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Severe parathyroid hormone-independent hypercalcemia in disseminated juvenile paracoccidioidomycosis mimicking a hematologic malignancy: a case report

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ABSTRACT

Background: Juvenile paracoccidioidomycosis (PCM) can resemble hematologic malignancy; severe hypercalcemia is an uncommon complication.

Case Presentation: A 9-year-old girl from urban southeastern Brazil presented with generalized lymphadenopathy, weight loss, hepatosplenomegaly, and skin lesions. Uncorrected total calcium was 15.4 mg/dL with albumin 2.4 g/dL, ionized calcium was 2.27 mmol/L, and parathyroid hormone (PTH) <4 pg/mL. Imaging suggested lymphoproliferative disease without relevant osseous abnormalities, but skin and lymph node histopathology demonstrated *Paracoccidioides* spp. Hypercalcemia persisted despite hydration and furosemide. A single zoledronic acid dose of 0.0125 mg/kg preceded antifungal initiation, and calcium was already decreasing before amphotericin B. She required ventilation and vasoactive support and developed reversible stage 1 acute kidney injury and asymptomatic hypocalcemia requiring oral supplementation. After approximately six weeks of amphotericin B lipid complex, she was discharged on trimethoprim-sulfamethoxazole. At nine months, no readmissions or clinical complications were reported; calcium had normalized during ongoing supplementation.

Conclusion: Disseminated juvenile PCM should be considered in children with a malignancy-like presentation and PTH-independent hypercalcemia. The mechanism remains unconfirmed; serial calcium and renal monitoring are essential.

Keywords: Paracoccidioidomycosis, hypercalcemia, child, lymphadenopathy, diagnosis, differential, critical care, case reports.

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Background

Paracoccidioidomycosis (PCM) is endemic in Latin America, particularly Brazil. Its acute/subacute juvenile form commonly involves lymph nodes, liver, spleen, and skin [1–3]. Severe hypercalcemia is unusual and can reinforce suspicion of malignancy [4–6]. We describe disseminated juvenile PCM with parathyroid hormone (PTH)-independent hypercalcemia, documenting treatment chronology, subsequent hypocalcemia, renal recovery, and outpatient follow-up.

Case Presentation

A previously healthy 9-year-old girl from a peripheral urban neighborhood in metropolitan São Paulo, southeastern Brazil, developed progressive lymphadenopathy, hyporexia, fatigue, and a 6-kg weight loss over 3 months. Fever, vomiting, and nodular and pustular skin lesions followed. Rural residence, agricultural exposure, and relevant travel were not documented. She was dehydrated, tachycardic, and tachypneic, with generalized lymphadenopathy and hepatosplenomegaly. Hospital and pediatric intensive care unit admission define hospital day (HD) 1; emergency evaluation occurred the preceding day.

Hemoglobin was 8.6 g/dL, leukocytes 18,060/mm^3, eosinophils 2,709/mm^3, platelets 469,000/mm^3, and C-reactive protein 234.7 mg/L. Initial total calcium was 15.4 mg/dL, uncorrected for albumin (2.4 g/dL). Conventional retrospective albumin adjustment yields approximately 16.7 mg/dL, but severe hypercalcemia was

independently confirmed by ionized calcium 2.27 mmol/l on HD1. PTH was <4 pg/ml on HD1-2. Serial biochemical results are provided in Tables 1 and 2. Calcitriol was not measured; PTH-related peptide testing was unavailable locally.

Computed tomography demonstrated generalized lymphadenopathy and splenomegaly, without relevant osseous abnormalities, suggesting lymphoproliferative disease. Bone marrow examination showed no neoplasia. Cervical lymph node and skin biopsies revealed suppurative granulomas, multinucleated giant cells, and multiple budding yeasts highlighted by periodic acid-Schiff and Grocott stains, consistent with *Paracoccidioides* spp. (Figure 1). Species-level identification was unavailable. Figure 2 shows the cutaneous manifestations.

Intravenous hydration at 3,000 ml/m^2/day was administered on HD1-6. Furosemide was given at 1 mg/kg/day on HD1-2, increased to 40 mg/day on HD3, and discontinued on HD7. Persistent hypercalcemia, initially considered malignancy-associated, prompted nephrology-recommended zoledronic acid: one dose of 0.0125 mg/kg infused over one hour on HD5 (weight 29 kg). No repeat dose was given. A more specific rationale for dose selection was not documented. Total calcium decreased to 13.2 and 12.4 mg/dL on HD6 and HD7, before antifungal initiation.

Amphotericin B deoxycholate 1 mg/kg was administered on HD9 while Ministry of Health authorization for the lipid complex formulation was requested. Amphotericin B lipid complex 5 mg/kg/day was then administered without interruption from HD10 to HD52, approximately six weeks, with duration determined by the hospital infection control team. The change followed access to the requested formulation; toxicity was not documented as the reason. Invasive ventilation was required on HD9-31, with vasoactive/inotropic support during the critical phase.

The nephrology team classified acute kidney injury as Kidney Disease: Improving Global Outcomes (KDIGO) stage 1. Creatinine peaked at 1.62 mg/dl on HD3, before

Table 1. *Calcium and renal course with treatment chronology.*

HOSPITAL DAY	TOTAL CALCIUM (MG/DL)	IONIZED CALCIUM (MMOL/L)	CREATININE (MG/DL)	CONTEXT
Pre-admission	15.4	—	1.06	Emergency evaluation; albumin 2.4 g/dl
1	15.4	2.27	—	Hydration and furosemide started
3	—	—	1.54 / 1.62	Morning / afternoon creatinine; peak 1.62
5	—	—	—	Single zoledronic acid dose
6	13.2	—	1.13	Last day of hyperhydration
7	12.4	1.81	0.83	Furosemide discontinued
9	10.4	1.58	—	One dose amphotericin B deoxycholate
10	—	—	0.78	Amphotericin B lipid complex started
11	9.2	1.33	1.04	Ionized calcium remained elevated
13	7.4	1.18	1.22	Low total calcium; ionized within range
17	7.3	1.05	1.07	Calcium nadir; albumin 2.8 g/dl
22	—	—	1.29	Creatinine fluctuation during treatment
25	8.8	—	0.93	Transient total calcium normalization; albumin 3.1
26	—	—	0.73	Renal improvement
30	7.4	1.12	—	Recurrent hypocalcemia; calcium carbonate started
31	8.2	—	—	Below total calcium reference interval
33	—	—	0.38	25-hydroxyvitamin D 16 ng/ml
34	—	—	—	Weekly cholecalciferol started
46	8.4	—	—	Below total calcium reference interval
47	8.8	—	—	Total calcium normalized on supplementation
52	—	—	—	Hospital discharge; oral antifungal therapy
13 days after discharge	—	—	0.46	PTH 82.8 pg/ml
5 months after discharge	9.7	—	0.50	25-hydroxyvitamin D 34 ng/ml; supplements ongoing

HD1 denotes hospital admission. Pre-admission measurements were obtained one day earlier. —: result unavailable for that time point. Laboratory reference intervals: total calcium 8.8–10.8 mg/dL; ionized calcium 1.15–1.29 mmol/l. All listed total calcium values are uncorrected. The retrospective admission estimate is 15.4 + 0.8 × (4.0–2.4) = 16.68 mg/dl; this estimate does not replace measured ionized calcium. Follow-up intervals are approximate.

Table 2. *Additional biochemical characterization.*

MEASUREMENT	TIMING	RESULT
Albumin (g/dl)	Pre-admission; HD17; HD25	2.4; 2.8; 3.1
Phosphate (mg/dl)	Pre-admission; HD1; HD2	5.4; 5.5; 5.2
Magnesium (mg/dl)	HD1; HD2	2.00; 1.69
Urea (mg/dl)	Pre-admission; HD2; HD3	38; 44; 50
Alkaline phosphatase (U/l)	HD3	242
PTH (pg/ml)	HD1; HD2; 13 days after discharge	<4; <4; 82.8
25-hydroxyvitamin D (ng/ml)	HD4; HD33; 5 months after discharge	19.5; 16; 34
1,25-dihydroxyvitamin D	—	Not measured
PTH-related peptide	—	Not measured; assay unavailable locally

HD = hospital day; PTH = parathyroid hormone. Urea values denote total urea, not blood urea nitrogen.

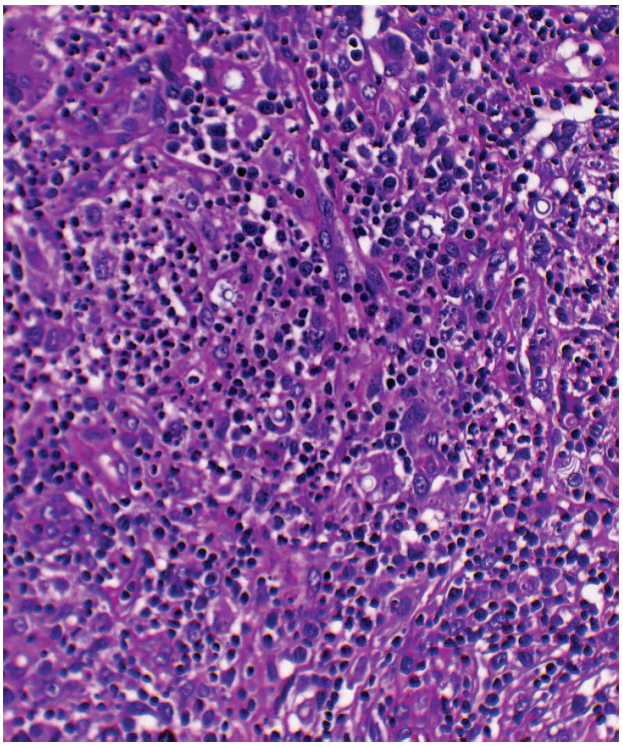


Figure 1. *Cervical lymph node histopathology showing round, thick-walled fungal structures morphologically compatible with Paracoccidioides spp. within a granulomatous inflammatory infiltrate (hematoxylin and eosin; original magnification ×400).*



Figure 2. *Erythematous-violaceous infiltrated plaques on the upper limb at presentation. The clinical photograph was previously cropped to remove identifying elements.*

zoledronic acid and amphotericin B. No pre-illness baseline was available. There was no oliguria, anuria, or dialysis. Creatinine fell to 0.78 mg/dl on HD10, fluctuated between 0.93 and 1.29 mg/dl on HD11-25, and decreased to 0.73 mg/dl on HD26 and 0.38 mg/dl on HD33. Height was unavailable for estimating glomerular filtration rate.

Asymptomatic hypocalcemia followed. The lowest documented total and ionized calcium values were 7.3 mg/dL and 1.05 mmol/l on HD17 (albumin 2.8 g/dl). Total calcium transiently normalized on HD25, but total and ionized calcium were again low on HD30. Calcium carbonate 1 g/day was started that day; intravenous calcium was not required. Cholecalciferol 50,000 IU weekly was started on HD34 for three weeks. Total calcium first returned to the reference interval after recurrence on HD47; intervening measurements do not establish continuous hypocalcemia.

She left intensive care on HD35 and was discharged on HD52. Discharge medications were trimethoprim-sulfamethoxazole 160/800 mg orally every 12 hours (10 ml of suspension containing 80/400 mg per 5 ml), calcium carbonate 500 mg/day, and cholecalciferol 2,000 IU/day. Calcium carbonate doses denote salt mass. At nine-month follow-up, all three medications continued without a defined antifungal stop date. Weight increased from 25 to 29 kg,

with no readmissions or reported complications. Five-month laboratory results showed calcium 9.7 mg/dl, creatinine 0.50 mg/dL, and 25-hydroxyvitamin D 34 ng/ml. Detailed follow-up of individual lesions was unavailable.

A summary of the case, including clinical presentation, investigations, treatment, complications, and outcomes, is provided in Table 3.

Discussion

Both suppressed PTH and markedly elevated ionized calcium support PTH-independent hypercalcemia. Albumin correction is imperfect in critical illness; direct ionized calcium measurements strengthen interpretation [7]. Hypercalcemia has been reported in PCM with osteolysis and with kidney injury [4–6]. Here, no osseous abnormality was documented. Granuloma-associated extrarenal calcitriol production is biologically plausible, but neither calcitriol nor PTH-related peptide was measured. Low 25-hydroxyvitamin D does not establish the mechanism, which remains unresolved.

This presentation illustrates the overlap between juvenile PCM and hematologic malignancy. Tissue examination established the diagnosis despite nonspecific imaging and marked systemic involvement [1–3]. Urban residence does not exclude PCM: juvenile cases have been described in São Paulo urban residents, and southeastern Brazil remains an established endemic setting [8,9]. Deficient sanitation indicates social vulnerability but does not establish the source of fungal exposure.

The chronology prevents attributing calcium normalization solely to antifungal therapy: calcium fell after hydration, furosemide, and zoledronic acid, before amphotericin B. Treatment of the underlying infection may have contributed to later control, but individual effects cannot be separated. Amphotericin induction followed by oral trimethoprim-sulfamethoxazole is consistent with management options for severe pediatric PCM [1,3].

The selected zoledronic acid dose has been studied as a lower initial dose in children with bone disorders to reduce hypocalcemia [10]. This provides pediatric dosing context, not evidence of a PCM-specific protocol or proof of the treating team's reasoning. Subsequent hypocalcemia was temporally associated with treatment; low vitamin D and critical illness complicate causal attribution. Continued outpatient calcium and vitamin D preclude claiming sustained normocalcemia without supplementation.

Peak creatinine preceded both potentially nephrotoxic treatments. Later fluctuations occurred during amphotericin exposure but cannot establish drug-induced injury. Recovery without dialysis and subsequent creatinine of 0.46–0.50 mg/dL are reassuring. Remaining limitations include absent pre-illness creatinine, calcitriol, and PTH-related peptide measurements, species identification, and detailed lesion follow-up. Clinical stability during ongoing antifungal treatment does not establish definitive cure.

Conclusion

Juvenile PCM belongs in the differential diagnosis of malignancy-like illness with severe PTH-independent hypercalcemia in endemic settings. Histopathology establishes the infection; serial biochemical assessment clarifies treatment response and complications. A calcitriol-mediated mechanism remains a hypothesis in this case.

What is new?

Severe parathyroid hormone-independent hypercalcemia can accompany disseminated juvenile paracoccidioidomycosis even without radiographic osteolysis and may mimic hematologic malignancy. In children from endemic regions, generalized lymphadenopathy, hepatosplenomegaly, skin lesions, and suppressed-parathyroid-hormone hypercalcemia should prompt early tissue biopsy for fungal disease.

Acknowledgments

None.

List of Abbreviations

HD	Hospital day
KDIGO	Kidney Disease: Improving Global Outcomes
PCM	Paracoccidioidomycosis
PTH	Parathyroid hormone

Conflict of interest

The authors declare that they have no conflicts of interest regarding the publication of this case report.

Funding

None.

Consent for publication

Written informed consent for publication was obtained from the patient's mother and legal guardian. Patient assent was not obtained during critical illness because her condition precluded participation. Clinical information was de-identified.

Ethical approval

The Research Ethics Committee of Casa de Saúde Santa Marcelina approved this report on July 20, 2026 (CAAE 99090426.8.0000.0066; approval No. 8.596.895).

Declaration of generative artificial intelligence use

The authors used ChatGPT (OpenAI) for English-language drafting, editing, and organization. The authors reviewed and revised the output and take responsibility for verifying the clinical data, references, and final manuscript.

Patient perspective

A patient perspective was not obtained during critical illness.

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Table 3. *Summary of the case.*

ITEM	DESCRIPTION
Patient	Female, 9 years old
Final diagnosis	Disseminated juvenile PCM with severe PTH-independent hypercalcemia
Presentation	Weight loss, fever, lymphadenopathy, hepatosplenomegaly, skin lesions, and a malignancy-like presentation
Investigations	Computed tomography, bone marrow examination, skin and cervical lymph node biopsies, serial calcium and renal measurements
Treatment	Hydration, furosemide, single-dose zoledronic acid, amphotericin B, oral trimethoprim-sulfamethoxazole, calcium carbonate, and cholecalciferol
Complications	KDIGO stage 1 acute kidney injury; asymptomatic hypocalcemia
Outcome	No readmissions or reported complications through nine months; ongoing antifungal therapy and calcium/vitamin D supplementation
Specialties	Pediatric critical care, infectious diseases, nephrology, and pathology