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Dengue in children and adolescents with onco-hematological disease: A case series

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ABSTRACT

Dengue is a viral disease transmitted mainly by the *Aedes aegypti* mosquito. Argentina has seen a significant increase in epidemics in recent years. Pediatric patients with oncohematological diseases are particularly vulnerable due to their immunosuppression, which can predispose them to severe cases. This report presents five clinical cases of pediatric patients with oncohematological diseases who developed dengue infection, illustrating the variability in its clinical presentation. Symptoms were heterogeneous, ranging from mild forms to severe cases with liver failure, bleeding, and the need for intensive care.

Early identification, close monitoring, and an interdisciplinary approach are key to management. This series of cases reinforces the need for active clinical surveillance for fever in an epidemiological context, even in the absence of typical symptoms.

Keywords: *dengue; pediatrics; immunosuppression; hematological neoplasms.*

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INTRODUCTION

Dengue is an infectious disease caused by the dengue virus (DENV), a member of the Flaviviridae family, and four serotypes affecting humans are recognized (DENV1-DENV4). Transmission occurs through mosquitoes of the genus Aedes, mainly *Aedes aegypti*.[1]

In Argentina, it occurs epidemically, with increases in cases during the warm months. According to the National Epidemiological Bulletin of the Ministry of Health, in the 2023-2024 season, more than 580 000 cases were reported, with a cumulative incidence of 1239 per 100 000 inhabitants, which is three times the number reported in the previous period.[2]

During the same period, the Hospital de Niños Pedro de Elizalde confirmed 205 cases, five of which were patients with oncohematological diseases admitted during the first four months of 2024.

This is a systemic viral infection that can be potentially serious. In patients with oncohematological diseases, the clinical presentation may resemble that of immunocompetent individuals, with a spectrum ranging from asymptomatic forms to hemorrhagic or shock symptoms. Manifestations such as fever, rash, thrombocytopenia, and abnormal liver function tests can be mistaken for adverse effects of antineoplastic treatment or other infectious complications, including febrile neutropenia of bacterial, viral, or fungal origin.[1]

Several international reports describe variable clinical presentations of dengue in patients with oncohematological disease, including those with a history of transplantation.[3-7] In this context, we present the local experience of five pediatric patients with oncohematological disease who developed dengue infection, to describe their clinical course and inform management of this population.

CLINICAL CASE 1

A 12-year-old girl was diagnosed with high-risk type B acute lymphoblastic leukemia in the consolidation phase. She received her last cycle of chemotherapy ten days before admission. She was admitted for high-risk febrile neutropenia associated with grade II mucositis and thrombocytopenia requiring transfusion (*Table 1*). Empirical broad-spectrum antibiotic therapy was indicated, with adjustment of the regimen due to the progression of mucositis and the onset of dysphagia.

On the fifth day of hospitalization, given the persistence of fever without an obvious source, a dengue panel was requested. IgM was positive, and polymerase chain reaction (PCR) was negative, confirming the infection. Laboratory tests showed persistent leukopenia and thrombocytopenia.

On the tenth day, the fever persisted, and abdominal pain was added. The ultrasound was normal. The liver function tests showed progressive elevation of transaminases and coagulation abnormalities (*Table 1*). She developed liver failure, neurological compromise, and hypoxemia; she required admission to the pediatric intensive care unit with mechanical ventilation for seven days and inotropes for five days.

During hospitalization, she presented with

Table 1. Laboratory parameters

Parameter	Case 1			Case 2		Case 3			Case 4		Case 5		
	D1	D5	D10	D1	D3	D1	D3	D8	D1	D3	D1	D8	D30
WBC (cells/mm³)	1400	700	3100	6000	3200	4400	3000	2300	550	3980	1200	2500	4300
Neutrophils (%)	88	–	95	75	41	74	78	44	–	84	30	73	60
Lymphocytes (%)	11	–	2	7	27	20	2	48	–	6	70	19	38
Hb (g/dL)	7.6	7.8	9.6	12	12.6	9.2	7.8	9	9.6	9.8	7	7.8	8.9
HCT (%)	22	23	28	35.2	37	27	23	27	29.8	30	21	23.4	27
Platelets (×10³/µL)	5	5	10	204	170	426	435	542	132	98	206	60	30
CRP (mg/L)	83	45	80	8.1	–	42	30	3	6	1	49	140	70
GOT (U/L)	47	33	1455	26	25	33	22	28	47	48	102	100	32
GPT (U/L)	59	50	1300	32	30	21	14	20	21	23	92	80	20

D: day; WBC: white blood cells; Hb: hemoglobin; HCT: hematocrit; CRP: C-reactive protein; GOT: glutamic oxaloacetic transaminase; GPT: glutamic pyruvic transaminase.

active bleeding requiring transfusion and fluid support. Management was interdisciplinary, with therapeutic adjustments based on clinical evolution and liver involvement. She remained afebrile, with negative cultures and progressive improvement. She resumed chemotherapy one month later.

CLINICAL CASE 2

A 16-year-old male adolescent with a recent diagnosis of central nervous system germ cell tumor (last cycle of chemotherapy twenty days before admission). He consulted for fever, headache, and myalgia. Initial hematological studies showed no significant abnormalities (*Table 1*), so empirical antibiotic therapy was indicated in the context of fever in a non-neutropenic cancer patient.

Given the persistent fever and epidemiological context, dengue tests were requested, which confirmed acute infection by detecting the NS1 antigen and a positive PCR result 72 hours after admission. Cultures were negative for bacteria; therefore, antibiotic therapy was discontinued, and symptomatic treatment was continued. The condition was classified as dengue without warning signs.

The patient progressed favorably. He presented with lymphopenia, mild hemoconcentration, and thrombocytopenia (*Table 1*). He was discharged after 96 hours with outpatient follow-up.

CLINICAL CASE 3

A 3-year-old girl with standard-risk type B acute lymphoblastic leukemia, in maintenance phase (last chemotherapy four weeks prior). She consulted for fever without neutropenia (*Table 1*). On physical examination, she presented with grade I mucositis as the only finding, so empirical antibiotic therapy was initiated. After 72 hours, she remained febrile and developed lesions consistent with herpes simplex infection and cellulitis on her index finger. Antimicrobial treatment was adjusted.

She was hospitalized without fever or microbiological findings. On the eighth day, she presented with a generalized pruritic maculopapular rash. Dengue infection was confirmed (NS1 and PCR positive) with lymphopenia as the only associated finding (*Table 1*). She remained stable and without warning signs; after 72 hours, she was discharged with outpatient follow-up.

CLINICAL CASE 4

A 9-year-old girl with right supraclavicular Ewing's sarcoma, last chemotherapy two weeks before admission. She was admitted for high-risk febrile neutropenia associated with headache and myalgia *(Table 1*). Cultures were obtained, and empirical antibiotic therapy was initiated. At 72 hours, due to persistent fever, a dengue panel was requested. Positive results for the NS1 antigen and PCR confirmed acute infection. The condition was classified as dengue without warning signs. She recovered from neutropenia and transient thrombocytopenia, with no other relevant laboratory abnormalities (*Table 1*). As she was afebrile, without warning signs, and with negative cultures, she was discharged on the fifth day of hospitalization with outpatient follow-up.

CLINICAL CASE 5

A 17-year-old male adolescent with type B acute lymphoblastic leukemia in recent extramedullary relapse. He had a history of multiple hospitalizations due to infectious complications, adverse effects of treatment, and poor pain control. Last chemotherapy seven days before admission.

He was admitted for severe pain in his left knee with functional impairment and a positive key sign. Intravenous analgesia was initiated, and diagnostic arthrocentesis was performed, with no microbiological rescue.

On the eighth day of hospitalization, he developed healthcare-associated pneumonia in the context of fever, lymphopenia, thrombocytopenia, and elevated C-reactive protein (*Table 1*). Empirical antibiotic coverage was initiated.

On the tenth day of hospitalization, given the persistence of fever, thrombocytopenia, and abdominal pain, and considering the epidemiological context, a dengue panel was requested, which confirmed acute infection by PCR. It was classified as dengue with warning signs, with a predominance of osteoarticular manifestations.

The patient progressed unfavorably, with fever, persistent joint pain, and multiple transfusion requirements. On the 20th day of hospitalization, septic arthritis was confirmed by isolation of *Escherichia coli* in joint fluid from the right hip, and treatment was adjusted according to the antibiogram.

Subsequently, he developed necrotizing fasciitis due to *Klebsiella pneumoniae* in his left

thigh, requiring multiple surgical debridements.

Thirty days after hospitalization, clinical improvement was noted, and by day 40, progressive normalization of laboratory parameters was documented (*Table 1*). He remained hospitalized to complete a prolonged course of intravenous antibiotic therapy for osteoarticular focus and to resume chemotherapy.

DISCUSSION

The growing incidence of dengue in Argentina poses a challenge in the treatment of immunocompromised patients, particularly those with oncohematological diseases, given their vulnerability and the heterogeneity of clinical presentation.[1]

The available evidence shows a greater number of international reports, mainly from Asian countries, where variable clinical forms have been reported, especially in patients with leukemia and transplant recipients.[3-7]

In the cases analyzed, wide clinical variability was observed, with presentations ranging from mild to severe forms (*Table 2*). In some patients, the initial presentation was attributed to cancer treatment, underlying disease, or a possible concomitant infection, which delayed the diagnosis of dengue. This finding is consistent with that described by Pereira et al., who also reported diagnostic delays in patients with hematological diseases for similar reasons.[7]

Thrombocytopenia was the most common hematological finding, present in 4 of 5 patients, with counts <20 000/µL in some, requiring transfusions. This finding is consistent with that reported by Ramzan et al. and Chuansumrit et al., who described marked platelet decreases in patients with leukemia undergoing treatment.[4,5]

Liver abnormalities were observed in two patients, one of whom had liver failure. This is consistent with the importance of liver involvement as a manifestation of dengue, regardless of immune status. In a national retrospective study of severe dengue, the liver was the most affected organ, with transaminases >1000 U/L in 60% of cases, and hepatomegaly was identified as a warning sign.[8,9]

All patients survived, although two had serious complications. Case 5 had a complex condition that was not directly attributed to dengue infection. These results differ from the 3.6% mortality reported by Chuansumrit et al. and are consistent with the reports by Ramzan et al. and Sharma et al., who did not record any deaths in their patient cohorts.[3-5]

The findings of this series provide information on the clinical behavior of dengue in pediatric patients with oncohematological disease and contribute to raising awareness of this presentation at the local level. Dengue infection in this population represents a diagnostic challenge that requires early suspicion, close monitoring, and interdisciplinary coordination to prevent complications and reduce morbidity and mortality.■

Table 2. Summary of cases

Case	Age (years)	Oncohematological diagnosis	Confirmation of dengue	Complications	Classification of dengue	Progression
1	12	Common B ALL HR - consolidation	IgM (+), CRP (-)	Liver failure, MV, PTT, active bleeding	Severe dengue	Favorable after intensive care
2	16	Germ cell tumor CNS - 1st CT cycle	NS1 (+), CRP (+)	None	No signs of alarm	Favorable, high at 96 hours
3	3	Common LLA B SR - maintenance	NS1 (+)	None	No warning signs	Favorable, discharge in 72 hours
4	9	Ewing's sarcoma	NS1 (+), CRP (+)	Thrombocytopenia	No warning signs of alarm	Favorable, discharge in 5 days
5	17	Common B ALL - extramedullary relapse	CRP (+)	Septic arthritis, necrotizing fasciitis	With warning signs of alarm	Torpid

ALL: acute lymphoblastic leukemia; HR: high risk; SR: standard risk; CT: chemotherapy; PICU: pediatric intensive care unit; CRP: polymerase chain reaction; NS1: nonstructural antigen 1 for dengue; PTT: pleural drainage tube; MV: mechanical ventilation.

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