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Divergent Myeloid Transformation in Genetically Confirmed Chediak– Higashi Syndrome–Associated Hemophagocytic Lymphohistiocytosis: A Two-Case Series and Literature Review

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Case Report

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Abstract

We describe two genetically confirmed pediatric patients with Chediak–Higashi syndrome (CHS) who initially presented with hemophagocytic lymphohistiocytosis (HLH) and subsequently developed distinct myeloid malignancies. Clinical, morphologic, immunophenotypic, cytogenetic, molecular, and genetic findings were retrospectively reviewed, and the diagnosis of CHS was confirmed by identification of pathogenic LYST variants in both patients. Both patients initially responded to HLH-directed therapy with etoposide and dexamethasone but subsequently underwent divergent myeloid transformation, with one patient developing non-M3 acute myeloid leukemia (AML) and the other developing PML::RARA-positive acute promyelocytic leukemia (APL). A review of the published literature indicates that leukemic transformation in CHS is exceptionally rare and demonstrates heterogeneous clinical and biological features. These two cases expand the limited evidence regarding myeloid malignancy arising in genetically confirmed CHS and highlight the potential interplay between inherited lysosomal trafficking defects, chronic immune dysregulation, inflammatory bone marrow stress, and therapeutic exposures in clonal myeloid evolution. Long-term hematologic surveillance, including timely bone marrow reassessment in patients with persistent or recurrent cytopenias following HLH, may facilitate earlier recognition of malignant transformation.

Introduction

CHS is a rare autosomal recessive immunodeficiency caused by pathogenic variants in the LYST gene, resulting in defective lysosomal trafficking and abnormal cytoplasmic granule formation [1, 3] Impaired vesicular transport compromises the cytotoxic function of natural killer (NK) cells and cytotoxic T lymphocytes (CTLs), leading to the characteristic accumulation of giant lysosomal inclusions. Clinically, CHS is characterized by oculocutaneous albinism, recurrent infections, cytopenias, and progressive immune dysregulation [2, 3].

HLH represents one of the most severe complications of CHS and is a major determinant of morbidity and mortality [3, 4]. Defective cytotoxic lymphocyte function results in uncontrolled immune activation and sustained cytokine signaling, typically manifesting with persistent fever, cytopenias, hyperferritinemia, hepatosplenomegaly, and other features of systemic inflammation [4, 15, 22]. In CHS, impaired lysosomal trafficking directly contributes to defective granule-mediated cytotoxicity and predisposition to HLH [3, 4].

Although HLH is primarily recognized as an acute hyperinflammatory disorder, persistent immune activation may have broader effects on hematopoietic homeostasis [8, 22]. Chronic inflammatory signaling can impose proliferative and oxidative stress on hematopoietic stem and progenitor cells and may promote genomic and epigenetic alterations associated with clonal evolution [8, 19]. Similar interactions between chronic inflammation, hematopoietic stress, and myeloid neoplasia have been proposed in other inflammatory and immunodeficiency disorders. In CHS, the combination of inherited lysosomal dysfunction and prolonged inflammatory activation may therefore create a biologic environment permissive for secondary myeloid transformation [1, 8, 19].

Therapeutic exposure may represent an additional contributing factor. Etoposide, a topoisomerase II inhibitor widely used in the treatment of HLH, induces DNA double-strand breaks and has been associated with therapy-related myeloid neoplasms [6, 7, 18]. However, the development of AML following etoposide exposure in an individual patient cannot be attributed to treatment alone, particularly when pre-existing genetic and inflammatory abnormalities may independently contribute to clonal selection [6, 7, 19].

The genomic classification of myeloid neoplasms further emphasizes the biological heterogeneity of AML and the importance of molecular characterization in distinguishing distinct leukemic entities [5, 12, 13]. Recurrent genetic abnormalities play an important role in AML classification and disease biology [20]. In this context, the occurrence of different AML phenotypes in patients with the same inherited immunodeficiency may provide an opportunity to explore the complex interaction between constitutional genetic defects, chronic immune dysregulation, inflammatory marrow stress, and treatment-related genotoxicity.

Here, we describe two pediatric patients with genetically confirmed CHS who developed distinct myeloid malignancies following CHS-associated HLH. One patient evolved to non-M3 acute myeloid leukemia following prolonged exposure to etoposide, whereas the second developed molecularly confirmed PML::RARA-positive acute promyelocytic leukemia. By integrating longitudinal clinical, morphologic, immunophenotypic, cytogenetic, and molecular findings with a review of the available literature, we highlight the rarity and biological heterogeneity of leukemic transformation in CHS and propose potential mechanisms linking inherited lysosomal dysfunction, persistent inflammation, and myeloid clonal evolution.

Case presentation 1

In March 2022, a 9-year-old girl presented with persistent fever, marked pallor, progressive fatigue, and significant splenomegaly. Laboratory evaluation revealed pancytopenia, marked hyperferritinemia and elevated C-reactive protein, together with relative lymphocytosis, neutropenia, elevated liver enzymes, and lactate dehydrogenase, indicating substantial systemic inflammatory activity. Elevated LDH may accompany severe systemic disease and may have diagnostic or prognostic relevance in hematologic and inflammatory disorders [14]. Peripheral blood smear demonstrated characteristic giant azurophilic granules within leukocytes, raising strong suspicion for CHS with secondary HLH [3, 4].

During the subsequent weeks, pancytopenia persisted and progressively worsened, accompanied by increasing ferritin and triglyceride levels and abnormalities in fibrinogen, supporting ongoing hyperinflammation [4, 15, 22]. Progressive splenomegaly was documented on serial imaging. Cerebrospinal fluid examination was unremarkable, with no evidence of central nervous system involvement. The combination of persistent cytopenias, hyperinflammation, splenomegaly, and characteristic marrow abnormalities supported the diagnosis of CHS-associated HLH, and HLH-directed therapy was initiated [4, 15, 22] [Figure 1].

Given the clinical suspicion of an inherited immune dysregulatory disorder and the association of HLH with pathogenic variants in genes involved in cytotoxic lymphocyte function, whole-exome sequencing was performed to investigate potential genetic causes [16]. Whole-exome sequencing identified a homozygous pathogenic LYST variant (NM_000081.4, exon 25, c.7159C > T, p.R2387X), confirming the diagnosis of CHS [1, 3]. The broad spectrum of pathogenic LYST variants and their relationship with the clinical manifestations of CHS have been comprehensively described [1, 3]. A heterozygous pathogenic MMACHC variant (NM_015506.3, exon 4, c.616C > T, p.R206W; rs538023671) was also identified. Its clinical relevance to the patient's phenotype was uncertain, and no established association with the patient's CHS phenotype was identified [17].

The patient received etoposide-based HLH therapy with systemic dexamethasone according to established treatment protocols [11, 18]. She demonstrated progressive hematologic and clinical improvement, accompanied by declining inflammatory markers and substantial regression of splenomegaly. Etoposide was continued through multiple treatment cycles, with the final dose administered in April 2025. At completion of therapy, she remained clinically stable without evidence of central nervous system involvement.

In September 2025, several months after completion of HLH-directed therapy, the patient developed recurrent and progressively worsening cytopenias. Unlike her initial presentation, there was no prominent biochemical evidence of HLH reactivation. A small subpleural pulmonary micronodule with respiratory symptoms was also identified, initially raising concern for an infectious process. However, persistent marrow suppression prompted repeat bone marrow evaluation in October 2025.

Bone marrow examination demonstrated approximately 80% blasts among nucleated cells, consistent with acute leukemic transformation. Flow cytometry showed a predominantly myeloid phenotype, with expression of MPO (79%), CD33 (55%), CD117 (45%), CD13 (40%), HLA-DR (80%), and CD11a (60%), while CD34 was expressed in only 5% of cells. The blast population was largely negative for lymphoid and other lineage-defining markers, supporting myeloid differentiation. Immunophenotypic characterization is central to establishing lineage and defining the phenotype of AML [23].

Cytogenetic and molecular studies were negative for recurrent AML-associated abnormalities, including RUNX1::RUNX1T1, PML::RARA, CBFB::MYH11, and BCR::ABL1, supporting a diagnosis of acute myeloid leukemia without defining recurrent genetic abnormalities (AML, non-M3) [5, 12, 13, 20] [Table 1].

Table 1
Timeline of Case 1

Date	Clinical Event	Laboratory Findings	Imaging / Pathology	Intervention	Outcome
March 2022	Initial presentation at age 9 with pallor, fever, splenomegaly	Ferritin 368.5 ng/mL; CRP 85 mg/L; Pancytopenia: WBC 2.2×10³/μL, RBC 3.4×10⁶/μL, Hb 7.5 g/dL, Hct 25.6%, PLT 46×10³/μL; Neutrophils 10%, Lymphocytes 66%, Blasts 22%; AST 107 U/L, ALT 144 U/L, LDH 704 U/L	Peripheral smear: giant azurophilic granules (consistent with CHS); Spleen 210×100 mm	Hospital admission	Suspicion of CHS with secondary HLH
March 2022	Worsening cytopenia; mild viral pneumonia	WBC 1.9×10³/μL; RBC 3.68×10⁶/μL; Hb 9 g/dL; PLT 27×10³/μL; Ferritin 693.1 ng/mL; Triglycerides 282 mg/dL; Fibrinogen 582 mg/dL; Perforin expression 61%	Liver normal; Spleen 225×54 mm; BM flow cytometry: CD33 70%, CD11b 50%, CD15 45%, HLA-DR 37%, CD34 0.5%; CSF negative for malignant cells	HLH-directed therapy initiated (Etoposide + Dexamethasone)	Diagnosis confirmed: HLH secondary to CHS
March 2022	Genetic confirmation	WES: Homozygous LYST c.7195C > T (p.R2387X); Heterozygous MMACHC c.616C > T (p.R206W)	—	Genetic counseling	Molecular confirmation of Chediak–Higashi syndrome
July 2022	Hematologic improvement	Gradual CBC recovery	Spleen reduced to 150×55 mm	Continuation of etoposide cycles	Partial remission of HLH
August 2023	Continued response	Stable blood counts	Spleen 139×42 mm	Ongoing therapy	Sustained remission
April 2025	Completion of HLH protocol	Stable hematologic profile	—	Final etoposide dose administered	Clinical stability maintained
July 2025	Recurrence of pancytopenia	WBC 1.9×10³/μL; RBC 4.12×10⁶/μL; Hb 10.4 g/dL; Hct 31.3%;	—	Further monitoring	Hematologic relapse

Date	Clinical Event	Laboratory Findings	Imaging / Pathology	Intervention	Outcome
		PLT 120×10³/μL			
September 2025	Severe pancytopenia with infection and bleeding	WBC 1.1×10³/μL; RBC 3.4×10⁶/μL; Hb 8.4 g/dL; Hct 28.4%; PLT 40×10³/μL; CRP 38→52 mg/L	CT scan: tiny subpleural solid micronodule in apical segment of RUL; Spleen > 200 mm	Hospitalization; infection management	Clinical deterioration
October 2025	Bone marrow re-evaluation	80% blast gate; MPO 79%; CD11a 60%, CD13 40%, CD33 55%, CD117 45%, CD34 5%, HLA-DR 80%, TdT 5%; Ferritin 5000 ng/mL; Fibrinogen 42 mg/dL;	Cytogenetics negative for t(8;21), inv(16), t(15;17), t(9:22)	Diagnosis of AML	Secondary AML transformation

Although prolonged etoposide exposure is a recognized risk factor for therapy-related myeloid neoplasms, the relationship between cumulative exposure and leukemic transformation is complex and influenced by host-specific biological factors [6, 7, 18, 19]. In this patient, AML developed in the setting of genetically confirmed CHS, prolonged inflammatory stress, and extensive HLH-directed therapy. Therefore, the leukemic transformation cannot be attributed to etoposide exposure alone and is more appropriately interpreted within a multifactorial framework involving inherited lysosomal dysfunction, chronic immune activation, marrow stress, and potential therapy-related genotoxic injury [6, 8, 19].

Case presentation 2

In October 2019, an 8-month-old boy presented with persistent fever, reduced activity and responsiveness, and hepatosplenomegaly. Laboratory evaluation revealed pancytopenia with relative lymphocytosis, mild hyponatremia, and modest elevation of hepatic transaminases, suggesting significant systemic and hematologic involvement. Hyponatremia may accompany severe systemic disease, although its clinical interpretation should remain contextual [21]. Bone marrow aspiration and biopsy showed a normocellular marrow with prominent hemophagocytosis and approximately 80% cellularity, supporting the diagnosis of HLH [4, 15, 22].

Flow cytometric evaluation demonstrated a mixed lymphoid–myeloid population. Within the evaluated population, myeloid-associated markers included CD33 (62%) and CD18 (85%), while CD117 and CD13 were detected in only 0.2% and 10% of cells, respectively. The lymphoid compartment showed predominantly T-cell features, with CD3 expression in 50%, CD7 in 41%, and CD8 in 35% of cells. Morphologic examination additionally identified basophilic cytoplasmic inclusions compatible with CHS granules. Together with the clinical presentation and prominent hemophagocytosis, these findings raised suspicion for an underlying lysosomal trafficking disorder [3].

Targeted genetic evaluation subsequently identified a pathogenic variant in the LYST gene, establishing the diagnosis of CHS. Abdominal ultrasonography confirmed marked hepatosplenomegaly. Biochemical evaluation demonstrated hyperinflammation, including ferritin levels exceeding 1200 ng/mL, hypertriglyceridemia, and hypofibrinogenemia, while cerebrospinal fluid examination was unremarkable. The overall clinical, laboratory, morphologic, and genetic findings supported a diagnosis of CHS-associated HLH [3, 4, 15, 22].

HLH-directed therapy with etoposide and dexamethasone was initiated, resulting in gradual clinical and hematologic improvement [11, 18]. Serial ultrasonography demonstrated a substantial reduction in splenic size by January 2020. Treatment was subsequently continued on an outpatient basis with maintenance etoposide, and the patient achieved partial remission with sustained clinical stability.

In October 2023, approximately four years after the initial presentation, the patient developed recurrent splenomegaly, rising ferritin levels, and recurrent hypofibrinogenemia, consistent with reactivation of HLH. Given the history of chronic inflammatory disease and previous cytotoxic exposure, repeat bone marrow evaluation was performed to distinguish recurrent HLH from possible clonal hematologic evolution.

Bone marrow examination demonstrated approximately 33% abnormal promyelocytes. Flow cytometry identified a dominant mononuclear population comprising approximately 89% of analyzed cells, with strong expression of myeloid-associated markers CD13 (82%), CD33 (83%), CD117 (80%), CD64 (81%), and CD123 (81%). CD34 was expressed in 18% of cells, whereas HLA-DR was detected in only 8%. Cytochemical staining demonstrated strong MPO positivity, supporting myeloid differentiation and raising suspicion for an acute myeloid neoplasm [23].

Morphologic examination confirmed prominent abnormal promyelocytes, some containing cytoplasmic inclusions morphologically compatible with CHS granules. Molecular analysis of bone marrow by RT-PCR subsequently demonstrated a PML::RARA fusion transcript, specifically the bcr1 (long-type) isoform, establishing the diagnosis of APL [24] [Table 2]. The occurrence of APL in the setting of genetically confirmed CHS and recurrent HLH represents an exceptionally uncommon clinical evolution.

Table 2
Timeline of Case 2

Date	Clinical Event	Laboratory Findings	Imaging / Pathology	Intervention	Outcome
October 2019	Initial presentation at age 8 months with persistent fever	WBC 3.1×10³/μL; RBC 2.93×10⁶/μL; Hb 7.4 g/dL; Hct 22.7%; PLT 32×10³/μL; Lymphocytes 77%; Sodium 131 mEq/L; Mildly elevated liver enzymes (~ 40 U/L)	Ultrasound: Hepatomegaly (107 mm); Splenomegaly (122×29 mm)	Hospital admission	Suspicion of marrow dysfunction
Late October 2019	Bone marrow evaluation	Ferritin > 1200 ng/mL; Fibrinogen 131mg/dL; Triglycerides 638 mg/dL	BM biopsy: Normocellular marrow (~ 80%) with marked hemophagocytosis → consistent with HLH; Flow cytometry: 30% lymphocytes, 60% myeloid population with basophilic cytoplasmic inclusions resembling CHS	Diagnosis: HLH secondary to suspected CHS	HLH confirmed
Late October 2019	CSF analysis	No malignant cells	CNS not involved	—	CNS disease excluded
October 2019	Initiation of HLH protocol	—	—	Etoposide + Dexamethasone started	Gradual clinical and hematologic improvement
January 2020	Follow-up imaging	Ferritin declining	Splenic size reduced to 93×31 mm	Continued outpatient etoposide	Partial remission achieved
October 2023	Clinical relapse	Ferritin > 1200 ng/mL; Fibrinogen 151 mg/dL	Ultrasound: Splenomegaly progressed to 170×40 mm	Re-evaluation initiated	HLH relapse suspected
Late 2023	Bone marrow re-evaluation	Immunophenotype: CD13+, CD33+, CD34 (subset)+, CD45+, CD64+, CD117+, CD123+; MPO positive	BM smear: 33% leukemic promyelocytes; numerous Chédiak–Higashi inclusion bodies; Molecular: PML-RARA (bcr1, L-type transcript) positive by RT-PCR	Diagnosis: **APL**	Leukemic transformation confirmed
Early 2024	AML-M3 treatment initiated	—	—	Standard APL protocol initiated	Initial response achieved
~ 3 months later (2024)	Acute clinical deterioration	Fever, tachypnea, jaundice	Suspected severe pulmonary opportunistic infection; Gastroenterology consult: suspected veno-occlusive disease (VOD)	Broad-spectrum antibiotics + supportive care	Progressive respiratory failure

Date	Clinical Event	Laboratory Findings	Imaging / Pathology	Intervention	Outcome
2024	Terminal event	Severe hypoxia; cardiopulmonary arrest	—	Full resuscitative efforts	Patient expired

The patient received AML-M3-directed therapy. Approximately three months after initiation of treatment, however, he developed acute clinical deterioration characterized by high-grade fever, tachypnea, progressive jaundice, and pulmonary involvement. Clinical and radiologic findings raised concern for an opportunistic infectious process in the setting of severe immunosuppression. Concurrent evaluation also raised the possibility of hepatic veno-occlusive disease, a serious complication associated with endothelial injury and poor clinical outcomes [25].

Despite intensive supportive care and broad-spectrum antimicrobial therapy, the patient's respiratory status progressively deteriorated, with refractory hypoxemia and increasing respiratory distress. He subsequently developed cardiopulmonary arrest and died despite attempted resuscitation, with the clinical course ultimately complicated by multiorgan failure.

Discussion

CHS is an inherited immunoregulatory disorder in which pathogenic LYST variants impair lysosomal trafficking and cytotoxic granule exocytosis, predisposing patients to persistent immune activation and HLH [1, 3]. Although HLH is a well-recognized and potentially life-threatening accelerated phase of CHS, progression to myeloid malignancy appears to be exceptionally rare. Reports describing LYST-associated disease and HLH illustrate the complex relationship between LYST dysfunction and hematologic complications [1, 9, 10, 26].

A review of the published literature identified only a limited number of reports describing AML in patients with LYST alterations before the present report. In particular,Wu et al. reported a case of AML complicated by hemophagocytic lymphohistiocytosis, further illustrating the clinical association between AML and HLH [26]. Other reports have described LYST mutations associated with HLH and other hematologic malignancies, further emphasizing the potential clinical overlap between inherited immune dysregulation and hematologic neoplasia [9, 10] [Table 3].

Table 3
Published cases of leukemia arising in patients with CHS or LYST mutation

Author	Year	Age	Sex	LYST mutation	CHS status	HLH	Leukemia	Cytogenetics	Outcome
Wu et al. (57)	2018	15	F	Compound heterozygous	Heterozygous LYST variants; CHS not clinically established	✓	AML	t(8;21;22)	Alive after HSCT
Present Case 1	2026	9	F	p.Arg2387Ter	Clinically and genetically confirmed CHS	✓	Non-M3 AML	Normal karyotype	Alive
Present Case 2	2026	8 months	M	Homozygous LYST	Clinically and genetically confirmed CHS	✓	PML::RARA APL	t(15;17)	Died

In contrast, several reports have described pseudo-Chediak–Higashi anomaly in leukemia, an acquired morphologic phenomenon resembling CHS granules but not representing germline CHS. Reported leukemic phenotypes have included acute promyelocytic leukemia, including the hypogranular variant, and other myeloid or lymphoid malignancies [27–30]. These entities should therefore be distinguished from genetically confirmed CHS-associated leukemic transformation.

An important distinction exists between the previously reported Wu et al. case and the present patients. In the Wu et al. report, AML and HLH were diagnosed concurrently, and LYST-associated abnormalities were identified; however, classical CHS was not established in the same clinical context as in the present cases [26]. In contrast, both patients in the present series had clinically and genetically confirmed CHS with antecedent HLH and subsequently developed two distinct myeloid malignancies: non-M3 AML and PML::RARA-positive APL.

LYST dysfunction itself has not been established as a direct leukemogenic driver. Nevertheless, recurrent HLH, persistent cytokine-mediated inflammation, and repeated hematopoietic stress may create a permissive environment for genomic instability and clonal selection [8, 19, 22]. Similar inflammation-associated mechanisms have been proposed in other hematologic disorders, although direct evidence in CHS remains limited. Accordingly, these processes should be considered potential contributors rather than primary initiating events.

Therapeutic exposure adds further complexity. Etoposide, a key component of HLH-directed therapy, has been associated with therapy-related AML in specific clinical contexts [6, 7]. Consensus recommendations support the use of etoposide-based therapy in selected patients with severe HLH while recognizing the need to balance treatment benefits against potential toxicity [18]. However, leukemogenic risk is influenced by cumulative exposure, treatment schedule, latency, and host susceptibility [6, 7, 19]. In Case 1, AML developed after prolonged etoposide exposure, making a therapy-related contribution biologically plausible; nevertheless, causality cannot be established in the setting of pre-existing CHS and prolonged inflammatory stress.

The development of PML::RARA-positive APL in Case 2 further argues against a uniform treatment-related mechanism. The PML::RARA rearrangement represents the defining molecular abnormality of APL and can be detected by molecular methods such as RT-PCR [24]. Whether inflammatory or therapeutic stress contributed to susceptibility to the PML::RARA rearrangement remains unknown, and its occurrence may also have been coincidental.

From a clinical perspective, distinguishing leukemic transformation from recurrent HLH can be challenging because both may present with cytopenias, hepatosplenomegaly, fever, and inflammatory abnormalities [4, 15, 22]. In our patients, repeat bone marrow evaluation and multiparametric flow cytometry were essential for recognizing evolving myeloid neoplasia. Persistent or unexplained cytopenias after apparent control of HLH should therefore prompt reassessment rather than being presumed to represent inflammatory relapse [8, 15].

Despite sharing genetically confirmed CHS and antecedent HLH, the two patients demonstrated markedly different leukemic phenotypes and clinical trajectories. This divergence supports a multifactorial model in which inherited lysosomal dysfunction and chronic immune dysregulation may provide a permissive background, while additional acquired genetic or environmental factors determine the eventual malignant phenotype. The presence of CHS-like cytoplasmic inclusions within leukemic cells is noteworthy but does not, by itself, establish that the malignant clone arose directly from the constitutional LYST defect [27–30].

Taken together, these cases expand the limited literature on myeloid malignancy following CHS-associated HLH and highlight the biological heterogeneity of this rare clinical evolution. Although no specific surveillance strategy for leukemic transformation in CHS has been established, persistent or recurrent cytopenias should prompt timely marrow reassessment, with immunophenotypic and molecular studies when indicated [13, 23]. Larger multicenter cohorts with longitudinal genomic data will be necessary to determine whether CHS-associated HLH confers an increased risk of myeloid neoplasia and to clarify the relative contributions of inherited disease, inflammatory stress, and therapeutic exposure.

Declarations

Statement of Ethics

This case series involved retrospective reporting of clinical, laboratory, morphologic, and genetic findings from two pediatric patients and did not involve a clinical intervention or clinical trial. According to the policies of the participating institution, formal ethics committee approval was not required for this retrospective case report. Written informed consent for publication of the clinical details and accompanying images was obtained from the parents/legal guardians of both patients.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contribution

S.H. contributed to the conception and design of the study, clinical case evaluation, interpretation of the clinical and laboratory findings, supervision of the study, and critical revision of the manuscript.

M.B. contributed to the conception of the report, literature review, data collection and interpretation, preparation of the initial manuscript, and integration of the clinical, hematologic, molecular, and literature findings.

H.S.M. contributed to clinical evaluation and management of the patients, interpretation of clinical and hematologic findings, and critical revision of the manuscript.

M.K. contributed to laboratory data collection, hematologic and flow-cytometric data interpretation, literature review, and manuscript preparation.

B.P. contributed to laboratory and diagnostic interpretation, review of hematologic and molecular findings, and critical revision of the manuscript.

A.E. contributed to clinical evaluation and management, interpretation of clinical findings, and critical revision of the manuscript.

All authors critically reviewed and approved the final version of the manuscript and agreed to be accountable for all aspects of the work.

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Data Availability

The de-identified data supporting the findings of this study are included within the manuscript and its supplementary materials.

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Figures

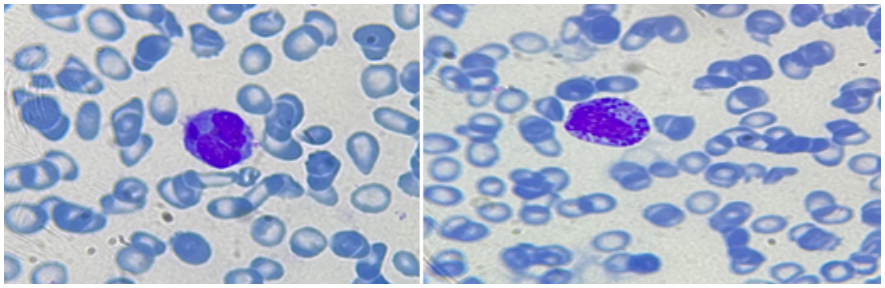


Figure 1

Peripheral blood leukocytes containing giant lysosomal granules characteristic of Chediak–Higashi syndrome.