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ANTITHROMBIN DEFICIENCY IN PEDIATRIC PATIENT WITH MULTISYSTEM INFLAMMATORY SYNDROME IN CHILDREN (MIS-C)

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OBJECTIVES

MIS-C is hyperinflammatory condition arising secondary to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. Antithrombotic prophylaxis is recommended in children hospitalized with severe disease who have at least one risk factor for thrombosis or a high plasma concentration of D-dimers. Heparins exert their anticoagulant effect through activation of antithrombin (AT). The efficacy of low molecular weight heparin (LMWH) therapy in pediatric patients is monitored using an anti-Xa activity assay.

MATERIALS & METHODS

We report a clinical case of MIS-C in critically ill pediatric patient with a six-day history of fever, multi organ dysfunction, laboratory evidence of hyperinflammation, positive antibody test for SARS-CoV-2 IgG and the absence of alternative cause that would explain the clinical presentation. The patient was treated according to the treatment guidelines and subsequently was discharged with the resolution of his symptoms.

CASE PRESENTATION

A previously healthy 15-year-old boy was admitted to the pediatric department. He was noted to have fever, abdominal pain, diarrhea, cardiac dysfunction and neurological signs and symptoms. Skin findings were present with maculopapular and petechial lesions. His pulse and respiratory rates were 125/minute and 40/minute respectively. Chest X-ray showed interstitial abnormalities that indicated pneumonia (Fig. 1). Echocardiography was performed and myocarditis, pericarditis and pleural effusions bilaterally were noted. Left ventricular ejection fraction was 43%.

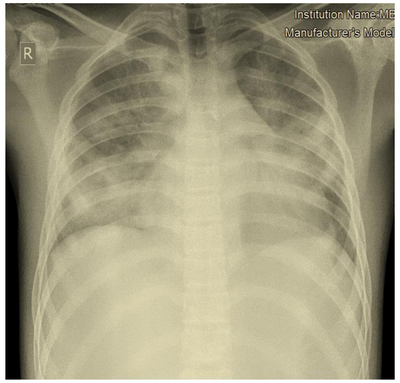

Fig. 1 Abnormal results of chest imaging

Table 1 Summary of pertinent laboratory values with institutional ref. ranges

Admission	Day 7 of admission
CRP 309.8 (<5 mg/l)	**16.8**
Troponin 402.7 (<19.6 ng/l)	**91.6**
BNP 1534.13 (≤100 pg/ml)	**1621.9**
Ferritin 1500 (15-150 ng/ml)	**834.8**
PCT 61.8 (<0.5 ng/ml)	**17.05**
LDH 661 (0-248 U/l	**494**
Albumin 24.8 (35-52 g/l)	**29.1**

Table 2 Dynamics of the complete blood counts and hemostatic parameters

Laboratory values	Ref. range	Admission	Days 1 - 3	Days 4 - 7
RBC	4.5-5.3 T/L	5.7	4.9	4.2
HGB	115-148 g/L	140	126	111
HCT	0.37-0.49	0.41	0.36	0.31
PLT	140-400 G/L	73	76	82
WBC	4.5-11.0 G/L	25.8	56.2	13.1
GRA	25-60%	97.9	91.3	85.4
LYM	25-50%	1	0	13.0
ESR	< 12 mm	6	43	55
FIB	1.8-3.5 g/L	2.57	-	1.25
D-dimer	<0.55 mg/L FEU	35.2	18.4	5.6
AT	81.9-118.2%	-	28.2	31.1

RESULTS

Laboratory values were remarkable for high levels of C-reactive protein (CRP), B-type natriuretic peptide (BNP), ferritin, procalcitonin (PCT) and troponin (Table 1). The patient was noted to have neutrophilia, lymphopenia and decreased platelet count (Table 2). Because of markedly elevated levels of D-dimers at the admission 35.2 ng/L he was treated with therapeutic dose LMWH. Four hours after administration of Clexane 60 mg twice daily the measured anti-Xa level was very low (Table 3). AT deficiency was suspected and functional assay was performed. AT activity was 28% and anticoagulant therapy was switched to Vitamin K antagonist (VKA) acenocoumarol. Five days after initiation of treatment with acenocoumarol D-dimers concentration decreased to 5.6 mg/L. There was neither thromboembolic events nor bleeding during four months of follow-up.

Table 3 Laboratory monitoring of anticoagulant therapy

	Day 1 Clexane 2x60 mg	Day 2 VKA 4 mg	Day 3 VKA 1 mg	Day 4 VKA 2 mg	Day 5 VKA 2 mg	Day 6 VKA 2 mg	Day 7 VKA 2 mg
Anti-Xa Therapeutic range 0.5-1.2 IU/ml	0.1						
INR Therapeutic range 2.0-3.0		1.4	3.1	2.0	2.1	2.2	2.1

CONCLUSION

Reduced AT activity causes significantly low anti-Xa levels. Standart LMWH doses are likely to lead to under treatment in antithrombin-deficient individuals. Laboratory monitoring of LMWH in critically ill children with MIS-C may be useful to ensure adequate antithrombotic therapy.