation in TNFRSF1A. One patient had MEFV p.R202Q homozygous mutation, other patient had a NOD-2 heterozygous mutation and the patient with amyloidosis had NOBO8 deficiency and a NOD2 mutation (p.A918D). All patients responded to steroid therapy; subsequently 8/9 received anti IL-1Te recep- torkinert as first biological therapy and 1/9 with suspected vasculopathy received anti-TNF. Response to IL-1R antagonist was complete in 3/8 and partial in 4/8 children.1/8 showed no response. 2/8 patients were switched to anti-TNF. One each to etanercept and Ifliximab with good response. The patient with amyloidosis was changed to anti IL-6R with incomplete response but clear improvement compared to anti IL-1R response. The patient with suspected vasculopathy and initial anti-TNF treatment had partial response with no recurrent stroke but persistent neurological symptoms.

Conclusion: An important group of patients with sAID lack genetic confirmation. Empirical use of IL-1R antagonist is promising but not effective in all patients as it was observed in our case series,where 5/8 children showed partial or no response.3/5 needing a second biologic treatment in form of anti-TNF due to persistent moderate-severe symptoms.

A model to predict the response to different therapeutic strategies, based on clinical features and immunological profile (including inflammatory cytokines) might help to choose the most appropriate immunomodulatory treatment.

Disclosure of Interests: None declared


AB0976

PSYCHIATRIC DISORDERS DURING TRANSITION CARE IN ADOLESCENTS WITH RHEUMATIC DISEASES

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Background: Chronic rheumatic diseases (CRD) have a strong impact on psychosocial development of pediatric patients. There are several factors associated with psychiatric disorders (PD) in these children; physical disability, complex treatments, long-term follow-up, and flares, are the most cited in literature.

Juvenile Idiopathic Arthritis (JIA) is the first cause of disability in children with CRD, on the other hand, Major Depressive Disorder (MDDD) and Dysthymia are the third cause. Some PD, mostly MDDD, appear as a consequence of disability caused by CRD, but immune pathways might be implicated in pathogenesis as well.

Adolescents with CRD need to transition to an adult-centered care while deal with emotional and physical changes. This implies a difficult situation in which patients could be in higher risk for develop PD. There are a lack of information on how this process affects emotional health in this population.

Objectives: The aim of the study is to calculate the prevalence of PD in adolescents with CRD during transitional care and their relationship with clinical and social factors.

Methods: Patients older than 16 years with an established CRD, who were in transitional care during the period between July 2017 and January 2019 were included in this transversal study.

We used MINI KID assessment tool to characterize PD in our patients. Each patient performs an interview with both a clinical psychologist and