Autoimmune Lymphoproliferative Syndrome (ALPS): a pediatric single-center case series

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INTRODUCTION

ALPS is a primary immune regulatory disorder that typically presents in childhood, characterized by chronic non-malignant lymphadenopathy, hepatosplenomegaly, and autoimmune cytopenias. This study aimed to present a case series of pediatric patients with ALPS from a single center.

METHODS AND RESULTS

Patient	Gender	Age of onset (years)	DNT% (% of T cells)	VitB12 (pg/ml)	IgG (mg/dl)	Lymphoproliferation (age of onset)	Cytopenia (age of onset)	Other reported diagnosis (age)	Treatment	Maintenance treatment
P1	F	1	2.6%	>4,000	2,161 (RV: 857-1563)	Generalized lymphadenopathy + splenomegaly (2yo)	AIHA (1yo)	Learning disabilities, splenic cyst	High dose IV CS	No
P2	F	1	9%	>2,000	2,007 (RV: 549-1584)	Cervical lymphadenopathy (1yo)	AIHA (14yo)	Recurrent respiratory infections (1-5yo), Castleman´s syndrome, (4yo), short stature requiring GH (11-13yo)	High dose CS followed by oral CS for 3 months	No
P3	M	1	11%	>1,000	3,418 (RV: 857-1563)	Lymphadenopathy (1yo) splenomegaly (10yo)	Neutropenia (10yo); AHAI + IPT + neutropenia (13yo)	Leishmaniosis (7yo), ALL (7yo), short stature due to chronic CS; lower limbs asymetry; scoliosis	High dose IV CS chronic oral CS, MMF, Sirolimus	MMF for 9 months and then Sirolimus due to relapse of ITP
P4	F	0.58	5.84%	>2,000	3,904 (RV: 453-916)	Splenomegaly + lymphadenopathy (8mo)	AIHA + ITP (9mo)	Recurrent urticaria, CMV infection	High dose IV CS, high dose IVIG, oral CS, MMF	MMF
P5	M	3.75	6.5%	1,955	940 (RV: 540-1822)	Splenomegaly (6.4yo)	ITP (3.75 yo) AIHA (10.9yo)	none	High dose IV CS, high dose IVIG, oral CS, Rituximab, Sirolimus, MMF	Sirolimus for 14 month substitutde for MMF due to oral ulcers
P6	M	1,5	19.90%	1,830	609 (RV: 400-1250)	Lymphadenopathy (2yo)	ITP (1.5yo); Neutropenia (2yo)	Recurrent urticaria, allergic rhinitis	High dose IVIG, CS, Azathioprine, Sirolimus	Sirolimus

M: male; F: female; DNT: double negative T cells; VitB12: vitamin B12; yo: years-old; mo: months-old; AIHA: autoimmune hemolytic anemia; ALL: acute lymphocitic leucemia; ITP: immune trombocytopenic purpura; IV: intravenous; CS: corticosteroids; MMF:mycophenolate mofetil; DRESS: Drug reaction with eosinophilia and systemic symptoms

- Retrospective review of the medical records of 6 pediatric patients (3 male) with heterozygous germline pathogenic or likely pathogenic variants in the gene FAS
- P1 and P2 were sisters
- Median age at clinical diagnosis of ALPS (ESID 2019) was 8.4 years (range: 1.16–16.83 y)
- Genetic confirmation occurred at a median age of 12 years (range: 1.75–20.75 y)
- Median age of symptoms onset was 1 year (range: 0.58–3.75 y)
- The first clinical manifestations was autoimmune cytopenia in 4 patients (ITP: n=2; AIHA: n=1; Evans' syndrome: n=2) and benign chronic lymphadenopathy in 2
- During follow-up, all patients developed chronic lymphoproliferation (lymphadenopathy: n=5; splenomegaly: n=4) and autoimmune cytopenias (AIHA: n=5; ITP: n=3; neutropenia: n=2).
- Two patients underwent splenectomy before ALPS diagnosis (P3, P6)
- Four patients required long term treatment for cytopenias (P3-P6)
- Regarding family history, all parents were asymptomatic.
- The mother of P1 and P2 and the father of P4, carried the same genetic variants as their children. Other patients´ parents have not been tested.

CONCLUSION

Recognition of clinical and laboratory features of ALPS is essential for early diagnosis and can significantly impact management and improve survival outcomes.