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CASE REPORT

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Autoimmune polyendocrine syndrome type 2 in children: a case report and literature review

Yahong Liu[1*†], Fei Wang[1†], Lijuan Zhang[1], Hongxiao Zhang[1] and Yanfang Zhu[1]

Abstract

Background Autoimmune polyendocrine syndrome (APS) is a clinical disorder characterized by the loss of immune tolerance, leading to dysfunction in multiple endocrine glands. According to the latest disease classification, APS is categorized into three main subtypes: APS-1, APS-2, and IPEX (Immune Dysregulation, Polyendocrinopathy, Enteropathy, X-linked) syndrome. APS-2 is defined by the presence of at least two autoimmune endocrine disorders, such as type 1 diabetes mellitus, autoimmune thyroiditis, or Addison's disease. APS-2 typically manifests later than APS-1, with onset most commonly occurring in early adulthood. However, pediatric cases involving a combination of autoimmune thyroid disease, type 1 diabetes mellitus, and myasthenia gravis, are extremely rare.

Case presentation This article reported the case of a 3-year-old girl diagnosed with autoimmune polyendocrine syndrome type 2 (APS-2). The patient initially presented with hyperthyroidism and exophthalmos and was subsequently diagnosed with type 1 diabetes mellitus and myasthenia gravis. To our knowledge, this case represents the youngest reported patient of APS-2 at the time of diagnosis, as well as the shortest documented interval between the onset of autoimmune disorders affecting distinct endocrine glands.

Conclusions Through a retrospective analysis, we comprehensively reviewed the phenotypic characteristics of APS-2 and explored its potential immune mechanisms. This article aims to provide clinicians with a valuable reference case to enhance early recognition and facilitate the implementation of targeted prevention and treatment strategies.

Keywords Autoimmune polyendocrine syndrome type 2, Autoimmune thyroiditis, Type 1 diabetes mellitus, Myasthenia Gravis

Background

Autoimmune polyendocrine syndrome (APS) is a rare group of immune-mediated disorders characterized by the dysfunction of multiple endocrine glands [1]. According to the latest disease taxonomy, APS is classified into three main subtypes: APS-1, APS-2, and IPEX (Immune Dysregulation, Polyendocrinopathy, Enteropathy, X-linked) syndrome [2]. Among these, APS-2 is defined by the presence of at least two endocrine disorders, including type 1 diabetes mellitus (T1DM), autoimmune thyroid disease (AITD), Addison's disease, or other autoimmune conditions. It typically manifests in young adulthood, with a later onset compared to APS-1 [3, 4].

†Yahong Liu and Fei Wang contributed equally to this work.

*Correspondence:
Yahong Liu
2008liuyahong@163.com
[1]Department of Child Health Care and Rehabilitation, The Second Hospital & Clinical Medical School, Lanzhou University, Lanzhou, People's Republic of China

The incidence of APS-2 is higher than that of APS-1, with an estimated annual prevalence of 1–2 cases per 10,000 individuals. APS-2 is more common among females, showing a male-to-female ratio of 1:3 [5]. The genetic background of this syndrome is complex, involving interactions between multiple genetic and environmental factors that contribute to the loss of immune tolerance [6]. The human leukocyte antigen (*HLA*) gene complex plays a significant role in genetic susceptibility to APS-2, with HLA-B8 and DR3 alleles being strongly associated with an increased risk of developing APS-2 [7, 8].

Cases of APS-2 in childhood are relatively rare, with diverse clinical manifestations that pose challenges in both diagnosis and treatment [9]. This case report describes a young girl who initially presented with Graves' disease, subsequently developed T1DM and myasthenia gravis in succession, and was ultimately diagnosed with APS-2. She is currently six years old. By documenting this case, we aim to provide additional clinical data to improve the understanding of the rare manifestations of APS-2 in children and to promote early diagnosis and intervention.

Case presentation

This case involves a young girl, the second child in her family, who was born full-term via vaginal delivery with growth and development comparable to her peers. Both parents were in good health, with no history of consanguinity or hereditary diseases. On January 25, 2022, at the age of 3 years and 2 months, the patient was admitted to the Second Hospital of Lanzhou University due to bilateral exophthalmos that had persisted for two months. She exhibited no symptoms of hyperactivity, irritability, inattention, or sleep disturbances.

Physical examination revealed the following: body temperature 36.6 °C, pulse rate 139 beats per minute, blood pressure 102/56 mmHg, and respiratory rate 22 breaths per minute. The thyroid gland was enlarged, with palpable tremors and vascular bruits. Bilateral cervical lymph nodes were approximately the size of broad beans, with a medium texture. Ophthalmic examination showed bilateral exophthalmos, with no evidence of deformities, edema, pale palpebral conjunctiva, or scleral icterus. The pupils were equal in size, round, 3 mm in diameter, and responsive to light. No significant abnormalities were detected in the heart, lungs, or abdomen upon examination. Laboratory tests indicated abnormal thyroid function: triiodothyronine (T3) was 5.85 nmol/L (normal range: 1.51–3.35 nmol/L), thyroxine (T4) was 317.2 nmol/L (normal range: 66.86–158.02 nmol/L), free triiodothyronine (FT3) was greater than 30.8 pmol/L (normal range: 4.1–7.42 pmol/L), free thyroxine (FT4) was 108.23 pmol/L (normal range: 14.45–22.74 pmol/L), thyroid stimulating hormone (TSH) was 0.006 IU/mL (normal range: 0.27–4.2 μIU/mL), and thyrotropin receptor antibody (TRAb) was 9.41 IU/L (negative < 1.5 IU/L). The cortisol rhythm and adrenocorticotropic hormone levels were within normal ranges. Blood glucose, liver and kidney function, electrolyte levels serum, including serum calcium levels, and complete blood count showed no abnormalities. Cardiac ultrasound revealed no structural, hemodynamic, or functional abnormalities. Thyroid ultrasound demonstrated increased blood flow signals, diffuse thyroid enlargement, and multiple enlarged bilateral cervical lymph nodes (Fig. 1).

The patient was diagnosed with Graves' disease and initiated on oral methimazole 10 mg once daily. A one-month follow-up showed improvement in thyroid function. Figure 2 presents the alterations in TSH levels throughout the treatment course, while Fig. 3 depicts the changes in TRAb levels during the same treatment period. After 9–10 months of treatment, the patient's exophthalmos symptoms improved (Fig. 4). On July 26, 2022, at the age of 3 years and 8 months, the patient presented with polydipsia, polyuria, and polyphagia lasting over 20 days, accompanied by fatigue for 2 days. There was no dyspnea, cough, sputum, abdominal pain, or

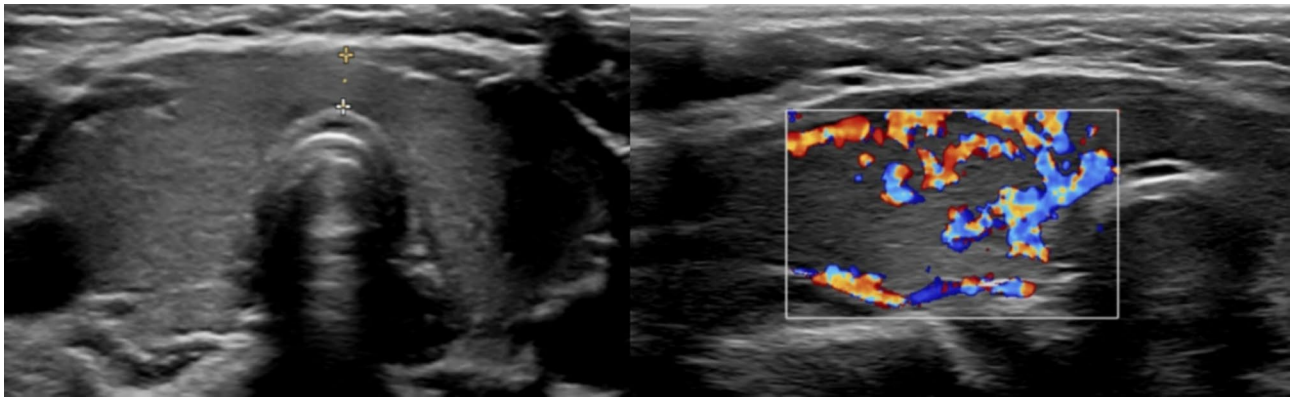

Fig. 1 Thyroid ultrasound of the child with APS-2

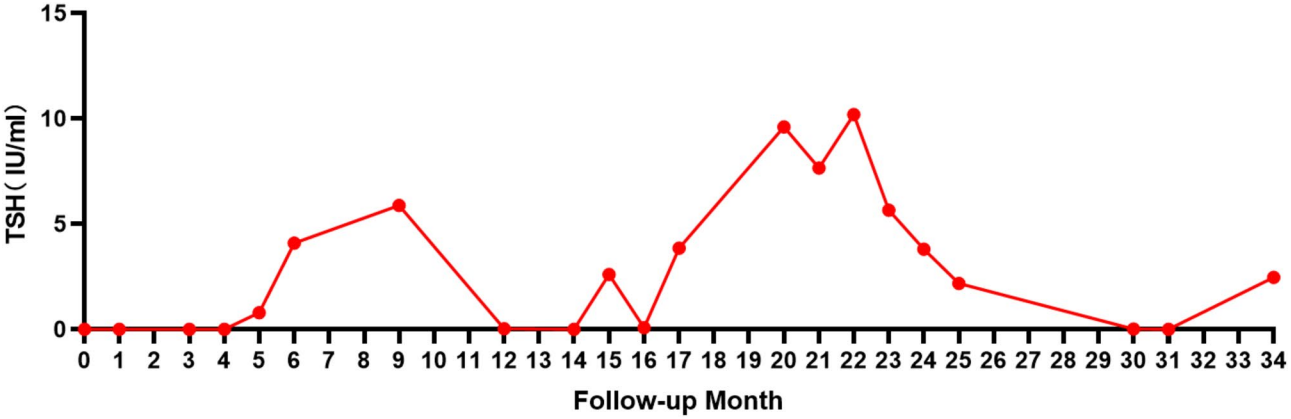

Fig. 2 Changes in TSH during the course of the disease

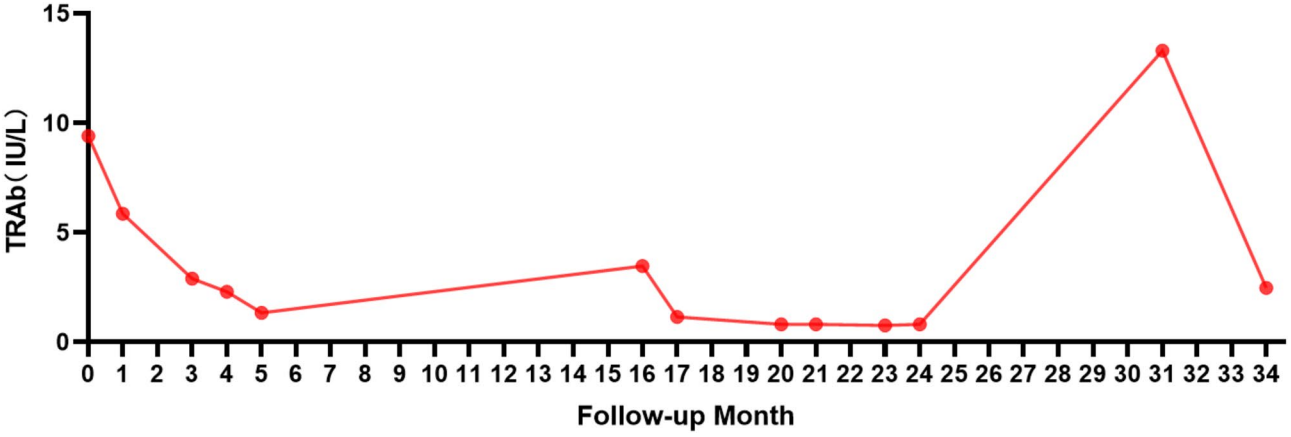

Fig. 3 Changes in TRAb during the course of the disease

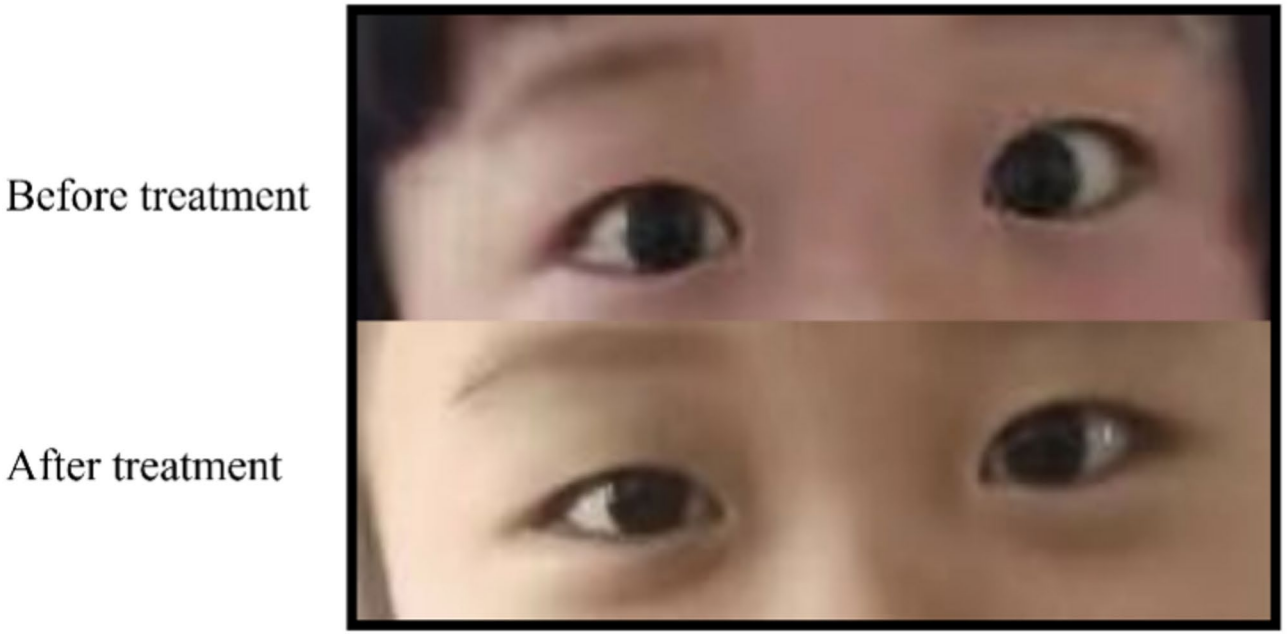

Fig. 4 Ocular manifestations of the child with APS-2 before and 9 months after methimazole treatment

diarrhea, but a low-grade fever of 37.4 °C was noted. Urinalysis revealed ketones 3+, glucose 3+, and protein 2+, but subsequent reexamination showed normal results. Electrocardiogram showed sinus tachycardia with ST-T segment abnormalities. Blood glucose was 17.9 mmol/L (normal range: 3.9–6.1 mmol/L), and the nine-item respiratory virus and mycoplasma antibody panel tested positive. The fasting C-peptide, insulin and anti-insulin antibody were 0.41 ng/mL (normal range: 0.48–5.05 ng/mL), 4.81 mU/L (normal range: 3.00–25.00 mU/L) and 6.33 IU/mL (normal range: 0.00–20.00 IU/mL), respectively. The postprandial 2 h insulin and C-peptide levels were 10.82 mU/L (normal range: 3.00–25.00 mU/L) and 0.86 ng/mL (normal range: 0.48–5.05 ng/mL), respectively. Glycated hemoglobin A1c (HbA1c) was 12.4% (normal range: 4–6%). The patient was diagnosed with T1DM and initiated on insulin therapy. Figure 5 illustrates the changes in HbA1c levels following insulin therapy. The changes in thyroid function, HbA1c levels, and the treatment regimen for the child with APS-2 are summarized in Table 1.

On April 25, 2023, at the age of 4 years and 5 months, the patient was admitted due to progressively worsening bilateral ptosis of the upper and lower eyelids over two months. There were no associated symptoms of chewing or swallowing difficulties, limb weakness, or dyspnea. Further investigations were conducted: brainstem thin-layer magnetic resonance imaging showed no significant abnormalities, and chest computed tomography (CT) revealed anterior mediastinal changes consistent with a normal thymus, additionally, orbital CT showed no abnormalities (Fig. 6). The acetylcholine receptor antibody (AChRAb) level was elevated at 4.21 nmol/L (positive, defined as ≥0.5 nmol/L). Electromyography demonstrated a low-frequency decrement in repetitive nerve stimulation of the bilateral facial nerves, while no significant abnormalities were observed in the ulnar, axillary, or accessory nerves. Based on these findings, the patient was diagnosed with myasthenia gravis (ocular type) and initiated on pyridostigmine bromide tablets, prednisone acetate tablets, and tacrolimus. Considering the patient's medical history and auxiliary examinations, a final diagnosis of APS-2 was established, with manifestations of Graves' disease, T1DM, and myasthenia gravis.

T3: Triiodothyronine (normal: 1.51–3.35 nmol/L), T4: Thyroxine (normal: 66.86-158.02 nmol/L), FT3: Free triiodothyronine (normal: 4.1–7.42 pmol/L), FT4: Free thyroxine (normal: 14.45–22.74 pmol/L), TSH: Thyroid stimulating hormone (normal: 0.27–4.2 uIU/mL), TRAb: Thyrotropin receptor antibody (negative < 1.5 IU/L), TPOAb: Thyroid peroxidase antibody (negative < 60 U/mL), TGAb: Thyroglobulin antibody (negative < 60 U/mL), HbA1c: Glycated hemoglobin A1c (normal: 4.0–5.6%), MMI: methimazole, /: not detected.

Discussion and conclusions

Clinical presentation and diagnostic journey

In this case, the patient initially presented with "exophthalmos", which led to a diagnosis of Graves' disease following a comprehensive examination. During subsequent visits, the child gradually exhibited typical symptoms of diabetes: polydipsia, polyuria, polyphagia, and fatigue, with laboratory results confirming a diagnosis of T1DM. As the condition progressed, she developed symptoms of bilateral ptosis, and after completing tests such as AChRAb, a diagnosis of myasthenia gravis (ocular type) was confirmed. The clinical presentation of this case is complex and particularly rare, as T1DM and myasthenia gravis emerged sequentially following the initial diagnosis of Graves' disease, ultimately meeting the criteria for APS-2. In fact, most autoimmune endocrine diseases involved in APS-2 exist in a latent state, with disease

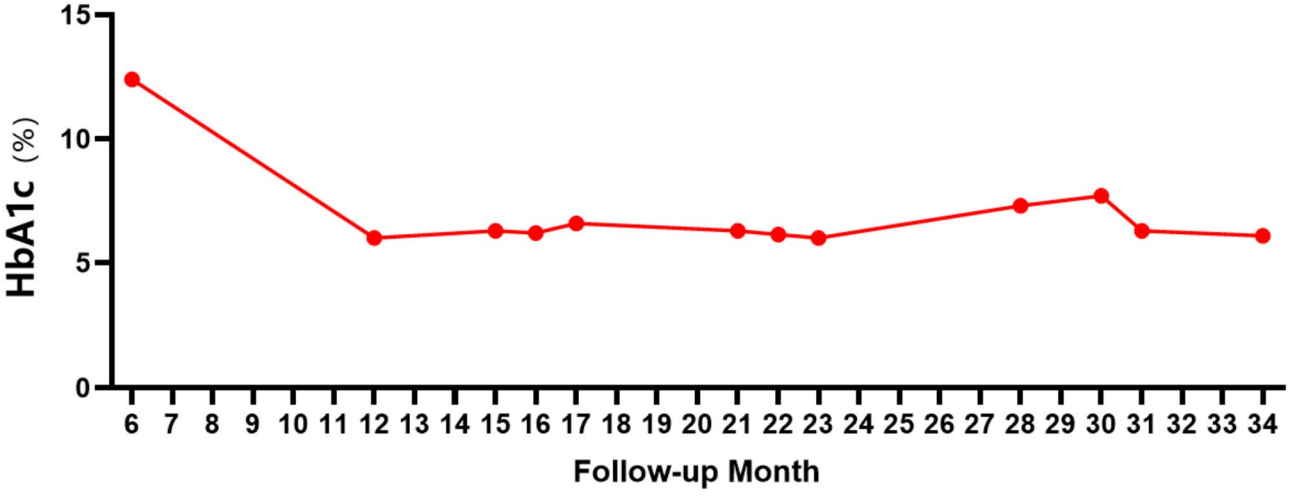

Fig. 5 Changes in HbA1c during the course of the disease

Table 1 Change of thyroid function and HbA1c and treatment of the child with APS-2

Months after treatment	T3 (nmol/L)	T4 (nmol/L)	FT3 (pmol/L)	FT4 (pmol/L)	TSH (IU/ml)	TRAb (IU/L)	TPOAb (U/mL)	TGAb (U/mL)	Treatment regimen	HbA1c(%)
0	5.85	317.2	> 30.8	108.23	0.006	9.41	/	/	MMI 10 mg qd	/
1	3.46	226.4	11.34	31.39	0.005	5.86	/	/	MMI 10 mg qd	/
3	3.05	186.7	8.59	22.45	0.009	2.89	/	/	MMI 5 mg qd	/
4	2.7	183.7	8.79	21.2	0.007	2.3	/	/	MMI 5 mg qd	/
5	1.4	114.0	4.39	15.13	0.789	1.33	/	/	MMI 3 mg qd	/
6	1.39	77.15	4.43	16.04	4.090	/	64.57	380.9	MMI 2.5 mg qd	12.4
9	1.82	164.49	5.67	21.19	5.88	/	/	/	+ Insulin	/
12	2.73	212.4	10.07	26.63	0.037	/	> 1300	> 500		6
14	3.47	252	13.36	37.15	0.002	/	/	/		/
15	2.27	115.3	5.54	16.05	2.61	/	/	/		6.3
16	2.37	136.0	6.14	23.4	0.08	3.47	> 600	668		6.2
17	2.4	133	5.2	18.4	3.86	1.14	329	387		6.6
20	2.36	109.0	6.61	19.2	9.61	< 0.8	101	23.6	MMI 1.6 mg qd	/
21	2.19	112.0	7.05	19.2	7.65	< 0.8	75	26.2	+ Insulin	6.3
22	1.83	189.21	5.18	19.23	10.19	/	/	/	Insulin	6.14
23	2.7	173.4	7.49	18.19	5.65	0.75	318.8	4.2	Insulin	6
24	3.05	129	6.46	21.9	3.81	< 0.8	245	129	Insulin	/
25	2.47	203.85	7.22	22.05	2.18	/	/	/	Insulin	/
28	/	/	/	/	/	/	/	/	Insulin	7.3
30	/	/	> 30.8	67.05	0.016	/	846.2	/	MMI 10 mg qd+	7.7
31	3.29	141	8.52	23.4	< 0.01	13.3	> 600	682	Insulin	6.3
34	2.79	124	5.64	14.6	2.47	2.47	> 600	966	MMI 5 mg qd	6.1

Footnote: The treatment timeline was calculated from the baseline assessment (month 0), which corresponded to the first admission date on 2022-01-25. Subsequent months represented the ordinal months of treatment following the baseline date

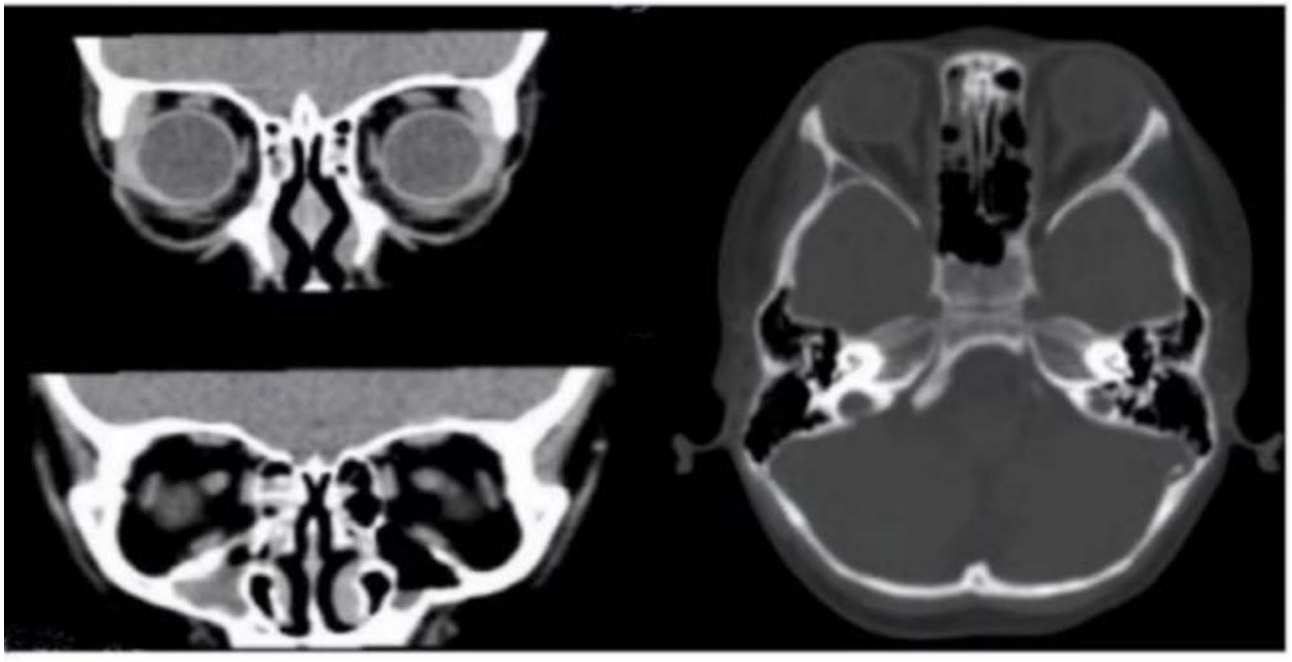

Fig. 6 Orbital CT images of the child with APS-2

onset occurring over several years. In this child, T1DM developed six months after the onset of hyperthyroidism, followed by myasthenia gravis appeared another six months later. The potential development of adrenal insufficiency or other autoimmune endocrine diseases in the future remains uncertain, underscoring the importance of long-term follow-up.

Evolution of APS classification

APS was first proposed by Michel Neufeld et al. [10] in 1980. It is a group of disorders characterized by a combination of endocrine and non-endocrine autoimmune diseases, with varying components and pathogenesis. Initially, APS was primarily classified into four types: APS-1 defined by the presence of at least two of the following conditions—chronic mucocutaneous candidiasis, acquired hypoparathyroidism, and idiopathic or autoimmune Addison's disease; APS-2 characterized by Addison's disease along with autoimmune thyroid disease and/or insulin-dependent diabetes mellitus; APS-3 involves autoimmune thyroid disease without Addison's disease, accompanied by insulin-dependent diabetes mellitus or pernicious anemia, and is further divided into subtypes III-A, III-B, and III-C. Additionally, there is a miscellaneous category of APS for cases that do not fit the above classifications. In this case, the child exhibited Graves' disease, T1DM, and myasthenia gravis. According to the diagnostic criteria established by Neufeld et al., this pediatric patient, who presented with Graves' disease, T1DM, and myasthenia gravis, was currently considered to have APS-3. However, due to the involvement of multiple autoimmune diseases in the progression of APS, the specific course of the disease was uncertain. For example, it was difficult to determine whether Addison's disease would be eventually manifest in this case, which added some confusion to the current diagnosis. Recent advances in APS research have led to a more widely applicable classification. Researchers believe that APS-2, APS-3, and APS-4 should not be considered distinct entities but rather part of a single syndrome, which referred to as APS-2. According to this updated classification, autoimmune thyroid diseases are the most common clinical component of this syndrome (70–75%), followed by T1DM (50–60%), Addison's disease (40%), and other autoimmune diseases, such as celiac disease, vitiligo, pernicious anemia, myasthenia gravis, and alopecia. Individual comorbidities may emerge many years later, long-term follow up on related diseases in children with Addison's disease, diabetes, or other autoimmune conditions is particularly critical [1, 3, 11]. Considering the patient's clinical manifestations, laboratory findings, and updated diagnostic recommendations, the final diagnosis for this case was APS-2.

Genetic architecture of APS subtypes

APS-1 and APS-2 represent two genetically distinct entities. APS-1 is an autosomal recessive disorder caused by biallelic mutations in the *AIRE* gene, localized to chromosome 21q22.3 (flanked by markers D21S49 and D21S171) as confirmed by linkage analyses [6, 12]. In contrast, APS-2 demonstrates polygenic predisposition involving chromosome 6 loci critical for immune regulation, including *HLA-DR* (major histocompatibility complex), *CTLA-4* (cytotoxic T-lymphocyte-associated protein 4), and *PTPN22* (protein tyrosine phosphatase non-receptor type 22), with additional contributions from *TNF-α* and *MICA* polymorphisms [5, 13]. Clinically, APS-1 predominantly manifests in childhood with classic triads (e.g., chronic mucocutaneous candidiasis, hypoparathyroidism), whereas APS-2 typically presents in adulthood with autoimmune thyroid disease, T1DM, and/or Addison's disease [5]. This divergence has led to a classification system stratifying APS into juvenile-onset monogenic (APS-1) and adult-onset polygenic (APS-2/3/4) subtypes based on genetic architecture, age of onset, and disease combinations [5, 14]. While *AIRE* genetic testing is diagnostic for APS-1 [6, 12], its utility in APS-2 remains limited due to multifactorial etiology; thus, genetic evaluation is not routinely recommended for APS-2 per current guidelines [5, 14]. In this pediatric APS-2 case, parental preferences aligned with these recommendations, as the absence of APS-1 phenotypic hallmarks (e.g., candidiasis, consanguinity) obviated urgent genetic investigation.

Pathogenic mechanisms of APS-2

The pathogenesis of APS involves multifactorial immune dysregulation, primarily driven by impaired suppressive function of regulatory T cells and reduced DNase1 activity, which collectively disrupt self-tolerance through defective apoptotic clearance of nuclear antigens and TLR9-mediated innate immune hyperactivation [5, 7, 15].

Building upon the multifactorial immune dysregulation in APS (Treg dysfunction and DNase 1 deficiency) [5, 7, 15], APS-2 pathogenesis specifically involves three interlinked axes: Th1/Th2 polarization defects in this case, Graves' disease manifested through Th2 dominance (IL-4/IL-13-driven TRAb production) [16], while T1DM reflected Th1 hyperactivation (IFN-γ-mediated β-cell MHC-I upregulation and CTL infiltration) [17, 18]. Autoantibody-epitope cascades-organ-specific antibodies (TRAb in thyroid, AChR-Ab in neuromuscular junctions) [19, 20]bind target antigens, triggering complement-mediated cytolysis and receptor internalization. APC-T cell cross-talk-Defective nuclear antigen clearance (via DNase 1↓) [7]enables dendritic cells to present self-antigens, amplifying TLR9-dependent B/T cell activation—a process exacerbated by impaired Treg suppression.

Table 2 Clinical profiles of APS2 with concurrent type 1 diabetes mellitus, myasthenia Gravis and autoimmune thyroid disease: insights from comparison with pediatric APS2 cases

Case Number	Gender	Age at Diagnosis	First Diagnosed Disease	Age at onset			Type of MG	Type of T1D	Type of Thyroid Disease
				T1DM	MG	AITD			
1[22]	F	8	Addison's disease	NA	NA	11	NA	NA	AITD
2[23]	M	1	MG	NA	1	1	Generalized type	NA	AITD
3[24]	M	11	Addison's disease	NA	NA	11	NA	NA	HT
4[25]	M	12	T1D + Thyroid disease	12	NA	12	NA	Acute onset	GD
5[26]	F	9	T1D	9	19	11	Ocular type	Acute onset	GD
6[27]	F	6	MG	8	6	9	Ocular type	Acute onset	GD
7[28]	F	32	MG	21	32	30	Generalized type	Acute onset	GD
8[29]	M	30	MG	37	31	30	Ocular type	Acute onset	GD
9[29]	M	27	MG	32	27	33	Ocular type	Slowly progressive type	GD
10[29]	F	27	MG + Thyroid disease	35	27	27	Ocular type	Slowly progressive type	GD
11[29]	F	19	T1D + Thyroid disease	19	29	19	Ocular type	Acute onset	GD
12[29]	M	37	MG + Thyroid disease	43	37	37	Ocular type + Upper limb involvement	Slowly progressive type	GD
13[29]	F	10	MG	15	10	35	Ocular type	Acute onset	GD
14[30]	F	5	MG	40	5	40	Ocular type	Acute onset	HT
15[29]	M	59	T1D	59	64	NA	Ocular type + dysphagia	Acute onset	HT
16[31]	M	20	T1D	20	52	52	Ocular type	Acute onset	AITD
17[32]	F	51	Thyroid disease	47	48	47	Generalized type	Acute onset	HT
18[33]	M	37	T1D	NA	37	37	Ocular type	NA	AITD
present case	F	3	Thyroid disease	3	4	3	Ocular type	Acute onset	HT

Footnote: T1DM: Type 1 Diabete Mellitus; MG: Myasthenia Gravis; AITD: Autoimmune Thyroid Disease; GD: Graves' Disease; HT: Hashimoto's Thyroiditis; NA: not applicable

Pediatric APS-2: unique trajectories and management paradigms

Additionally, autoimmune destruction of most target glands in APS-2 is a gradual process, often characterized by a prolonged preclinical prodromal phase. During this phase, patients may exhibit autoantibodies, lymphocyte abnormalities, and subclinical endocrine deficiencies. Furthermore, nearly one-fifth of first-degree relatives of APS-2 patients have unrecognized endocrine disorders, most commonly autoimmune Hashimoto's thyroiditis. We recommend routine thyroid function screening for this high-risk group and long-term follow-up for both patients and their first-degree relatives [21].

APS-2 is more commonly observed in adults. While in children, whose immune systems are still developing, the patterns of autoimmune responses and disease spectrum differ from those in adults. Children are more prone to congenital immune deficiency disorders or infection-related diseases, whereas complex autoimmune disease combinations like APS-2 remain rare in pediatric populations [5, 14]. Available literature indicates that in children, the co-occurrence of T1D, myasthenia gravis, and AITD usually involves only two of these three diseases, with few cases of all three diseases presenting simultaneously [22–25]. To date, based on current medical knowledge and literature review, only 14 patients concurrently diagnosed with AITD, T1DM, and MG have been reported in the literature. Among these cases, 9 patients presented with Graves' disease, T1DM, and MG [26–29], while the remaining 5 cases involved other autoimmune thyroid diseases combined with T1DM and MG [30–33] (Table 2). Among these cases, the age of onset is a critical factor. Based on the 14 previously reported cases, most patients developed the disease in adulthood, with only 3 cases occurring in childhood, who had a relatively long disease course, and the youngest age of onset was 6 years old. The time span from the first disease diagnosis to the confirmation of all three diseases was quite large, ranging from at least 3 years to several decades. The predominance of adult-onset APS-2 likely reflects age-related immunological shifts, including immunosenescence (progressive decline in Treg function) [5], cumulative antigen exposure [15], and epigenetic modifications from

chronic stressors [7], synergistically predisposing to loss of self-tolerance.

In stark contrast to adult-onset APS-2 driven by acquired immunosenescence [5, 7], this pediatric case manifested rapid progression at 3–4 years of age, suggesting distinct developmental immunopathology.

Three factors likely converge: Genetic priming-Potential AIRE gene variants (even without full APS-1 phenotype) [6] may disrupt thymic negative selection, allowing escape of self-reactive T cells targeting thyroid/pancreatic antigens; Immune ontogeny defects,:Immature Treg functional plasticity during early childhood [15] fails to restrain Th1/Th2 polarization extremes observed here; Environmental triggers: Neonatal viral exposures may accelerate epitope spreading via molecular mimicry with TSHR/GAD65 [17].

In this case, given the child's condition, a treatment plan involving the antithyroid drug methimazole was administered to correct thyroid dysfunction. Considering the physiological characteristics of children, the duration of ATD treatment may need to be extended compared to adults [27, 34]. Simultaneously, insulin therapy was implemented to precisely regulate blood glucose levels, thereby comprehensively improving the child's endocrine and metabolic status and promoting overall recovery.

This child's hyperthyroidism may affect growth and weight gain due to increased metabolic rate, managing T1DM needs to balance diet and growth, myasthenia gravis can limit physical activity and development, complex drug interactions in multiple treatments may influence efficacy or raise adverse effect risks so drug therapy complexity requires close attention, during treatment monitoring drug side effects and adjusting strategies according to growth stage and disease progression is essential, and long-term disease management has psychological and social implications as the child may have negative emotions and the relatives' quality of life and well-being may decline, thus strengthening psychological support for both the child and family with counseling and education to help them face the disease challenges positively is crucial.

In summary, in this case, a 3-year-old child was initially diagnosed with Graves' disease, followed by subsequent diagnoses of T1DM and myasthenia gravis, ultimately leading to a confirmed diagnosis of APS-2. The clinical presentation was complex and rare, involving dysfunction of multiple endocrine glands, highlighting the importance of early recognition and comprehensive management of APS-2. For pediatric patients initially diagnosed with AITD, heightened vigilance is necessary, considering the possibility of concurrent other autoimmune.

endocrine disorders. A thorough and systematic evaluation during diagnosis and treatment is essential, including detailed family medical history assessment. For such children, long-term follow-up and monitoring are indispensable to promptly identify new symptoms and abnormal indicators, adjust treatment strategies, and closely monitor growth, development, and psychological status. Collaboration with various relevant specialties is crucial to ensure the child's healthy growth and favorable prognosis. Through in-depth analysis of this case and literature review, we have gained a more comprehensive understanding of the clinical manifestations, pathogenesis, and treatment strategies of APS-2, providing valuable insights for future clinical work and research.

Abbreviations

AChRAb	Acetylcholine receptor antibody
AD	Adrenal insufficiency
AIRE	Autoimmune regulator
AITD	Autoimmune thyroid disease
APS	Autoimmune polyendocrine syndrome
APS-2	Autoimmune polyendocrine syndrome type 2
ATD	Antithyroid drug
CT	Computed tomography
CTLA-4	Cytotoxic T lymphocyte-associated antigen 4
DNA	Deoxyribonucleic acid
DNase	1 Deoxyribonuclease 1
FT3	Free triiodothyronine
FT4	Free thyroxine
HbA1c	Glycated hemoglobin A1c
HT	Hashimoto's thyroiditis
HLA	Human leukocyte antigen
iTreg	Inducible regulatory T cell
MHC	Major histocompatibility complex
MICA	Major histocompatibility complex class I chain-related gene A
MMI	Methimazole
PTPN22	Protein tyrosine phosphatase non-receptor 22
T1DM	Type 1 diabetes mellitus
T3	Triiodothyronine
T4	Thyroxine
TGAb	Thyroglobulin antibody
Th1	T helper type 1
Th2	T helper type 2
Th17	T helper type 17
TLR9	Toll-like receptor 9
TNF-α	Tumor necrosis factor-alpha
TPOAb	Thyroid peroxidase antibody
TRAb	Thyrotropin receptor antibody
Tregs	Regulatory T cells
TSH	Thyroid stimulating hormone

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Author contributions
All authors have made substantial contributions to this work. Yahong Liu made substantial contributions to the conception and design of this study. Fei Wang wrote the manuscript. Lijuan Zhang and Yanfang Zhu collected the data. Yahong Liu and Hongxiao Zhang critically reviewed the manuscript and supervised the whole study process. All authors read and approved the final manuscript and agreed to be accountable for all aspects of the work.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

This study was conducted in accordance with the principles of the Declaration of Helsinki. Ethical approval was granted by the Institutional Medical Ethics Committee of the Second Hospital & Clinical Medical School, Lanzhou University (No. 2025 A-046). Written informed consent was obtained from the legal guardian(s) of the pediatric patient prior to participation in this study.

Consent for publication

The parents of this patient consented to the publication of the case and any accompanying images with written informed consent.

Competing interests

The authors declare no competing interests.

Clinical trial number

Not applicable.

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