A Diagnostic Challenge: DIC versus Thrombotic Microangiopathy in Patient with Severe Disseminated Histoplasmosis

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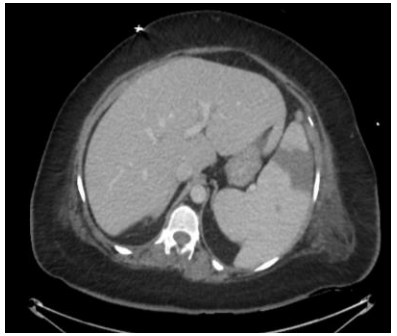
Case Study

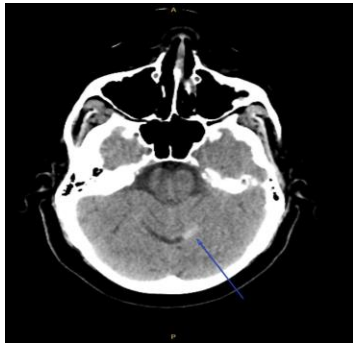
38-year-old female with PMH of lupus, HTN, CKD, asthma, anxiety and fibromyalgia presented with fever, bilateral hand/foot swelling, and ulcers around her lips typical of her usual lupus flare. Additionally, found to have leukopenia and thrombocytopenia. The patient was started on prednisone and showed improvement. Because of the patient's fever, pancytopenia, and elevated ferritin, there was suspicion of hemophagocytic lymphohistiocytosis. Bone marrow biopsy showed rare histiocytes and megakaryocytes with intracytoplasmic debris, without definitive evidence of hemophagocytosis. Results did demonstrate PAS and GMS-positive small, intracellular and extracellular fungal organisms with PCR confirmation of Histoplasma capsulatum. The patient was started on antifungal-therapy with amphotericin B. She developed worsening anemia with evidence of hemolysis and concomitant thrombocytopenia as well as SAH, SDH and vaginal bleeding. CT abdomen was done because of LUQ pain and showed evidence of splenic infarction and hepatosplenomegaly. Given concern for thrombotic microangiopathy, the patient was empirically initiated on plasma exchange. Another thought was that hemolytic anemia and thrombocytopenia are secondary to DIC in the setting of sepsis and secondary to disseminated Histoplasmosis in a critically ill patient. However, it can be difficult to differentiate between DIC and thrombotic microangiopathy. Patient also received several blood and platelets transfusions.

Labs and Imaging

	Result	Interpretations
Hemoglobin	5.7 g/dL	Low
Platelets	9 thousand/uL	Low
Reticulocytes	4.49 %	High
D Dimer	>20.00 ug/ml FEU	High
ADAMTS13	29.9 %	Low
Smear study	No schistocytes	No schistocytes
Creatinine	2.35 mg/dL	High
Fibrinogen	536 mg/dl	High
PT	19 seconds	High
PTT	60 seconds	High
INR	1.5	High
Coombs test	Negative	Negative



Splenomegaly with multiple splenic infarcts.



Small amount of subarachnoid hemorrhage in the left parietal region with trace subdural hemorrhage along the left tentorium.

Discussion

- DIC is a serious disease that causes microvascular thrombosis associated with thrombocytopenia, a bleeding tendency and organ failure. These symptoms and laboratory data are similar to those of thrombotic microangiopathy (TMA) which includes thrombotic thrombocytopenic purpura (TTP).
- The mechanism of onset for DIC is the marked activation and consumption of coagulation system followed by the activation of secondary fibrinolysis. In contrast, the mechanism of onset for TMA is the marked activation and consumption of platelets due to several factors followed by the activation and injury of vascular endothelial cells.
- As there is no gold standard for diagnosing DIC and no specific biomarker that clearly diagnoses DIC, the differential diagnosis between DIC and TMA is difficult.

		DIC	TMA
Symptoms	Organ failure	Often (lung, kidney, shock)	Usually (kidney, CNS)
	Bleeding	Frequent	Frequent
	Anemia	Often	Usually
Lab data	Platelet	Low	Low
	Hemoglobin	Low	Low
	Fibrin related markers	High	Normal or slightly high
	PT	Often prolonged	Normal
	Creatinine	High	High
	LDH	High	High
Treatment	Supportive	Recommended	Recommended
	Blood transfusion	Recommended	Recommended
	Plasma exchange	Not mentioned	Recommended
	Special treatment		Rituximab

Reference

Differences and similarities between disseminated intravascular coagulation and thrombotic microangiopathy Hideo Wada1*, Takeshi Matsumoto2, Kei Suzuki3, Hiroshi Imai3, Naoyuki Katayama4, Toshiaki Iba5 and Masanori Matsumoto6.