IMMUNOLOGICAL RECONSTITUTION INFLAMMATORY SYNDROME AND THROMBOTIC MICROANGIOPATHY
SEVERE COMPLICATIONS IN A CHILD WITH AIDS

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INTRODUCTION: Although rare in developed countries, immunological reconstitution inflammatory syndrome (IRIS) is still a severe problem in advance immunosuppression caused by HIV infection. This condition is associated with many complications, including secondary thrombotic microangiopathy (TMA). HIV may infect endothelial cells causing dysfunction and consumption of ADAMTS13.

- ♂, 10 months
- Clinical presentation
 - Neurodevelopment delay
 - Recurrent otitis media
 - Recurrent diarrhea
 - Intensive care unit: *Pneumocystis jirovecii* pneumonia → HIV infection (Viral load: 1460000 copies/mL; CD4 count: 9/uL)

Lamivudine, Zidovudine, Lopinavir/Ritonavir;
Co-infections: parainfluenza 3, parvovirus B19

Evolution

- 2 weeks after: progressive clinical decline with fever, diarrhea (that became bloody and mucous), weight loss, macular rash, stupor and hepatosplenomegaly
- Symptoms progressively worsen, although intercurrent infection (*Klebsiella pneumoniae*) was promptly treated
- Brain MRI – no HIV encephalopathy or CNS IRIS

BLOOD TESTS	Beggining of HAART	2 weeks of HAART/ beggining of symptoms	1 month of HAART	2 months and ½ of HAART	3 months of HAART
CD4 count (/uL)	9	109	54	59	88
Viral load (copies/mL)	1460000	3280	139	117	132
Hb (10.5-13.4 g/L)	12.2	8.6	7.6	8.9	4.2
WBC (6-16x10 ⁹ /L)	2.28	2.60	8.10	17.00	9.7
Neutrophils (0.1-1.0 x10 ⁹ /L)	6.56	0.97	6.05	12.60	7.5
Platelets (200-500 x10 ⁹ /L)	335	68	107	21	8
Reticulocysts (0.5-2.5%)	-	-	9.42	14	2.25
Fibrinogen (1.5-3.19 g/L)	-	0,8	0,7	1,0	0.5
TP (10.6-11.4 s)/ INR	-	18.7/1.63	12,6/1,13	15.4/1,36	21.1/1.83
APTT (24-36 s)	-	33,8	26.0	24.7	111.6
Ferritin (8.4-81.9 ng/mL)	-	1194	667,5	734	2530
ESR (<11 mm/h)	60	4	4	5	9
CRP (< 5mg/L)	1.2	191	3,4	5	0.6
AST (20-67 U/L)	62	141	15	40	61
ALT (5-33 U/L)	56	218	7	19	18
LDH (163-452 U/L)	558	-	224	586	1748
Bilirrubin (0.2-1.2 mg/dL)	0.11	-	0.45	0.24	1.15
Triglycerides (<178 mg/dL)	259	190	-	277	317
BUN (10,9-36,0 mg/dL)	13	5	18	55	103
Creatinine (0,1-0,36 mg/dL)	0,43	0,3	0.22	0.2	0,32
Haptoglobin (0.3-2.0 g/L)	-	-	0.98	0.07	<0.07
ADAMTS 13 activity (>0.67 UI/ML)/antibody (<15 UI/mL)	-	-	0.6/0.57	0.17/ 1.63	0.19/-
Blood smear	-	-	Rare schizocytes	Schizocytes	Schizocytes
Soluble CD25 (458-1197 pg/mL)	-	22167	2410	TMA secondary to HIV infection	Massive intestinal bleeding → death from probable intravascular disseminated coagulation
Infectious agents	B19 parvovirus, parainfluenza 3	-	<i>Klebsiella pneumoniae</i> ESBL (intestinal biopsy)	Plasma infusion (no response) ↓ Plasma exchange (no response)	
Macrophagic activation syndrome in the context of IRIS ↓ Metilprednisone + Iv Ig					

LEARNING POINTS: The clinical deterioration after HAART initiation was probably due to IRIS. Also, TMA secondary to HIV has very high mortality. HIV-associated TMA differs from the idiopathic trombocitopenic purpura: direct effect of virus in endothelium, higher levels of ADAMTS13 and absence of an inhibitor and, in agreement with this, plasma exchange is not effective. Still, after plasma infusion had failed, plasma exchange was tried, but the patient died with IDC. Severe persistent diarrhea may have been caused by HIV intestinal lymphatic tissue infection or intestinal microangiopathy.

References: 1. Warner et al. Hummen immunodeficiency virus associated thrombotic trombocitopenic purpura, a clinical conundrum. J Clinic Apher 2016;00:1-4; 2. Park et al. ADAMTS13 activity levels in patients with human immunodeficiency virus-associated thrombotic microangiopathy and profound CD4 deficiency. J Clin Apher 2009;24:32-36; 3. Brecher et al. Is it HIV TTP or HIV-associated thrombotic microangiopathy? J Clin Apher 2008;23:186-90