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Juvenile Systemic Lupus Erithemathosus And Dengue Fever: A Case Report

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ABSTRACT

The clinical management of patients with systemic lupus erythematosus in emergency situations requires a thorough understanding of the clinical features and complications associated with this condition. The objective of this study is to report a clinical case of an individual with systemic lupus erythematosus undergoing treatment with azathioprine associated with dengue virus infection and severe clinical manifestations. The 27-year-old male patient developed fever, myalgia, and diarrhea eight days before admission, was admitted to the emergency room of a private hospital in São Paulo with clinical worsening associated with hypotension and drowsiness, and a sepsis protocol was opened, as evidenced in the initial laboratory tests of acute renal failure Kdigo III, hydroelectrolyte disorders, blood dyscrasias, pancytopenia, antibiotic therapy for septic shock, abdominal focus in the first hour, use of vasopressor drugs, and admitted to an intensive care bed. During hospitalization, a patient diagnosed with group D dengue and active systemic lupus erythematosus, presenting renal dysfunction requiring renal replacement therapy, liver failure, collection secondary to dengue virus infection, necrotizing pancreatitis, blood dyscrasias, respiratory failure, and alveolar hemorrhage secondary to capillaritis due to dengue or systemic lupus erythematosus, treated with broad-spectrum antibiotics, human immunoglobulin, corticosteroid therapy, however, despite all the therapeutic arsenal and advanced support, the patient progresses to death after 42 days of hospitalization. These situations pose significant challenges in the management of medical emergencies and endemic diseases, and therefore require a comprehensive understanding to ensure appropriate treatment and improved clinical outcomes.

Keywords: Acute kidney injury; Dengue fever; Lupus erythematosus; Sepsis; Viral infection.

Introduction

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease characterized by widespread inflammation and multi-organ involvement (1). Patients with SLE are often immunocompromised due to both the disease itself and the immunosuppressive treatments they receive. This compromised immune state predisposes them to various infections, including viral infections such as dengue fever (2).

Dengue fever, caused by the dengue virus (DENV), is a mosquito-borne illness that can lead to severe clinical manifestations, particularly in individuals with pre-existing health conditions (3). Understanding the interplay between SLE and dengue fever is crucial for managing these patients and mitigating potential complications.

Previous research has demonstrated that patients with SLE and dengue fever have increased rates of hospitalization and death(4). In this article, we discuss a case of a young patient with juvenile SLE, who had a catastrophic presentation of dengue fever, highlighting some of the diagnostic challenges in these patients.

Case Report

A 27-year-old male patient, weighing 80 kg and 165 cm tall, in a stable relationship with no children, residing in São Paulo, Brazil, and working as a video game developer, had recently traveled to the beach in São Paulo. He presented to the emergency department of a private hospital in São Paulo on February 26, 2024, with myalgia and fever of 38°C for five days. He was medicated, underwent laboratory tests for dengue, which returned negative, and was discharged with instructions and a prescription for oseltamivir 75 mg twice a day for three days, prednisone 20 mg/day, and symptomatic medications including naproxen for five days.

On February 28, 2024, he returned to the emergency department with persistent symptoms, general malaise, fever, myalgia, and liquid diarrhea averaging five episodes per day without pathological products. He was hypotensive, somnolent, and confused.

The patient has a medical history of febrile illness, headache, and lymphadenopathy at the age of 7, diagnosed as Kikuchi-Fujimoto disease (necrotizing lymphadenitis) via lymph node biopsy, treated and followed up. At the age of 8, he met laboratory criteria for SLE but had been in remission for approximately 20 years. Two months before the current admission, he developed photosensitivity in the anterior chest wall region, arthralgia, and cutaneous symptoms. He was being followed up at another service and was prescribed hydroxychloroquine 400 mg/day and azathioprine (AZA) 100 mg/day, which he started on February 14, 2024.

In the emergency room, the patient was in a generally poor condition, pale (2+/4+), hydrated, febrile, anicteric, tachypneic, acyanotic, somnolent, confused in time and space, tachycardic with a heart rate (HR) of 111 bpm, systolic blood pressure (SBP) of 83 mmHg, diastolic blood pressure (DBP) of 48 mmHg, mean arterial pressure (MAP) of 60 mmHg, respiratory rate (RR) of 24 breaths per minute, oxygen saturation ($SatO_2$) of 97% on 1 L/min nasal oxygen, and a temperature of 39.4°C. Physical examination of systems did not reveal any notable changes.

Laboratory tests upon admission showed acute kidney injury (KDIGO III), elevated lactate, metabolic acidosis, electrolyte disturbances including hyponatremia, hypomagnesemia, hypocalcemia, anemia, leukopenia, severe lymphopenia, toxic granulations in neutrophils, rare atypical lymphocytes, normal platelets, mildly prolonged aPTT and INR, elevated CRP, and positive dengue IgM with negative IgG serology. See Table 1 for detailed results.

A sepsis protocol was initiated, with fluid resuscitation at 30 ml/kg/h in the first hour, persistent hypotension refractory to fluids, initiation of vasopressor therapy with norepinephrine to maintain MAP > 65 mmHg, blood cultures and urine cultures collected, and antibiotics administered within the first hour. The patient was then transferred to the intensive care unit.

Diagnostic Hypotheses and Investigations

The following diagnostic hypotheses were considered, and further investigations were initiated:

1. Acute kidney injury (AKI) KDIGO III (baseline creatinine 1.27 and admission creatinine 4.46 mg/dL) associated with pancytopenia of unclear etiology.
2. Septic shock of abdominal origin.
3. Dengue fever, severe (hemorrhagic).
4. Suspected active SLE.
5. Thrombotic microangiopathy.

An immunological profile showed ANA (antinuclear antibody) nuclear fine speckled 1/80 + dense fine speckled cytoplasmic 1/160. Anti-RNP, anti-SM positive, and anti-protein P ribosomal positive (>200 U/mL). Consumed CH50, C3, and C4. Anti-DNA (double-stranded), anti-Ro, anti-La, rheumatoid factor, anticardiolipin IgM/IgG, and anti-beta 2 glycoprotein 1 IgM/IgG negative.

Regarding other relevant laboratory results, schistocytes negative, a direct Coombs test was positive. Haptoglobin was normal, and LDH was elevated. Anemia profile: ferritin 38,7 µg/L, transferrin saturation index (TSI) 76%, folic acid >20 ng/mL, vitamin B12 > 2000 ng/L.

Serologies for CMV, COVID-19, influenza A and B, hepatitis B, hepatitis C, HIV, syphilis, hepatitis A, Chikungunya, Rickettsia rickettsii, leptospirosis, cryptococcus, and histoplasma were negative. Epstein-Barr virus detected at less than 1200 copies. Respiratory virus and bacteria panel was negative.

Urinalysis demonstrated pH 5.5, density 1.024, proteinuria 0.75 g/L, glucose 0.5 g/L, leukocytes 43,000/mL, erythrocytes 96,000/mL, no casts. Protein/creatinine ratio in a single urine sample: 1.97 g/L.

On February 29, 2024, due to the refractoriness of clinical measures, worsening laboratory and hemodynamic status, hemodialysis was indicated using continuous veno-venous hemodiafiltration (CVVHDF) for the first 72 hours.

Specialist consultations in hematology and rheumatology were requested due to the patient's juvenile SLE with signs of active SLE (malar rash and photosensitivity) associated with severe acute febrile syndrome, generalized lymphadenopathy (cervical, supraclavicular, infraclavicular, axillary), diarrhea, acute tonsillitis, cytopenias, AKI KDIGO III, elevated transaminases, canalicular enzymes, and direct bilirubin, suggesting hepatocellular damage or cholestasis of undefined etiology. This was likely associated with systemic autoimmune dis-

ease activity and dengue virus infection. The possibility of secondary hemophagocytic syndrome due to azathioprine use, active lupus, or infection (dengue virus) was also considered.

Imaging and laboratory findings indicated acute cholecystitis and acute pancreatitis, initially managed conservatively by the digestive surgery team due to the absence of severe symptoms, broad-spectrum antimicrobial therapy, hemodynamic instability, and the severity of the case. Parenteral nutrition (PN) was initiated due to prolonged fasting.

On March 1, 2024, the patient developed respiratory distress. High-flow nasal cannula therapy was attempted without success, progressing to orotracheal intubation. Hemodynamic worsening necessitated broad-spectrum antibiotics (meropenem, teicoplanin, and doxycycline) and antifungal (anidulafungin) therapy.

Hematology advised managing blood dyscrasias with daily vitamin K for three days, then weekly; haemocompletan if fibrinogen <100; fresh frozen plasma if INR >1.5; platelet apheresis if platelets <50,000; and daily monitoring of PT, aPTT, and fibrinogen.

On March 6, 2024, given the patient's dengue Group D associated with renal and hepatic dysfunction, blood dyscrasias, and an Hscore of 99% probability for hemophagocytosis without clinical improvement despite all measures, an empirical therapy with dexamethasone 10 mg/m²/day for two weeks (followed by tapering), human immunoglobulin (IVIG) 0.4 g/kg (35 g/day) for five days, and weekly vitamin K was initiated. Bone marrow biopsy, myelogram, and immunophenotyping in CIPD were performed without complications, revealing a hypocellular marrow, more pronounced in the erythroid series, with no hemophagocytosis figures and no abnormal cell population. The biopsy showed hypocellular marrow with a global reduction of all series (average global around 25%), irregular distribution of hematopoietic tissue, predominance of megaloblastoid forms in the erythroid and granulocytic series, mild dysmegakaryocytopoiesis, stromal changes with serous atrophy, edema, interstitial hemorrhage, and fibrin deposits without fibrosis (MF-0).

On March 12, 2024, the patient developed spontaneous endotracheal bleeding, desaturation, and required 100% FiO_2. Bronchoscopy revealed a small amount of bloody secretion in the distal trachea without an evident active bleeding focus, likely alveolar hemorrhage secondary to dengue or SLE capillaritis. Bronchoalveolar lavage revealed galactomannan positive for aspergillosis, leading to a switch from anidulafungin to liposomal amphotericin B.

The patient experienced abdominal distension and refractory constipation, leading to a new total abdominal CT scan, showing extensive necrotizing pancreatitis with a five-week evolution, the largest necrotic collection approximately 314 mL near the pancreatic head, initially managed conservatively. A new chest CT showed areas of consolidation associated with fungal infection. One week later, a new control imaging revealed worsening peripancreatic collections, suspected pancreatic fistula, with continued conservative management. However, on April 7, 2024, control imaging revealed signs of non-occlusive intestinal ischemia, pancreatic tail necrosis, and multiple organized necrotic collections (552 mL), associated with clinical and

hemodynamic deterioration, increased vasopressor drugs, episodes of fever, abdominal distension, high gastric output, rising inflammatory markers and bilirubin, indicating the need for surgical intervention.

On April 8, 2024, the patient was taken to the operating room for pancreatic sequestrectomy and ascites drainage, with pathological material sent for analysis. He returned to the intensive care unit hemodynamically unstable, progressing to cardiorespiratory arrest in asystole, and ultimately passed away.

Table 1. Evolution of laboratory parameters.

	29/02	05/03	10/03	15/03	20/03	25/03	30/03	05/04	08/04
Hb (g/dL)	11,3	8,3	7,4	8,3	8,7	7,6	6,9	6,8	8,0
Ht (g/dL)	31,7	25	22	23,3	24,9	21,7	21	20,2	23,9
Leukocytes/mm³	1480		3820	9020	8210	12030	27260	9300	8330
Platelets (thousands/mm³)	101	66	64	88	53	56	90	68	63
International normalized ratio	1,4	0,92	0,97	0,96	1,2	1,1	1,2	1,1	1,1
Fibrinogen (mg/dL)	129	77	428	419					228
Activated partial thromboplastin clotting time (s)	49,5	28,6	23,7	27,4	30,3	32,9	34,7	33,4	36,4
Urea (mg/dL)	133		170	116	131	101	97	88	95
Creatinin (mg/dL)	5,53		2,32	1,47	1,24	0,96	1,14	0,97	1,03
Na (mEq/L)	128	130	131	142	144	136	138	141	137
K (mEq/L)	3,6	5,1	4,5	3,5	3,6	3,7	4,2	4,4	4,2
Mg (mg/dL)	1,3	2,3	2,2	2,2	2,2	2,2	2,2	1,9	2,2
Ca (mmol/L)	0,88	1,3	1,13	1,23	1,07	1,26	1,2	1,26	1,33
AST U/L	369		89	56	29		75	112	98
ALT U/L	122		46	43	36		34	40	108
Total bilirubin (mg/dL)	2,79	6,15	6,67	4,93	3,85	4,21	3,64	5,99	10,31
Direct bilirubin (mg/dL)	2,65	5,75	6,15	4,62	3,43	3,79	3,16	5,44	9,15
Indirect bilirubin (mg/dL)	0,14	0,4	0,52	0,31	0,42	0,42	0,49	0,55	1,16
Amilase U/L	337		175	63		165	158	152	108
Lipase U/L	117		254	159		57	91	62	75
Alkaline phosphatase U/L	227		238	197		221	360	421	529
Gamma glutamyl transferase U/L	474		395	277		214	326	806	797
Lactate dehydrogenase U/L	2249		1203	648		555	689		545
Lactate (mg/dL)	34		12	10	16	19	22	29	29
C-reactive protein (mg/dL)	16,03			7,55	21,2	13,7	8,67	11,1	20,2
pH (blood)	7,27	7,27	7,33	7,31	7,49	7,41	7,36	7,47	7,34
Bicarbonate (mmol/L)	11	23	16	29	37	24	24	28	22

Abbreviation SLE: Systemic Lupus Erythematosus

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Conflict of interest: None.

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