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CASE REPORT

Chediak-Higashi Syndrome: a Comprehensive Case Report and Literature Review

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SUMMARY

Background: **Chediak-Higashi Syndrome (CHS) is a rare autosomal recessive disorder characterized by oculocutaneous albinism, immune dysfunction, and neurologic abnormalities.**
Methods: **This paper aims to provide a detailed understanding of the clinical presentation, laboratory examination, genetic basis, EEG/MRI, diagnostic challenges, and current management strategies for CHS through a new case report and a analysis of the current literature.**
Results: **The analysis of the case report and literature indicates that CHS requires vigilant clinical observation for early diagnosis and effective treatment. The analysis highlights the necessity for advanced therapies that are both more efficient and cost-effective, given the current limitations in treatment options.**
Conclusions: **The study concludes that further research is needed to develop more efficient and economical therapies for CHS that can enhance patient outcomes. The development of such therapies will be crucial in addressing the unmet needs of patients with this rare genetic disorder.**
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Supplementary Data

Table 1. Summary of case reports on CHS published in the last 5 years.

Investigations					Gene	Treatment	Prognosis
Clusters of melanin pigment on hair microscopy	Impaired transfer of melanin to keratino-cytes on skin biopsy	Hamo-phagocytic syndrome	CT/MIR	Others			
clusters of melanin pigment on hair microscopy	-	-	sustained fast wave rhythm discharge; bilateral frontal lobe, left parieto-occipital lobe cerebral edema	pathogen test showed that streptococcus pneumoniae, mycoplasma pneumoniae, influenza A virus, and novel coronavirus were all present	LYST Gene Mutation: NM_000081.4(c.1507 C>T; p.Arg503)	anti-infective and symptomatic therapies	discontinuation of treatment
-	-	-	-	-	a homozygous LYST/CHS1 mutation in exon 31, c.8186G>A (p.W2729Ter). In this case, a nonsense mutation at exon 31 (c.8186G>A) has not been reported in the HGMD database	underwent allogeneic hematopoietic stem cell transplantation (HCST) combined with umbilical cord blood transplantation (UCBT) after HLH-related chemotherapy	has been alive for nine months without recurrence
aberrant melanin particle distribution observed via hair shaft microscopy	-	compound hetero-zygous mutations in the LYST gene	-	cytopenia, fasting triglycerides 5.12 mmol/L, ferritin 600.7 ng/mL, and soluble interleukin-2 receptor >7,500 U/mL	c.8407C>T and another variant c.4020_4031del, which was located in exon 11	received ceftriaxone and meropenem for infection, intravenous immunoglobulin (IVIG) to boost immunity, dexamethasone for anti-inflammation, recombinant human thrombopoietin (rhTPO), Leucogen for platelet and WBC elevation, and RBC and platelet transfusions. Quetiapine fumarate was administered for sedation	succumbed to recurrent infections six months later
-	-	-	-	-	NM_000081.3:c.11173G>A p.(Gly3725Arg) in the LYST gene	prophylactic antibiotics	still waiting for an unrelated donor of stem cell transplantation

Cases	Year	Country /Region	F / M	Age years	Clinical features						
					Skin hypopig-mentation	Silvery gray hair	Neurological manifestations	Immunodefi-ciency	Recurrent infection	Additional findings	Giant intracytoplasmic granules in leukocytes
Our Case	2024	China	F	4	pigmen-tation of extremities	gray and rougher hair	sudden convulsions, motor difficulties, gait incoordination, and speech weakness	high total B lympho-cytes (CD3-CD19+, 26.95%) and low percentages of helper/ induced T cells (CD3+ CD4+, 26.51%) and total T lymphocytes (CD3+, 56.08%)	recurrent fever, cough, and dyspnea	-	abnormal round or round-like purplish-red granules of varying sizes and numbers in the cytoplasm of 20.0% of neutrophils
Liu C et al. [1]	2024	China	F	7	pale skin	silvery hair	none	-	recurrent fever	with splenomegaly, hepatomegaly (10 cm), and cervical lymph adenopathy. The EBV DNA test was positive	several abnormal giant granules in most white blood cells
Guo P et al. [2]	2024	China	F	14	-	-	-	-	frequent colds and fevers	a positive result for SARS-COV-2 mRNA from nasopharyngeal swabs, and SARS-COV-2 serum IgM test was positive. The patient was diagnosed with COVID-19, staphylococcal pneumonia, infectious mononucleosis, and polyserositis	abnormal inclusion bodies were found to present in the cytoplasm of neutrophils, lymphocytes, and eosinophils
Saiz-Sierra L et al. [3]	2024	Spain	M	3	some hypopig-mentation of the skin	lock of white hair on the front of the head	psychomotor abnormalities	-	recurrent respiratory infections	-	the presence of big cytoplasm granules in all the leukocytes, especially in neutrophils

Table 1. Summary of case reports on CHS published in the last 5 years (continued).

Investigations				Gene	Treatment	Prognosis
Clusters of melanin pigment on hair microscopy	Impaired transfer of melanin to keratinocytes on skin biopsy	Hamophagocytic syndrome	CT/MIR	Others			
-	-	-	-	-	-	died after 7 days of hospitalization
-	-	-	-	-	at age 12, he progressed to an accelerated phase and underwent allogeneic stem cell transplantation (AlloSCT) with an unrelated, HLA matched, ABO-mismatched donor	a mixed chimerism state post allogeneic stem cell transplant complicated by autoimmune hemolytic anemia
regularly arranged clumps of melanin	-	-	-	-	granulocyte-colony stimulating factor (G-CSF) therapy	subsequently referred to a tertiary center for further evaluation and consideration of bone marrow transplantation
-	-	-	no magnetic resonance imaging alterations	hemoglobin 11.7g/dL, white blood cells 10.4 x 10^9/L, absolute neutrophil count 0. x 10^9/L, and platelets 398 x 10^9/L; no biochemistry or coagulation defects were found	a homozygous pathogenic missense mutation (NM_000081.3:c.11173G>A;NP_000072.2:p.G3725R) in the LYST gene	-	-
hair microscopy revealed hypopigmented hair	-	-	diffuse brain parenchymal volume loss with cerebral white matter disease	-	-	in 2019, dexamethasone (10 mg/m^2/day) and intravenous Ig. in 2020, commenced emapalumab and underwent an uneventful hematopoietic stem cell transplantation	successfully salvaged

Cases	Year	Country/ Region	F / M	Age years	Clinical features						
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Eskio-glou S et al. [4]	2024	Greece	F	45	-	-	difficulty with balance and movement since childhood, learning difficulties, chronic tremors and weakness of the limbs, ataxia	-	recurrent urine and respiratory infections	Covid-19 infection	revealed many giant pink-to-purple azurophilic cytoplasmic granules in all WBCs
Mc Keague S et al. [5]	2024	Australia	M	36 (diag-nosed at age 11 with recur-rence)	-	-	-	a complete resolution of hematological and immunological dysfunction, but suffered progressive neurological deterioration over the subsequent two decades	-	-	-
Almesfe r A et al. [6]	2023	Saudi Arabia	F	8	abnormal pigmen-tation of her skin	fair hair	-	-	prolonged fever, a history of cough, shortness of breath, and decreased activity	hepatosplenomegaly	with giant intracytoplasmic granules in all the granulocytes
Bosch-Schips M et al. [7]	2023	Morocco	M	3.6	skin albinism	silver hair	strabismus, and benign Rolandic seizures	-	Several episodes of bacterial septicemia	light blue eyes, and right eye nystagmus	neutrophils showed multiple abnormally large intracytoplasmic blue-gray granules, and lymphocytes showed a single, extremely large, round, purple intracytoplasmic granule
Al Ahmari A et al.[8]	2023	Saudi Arabia	M	3	-	silvery hair	central nervous system (CNS) involvement	-	abdominal distension of moderate severity and persistent fever	hepatosplenomegaly	peripheral blood smear showed giant granules in the cytoplasm neutrophils

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Clusters of melanin pigment on hair microscopy	Impaired transfer of melanin to keratinocytes on skin biopsy	Hamophagocytic syndrome	CT/MIR	Others			
clumped melanin throughout the cortex and medulla of hair shaft and polychromatic birefringence respectively	-	-	-	-	-	empirical antibiotics	eferred to a higher center for bone marrow transplantation
-	-	-	-	-	-	-	-
hair-shaft microscopy revealed small regularly distributed clumps of melanin in the cortex	-	-	-	-	LYST gene (c.10371delT)	-	-
hair showed hypopigmentation consistent	-	-	-	-	LYST (c5023G>T, p.Gly1675)	received dexamethasone, etoposide, and cyclosporine A; initiated stem cell transplantation	the patient is alive and well
-	-	-	-	-	LYST c.8380dupT	dexamethasone and etoposide, a stem cell transplant	after 2 years the patient maintains complete donor chimerism, showing a normal physical and neurological development, and has not required subsequent admissions into the hospital

Cases	Year	Country/ Region	F/ M	Age years	Clinical features						
					Skin hypopig-mentation	Silvery gray hair	Neurological manifestations	Immunode-ficiency	Recurrent infection	Additional findings	Giant intracyto-plasmic granules in leukocytes
Khanal A et al. [9]	2022	India	M	5	hypopigmented skin	pallor, light brown hair	difficulty while walking	-	acute onset fever of moderate to high grade	generalized lymphadenopathy; Fundus examination showed grade-4 papilledema: hepato-splenomegaly with generalized lymphadenopathy	lympho cytes displayed basophilic cytoplasmic inclusions ; neutrophils exhibited lilac/grayish cytoplasmic inclusions
Shimizu K et al. [10]	2021	Japan	F	18	Hyperpigmen-tation on the facial skin	-	limb pain	-	repeated infections	extensive gingival swelling and redness and gingival retraction in the right lower central incisor	-
Singh A et al. [11]	2021	India	M	4	-	silver-grey hair	microcephaly	-	recurrent episodes of fever	pallor, periodontitis, generalized lymphadenopathy and hepatosplenomegaly	multiple irregular large round-to-oval purplecolored peroxidase positive intra-cytoplasmic inclusions in the neutrophils, lymphocytes and monocytes
Lange M et al. [12]	2021	Germany	F	0.1	-	-	-	-	-	hepatosplenomegaly, positive for SARS-CoV-2	a bone marrow aspirate showed CHS-characteristic inclusion bodies in band and segmented neutrophils
Boluda-Navarro M et al. [13]	2021	Spain	F	3	-	-	-	-	recurrent episodes of fever	ocular albinism characterized by absence of pigmentation in the peripheral retina splenomegaly varying between 5 and 15 cm	purple inclusions were detected in both lymphocytes and all stages of the granulocytic series. Intense vacuolization, sometimes with a purple inclusion, was also seen in all cell types

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-	-	-	-	-	-	treated by haplo-HSCT with reduced-toxicity conditioning and post-transplant cyclophosphamide	3 years post-transplant and is doing well with no signs of GvHD
hair microscopy of the silvery grey hairs showed evenly distributed melanin granules of regular diameter along the shaft	-	five out of the eight diagnostic criteria for hemophagocytic lymphohistio-cytosis	-	-	-	dexamethasone, cyclosporin and etoposide for management of HLH	died on day 4 of hospitalization due to multi-organ dysfunction
-	-	-	brain computed tomography was notable for fine hypodense foci scattered in the white matter of the cerebral hemispheres, suggestive of chronic microvasculopathy and cerebral atrophy	-	d exon 5 (c.433 C>T; p. Arg145*) of LYST (NM_000081.3)	-	-
-	-	-	-	-	one missense mutation NM_000081.2:c.5719A > G (p.Ile1907Val) and a intron mutation NC_000001.10:g.235945 391C > T (c.4863-4G > A)	waiting for a stem cell transplant	-
light microscopy of the patient's hair shafts showed absence of melanin granules in the white hair shafts and dispersion of melanin granules in the black hair shafts. Polaroscopic examination highlighted multiple bright individual colors in both the black and white hair shafts	-	-	-	-	e c2897_2902delins CAT p.(Met966_Arg968delins ThrCys)	-	-

Cases	Year	Country/ Region	F/ M	Age years	Clinical features						
					Skin hypopig-mentation	Silvery gray hair	Neurological manifestations	Immunode-ficiency	Recurrent infection	Additional findings	Giant intracyto-plasmic granules in leukocytes
Sachdev M et al. [14]	2021	India	M	1.4	-	silvery hair	-	-	recurrent infections	-	have intracytoplasmic inclusions seen on the peripheral smear
Gopaal N et al. [15]	2020	India	M	2.5	hypopigmented skin, pallor	silvery grey hair	-	-	seizures, fever, abdominal distention	yellowish discoloration of eyes and urine for one month, icterus, splenomegaly (span-12 cm), hepatomegaly (10 cm), cervical and axillary lymphadenopathy	peripheral blood smear revealed the classic giant azurophilic peroxidase-positive granules in neutrophil
Yarnell DS et al. [16]	2020	USA	F	67	fair skin complexion	silver colored hair	lifelong learning difficulties; cognitive impairment with memory changes and executive dysfunction	-	-	-	giant cytoplasmic granules in leukocytes
Song Y et al. [17]	2020	China	F	4	hypopigmen-tation of skin on neck and knee	-	-	-	recurrent upper respiratory	-	leukocytes with giant intracytoplasmic inclusions were observed with peripheral smear, which was evidenced by bone marrow aspirate
Veraitch O et al. [18]	2020	UK	M	38	patches of hypopigmen-ted skin consistent with vitiligo	silvery hairs	-	-	recurrent infections and an abnormal blood film	-	-

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-	-	-	-	-	(c.10010dupT) in LYST	-	-

Cases	Year	Country/ Region	F/ M	Age years	Clinical features						Giant intracyto-plasmic granules in leukocytes
					Skin hypopig-mentation	Silvery gray hair	Neurological manifestations	Immunode-ficiency	Recurrent infection	Additional findings	
Wang Z et al. [19]	2019	China	F	20	hyperpigmentation with bleaching spots were seen on her cheeks and limbs	silvery gray hair	-	-	-	fundus examination provided evidence of retinal mixed hypopigmentation and hyperpigmentation	large azurophilic and eosinophilic granules in neutrophils and monocytes were observed in the peripheral blood smear

CHS - Chediak-Higashi Syndrome, "-" - no data.