RECURRENT PNEUMONIA IN A PEDIATRIC PATIENT WITH CONGENITAL IMMUNODEFICIENCY DUE TO NUCLEOTIDE SUBSTITUTION MUTATION IN THE IKZF1 GENE

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ABSTRACT

Background: *Congenital immunodeficiency is an underlying cause of recurrent pneumonia in children. Mutations in the IKZF1 gene have been associated with immunodeficiency phenotypes that can lead to recurrent infections.*

Methods: *We report a case of a 7-month-old female infant with recurrent severe pneumonia and genetic testing revealing a pathogenic variant in the IKZF1 gene.*

Results: *The patient had recurrent pneumonia requiring prolonged hospitalization. Genetic analysis revealed a heterozygous, dominant missense mutation in the IKZF1 gene (chr7:50382594; c.476A>G;p.Asn159Ser), accompanied by deletions on chromosomes 17 (q12) and 18 (p11.32-p11.21). Treatment with intravenous immunoglobulin (IVIg) led to significant clinical improvement.*

Conclusion: *This case highlights the association between IKZF1 mutations and congenital immunodeficiency with recurrent pneumonia, underscoring the importance of early genetic diagnosis and targeted therapy.*

Keywords: *congenital immunodeficiency, recurrent pneumonia, IKZF1 gene, pediatric case report, IVIg therapy*

I. INTRODUCTION

According to statistics from Global Burden Disease, 15% of all child deaths in 2017 were caused by pneumonia. By 2019, the total number of deaths caused by pneumonia was 2.5 million, the highest pneumonia mortality cases in 2017 were among people aged 70 and olderof (1.2 million deaths), followed by children under 5 years old (672,000 deaths) (Figure 2.1). In Southeast Asia, the Philippine population has a particularly high mortality rate from pneumonia. Pneumonia is the second leading cause of death in both the population under 5 years old and over 70 years old in this country. and therefore it is one of the leading causes of death in children [1].

Some cases of recurrent pneumonia related to congenital immunodeficiency were consulted to perform genetic testing, and were found to be related to chromosomal and gene mutations, especially genetic mutations. At some locations on the IKZF1 gene, it causes a severe decrease in lymphocyte population, which has been recorded and reported around the world. Currently, the relationship between these mutations and immunodeficiency in children in Vietnam has not been thoroughly cared for and researched, making the management and treatment of these pediatric cases difficult. many difficulties, and a great disease burden for families and society. Early detection of genetically related congenital immunodeficiency will help change the direction of effective treatment, specifically Immunoglobulin treatment can help dramatically recover the clinical condition of pediatric patients.

Received: November 05th, 2025; Reviewed: November 15th, 2025; Accepted: December 15th, 2025

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For that reason, the research team carried out this topic as a premise for studies with larger sample sizes, thereby not only characterizing the IKZF1 gene mutation on the Vietnamese genetic map, but also It also changes the initial treatment approach with Immunoglobulin for pediatric patients with recurrent severe community-acquired pneumonia due to congenital immunodeficiency.

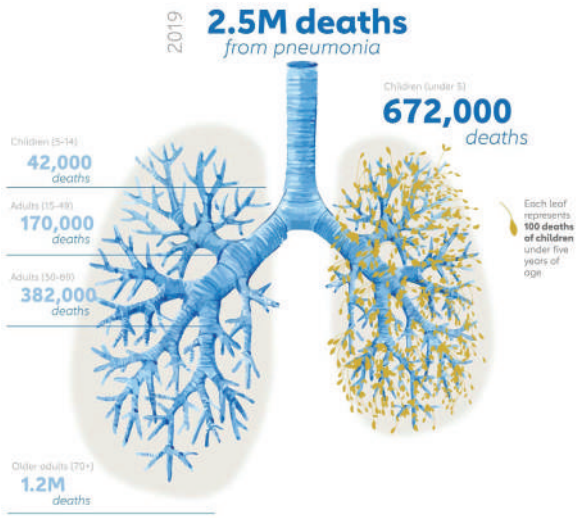

Figure 1. Number of deaths caused by pneumonia in different age groups in 2019 according to Global Burden Disease

It is estimated that approximately 6% of young children will experience at least one episode of pneumonia during the first 2 years of life [2,3]. In low- and middle- income countries, the pneumonia rate remains high and is still a major cause of morbidity and mortality in young children. Despite general improvements in living conditions, nutrition, and vaccination, more than 700,000 children under 5 years of age have died from pneumonia globally [4]. Among children with recurrent pneumonia, the group of children with severe pneumonia admitted to the Pediatric Intensive Care Unit (PICU) has high morbidity and mortality [5].

Recurrent pneumonia (RP) has been defined as at least 2 pneumonia episodes in 1 year or more than 3 at any time, with radiographic clearing between episodes [6,7]. Up to 9% of children with pneumonia will progress to RP, even in developed countries and more than 80% of children have underlying medical conditions [8-10].

Several causes of severe recurrent pneumonia (sRP) [11].

Table 2.1. Causes of severe recurrent pneumonia

Underlying causes	n	%
Congenital heart diseases	17	15.5
Immune disorders	24	21.8
Respiratory abnormalities	31	28.2
Pulmonary hemorrhagic syndrome	2	1.8
Post infectious bronchiolitis obliterans (PIBO)	5	4.5
Aspiration syndrome	12	10.9
Neuromuscular disorders	6	5.5
Recurrent wheezing	4	3.6
Unknown	9	8.2

Geneticists use a standardized way of describing a gene's cytogenetic location. The combination of numbers and letters provides a gene's "address" on a chromosome, this address is made up of several parts [12]:

- The chromosome on which the gene can be found. The first number or letter used to describe a gene's location represents the chromosome. Chromosomes 1 through 22 (the autosomes) are designated by their chromosome number. The sex chromosomes are designated by X or Y

- The arm of the chromosome. Each chromosome is divided into two sections (arms) based on the location of a narrowing (constriction) called the centromere. By convention, the shorter arm is called p, and the longer arm is called q. The chromosome arm is the second part of the gene's address. For example, 5q is the long arm of chromosome 5, and Xp is the short arm of the X chromosome.

- The position of the gene on the p or q arm. The position of a gene is based on a distinctive pattern of light and dark bands that appear when the chromosome is stained in a certain way. The position is usually designated by two digits (representing a region and a band), which

are sometimes followed by a decimal point and one or more additional digits (representing sub-bands within a light or dark area). The number indicating the gene position increases with distance from the centromere. For example: 14q21 represents position 21 on the long arm of chromosome 14. 14q21 is closer to the centromere than 14q22.

- Sometimes, the abbreviations "cen" or "ter" are also used to describe a gene's cytogenetic location. "Cen" indicates that the gene is very close to the centromere. For example, 16pcen refers to the short arm of chromosome 16 near the centromere. "Ter" stands for terminus, which indicates that the gene is very close to the end of the p or q arm. For example, 14qter refers to the tip of the long arm, or the very end, of chromosome 14.

Five members of the Ikaros family, this consists of Ikaros (IKZF1, encoded by IKZF1), Helios (IKZF2, encoded by IKZF2 at 2q34), Ailos (IKZF3, encoded by IKZF3; 17q12-21.1), Eos (IKZF4, encoded by IKZF4; 12q13.2), and Pegasus (IKZF5, encoded by IKZF5; 10q26.13) (Figure 2.2) [13-15]. IKZF1 gene is located on chromosome 7p12.2 band and consists of 8 exons, spanning a total of 62 kb and coding for a 519-amino acid protein and encoding transcription factor IKAROS, which plays a key regulatory role in lymphocyte production [16,17]. IKZF1 contains 6 zinc finger proteins and is mainly composed of 2 functional domains: an N-terminal DNA-binding domain (DBD) formed by 4 zinc fingers (ZF) and a C-terminal dimerization domain consisting of 2 additional ZFs. Exon 1 is not translated but may, together with the promoter region, regulate the transcription of the gene; little is known about the function of exons 2, 3, and 7. The remaining exons are crucial for the proper function of IKAROS: exons 4–6 encode the four N-terminal zinc fingers that are required for DNA binding and exon 8 codes for the two C-terminal zinc fingers that are used by IKAROS to dimerize either with itself or with other members of its family.

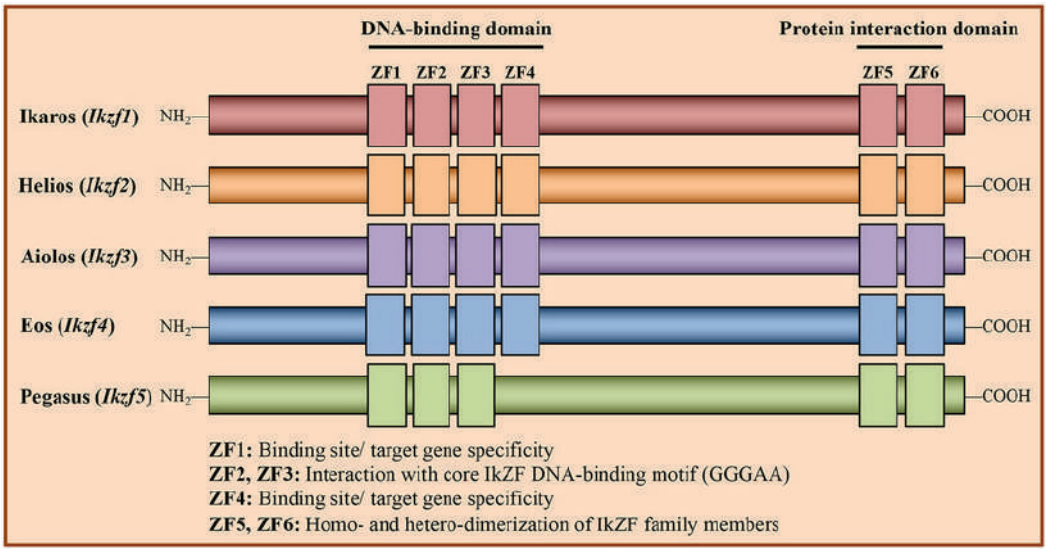

Figure 2. Structural domains of IKZF family proteins and their zinc finger functions

- Nowadays, roles for all family members except for Pegasus have been described in regulating hematopoietic cell populations [18]. Functions attributed to Ikaros family members were initially limited to roles in the early stages of lymphoid development, as the absence of functional Ikaros or Aiolos was found to result in severe disruption of T, B, and NK cell lineages. More recently, however, studies including conditional knockout of Ikaros factors in mature T cell populations have expanded understanding to include stage-specific transcriptional

regulation mediated by this family in mature lymphoid populations [18].

Recent studies have shown new findings about mutations in the IKZF1 gene [19,20]:

- While somatic IKZF1 alterations are associated with increased risk of B- progenitor acute lymphoblastic leukemia (B-ALL), autosomal dominant heterozygous germline mutations in IKZF1 are associated with immunodeficiency as well as B-ALL.

- Heterozygous germline IKZF1 mutations can be categorized into three allelic variants acting by haploinsufficiency (HI), dominant-negative (DN), or dimerization defective (DD).

- Patients with germline HI variants mostly present with a CVID phenotype that includes hypogammaglobulinemia, defective vaccine responses, progressive loss of B cell numbers, recurrent bacterial infections, and increased risk of autoimmunity/immune dysregulation and malignancy.

- Patients carrying DN mutations present with an early onset (<2 years) CID phenotype with severe immunological and clinical manifestations including opportunistic infections (i.e., *Pneumocystis jirovecii*) and increased leukemia susceptibility.

- Patients with DD variants show a higher incidence of autoimmune diseases/immune dysregulation and malignancy compared to the other allelic variants; recurrent or severe infections are less frequently seen in patients within this allelic variant.

Chromosomal mutations consist of four main types: deletion, inversion, insertion, and translocation. In chromosomal deletion mutations, the chromosome breaks, and the broken segment is lost, so it is no longer a part of the chromosome. The size of the lost part varies and the lost part can come from any part of the chromosome. Chromosomal deletion reduces the number of genes on the chromosome, often resulting in death. For example, in humans, a small deletion at the head of chromosome 21, (or a deletion of a long arm segment of chromosome 22) causes leukemia.

Chromosome 17 is one of the smallest chromosomes and has the highest gene density in humans. It is often rearranged in human tumors, especially severe in breast cancer, and is a breakpoint on its short or long branch [21]. The short arm and the long arm differ in the type of event they occur. Chromosome 17p is mainly related to deletions, some of which may be a refuge, while 17q shows a complex combination of overlapping increases and decreases. Most recent efforts have focused on two increases considered major events: 17q12-q21 corresponding to the amplification of ERBB2, and a large region at 17q23. Some new cancer-causing genes have been identified, where GRA7 and TOP2A at 17q21 or RP6SKB1, TBX2, PPM1D, and MUL at 17q23 have attracted the most attention [21].

18p deletion syndrome (18p-) also known as monosomy 18 [22]:

- It is a chromosomal disorder due to the deletion of all or part of the short (p) arm of chromosome 18. This is a rare chromosomal abnormality with many phenotypes, common clinical features include short stature; mild to moderate intellectual disability, especially slow clear speech; and facial dysmorphia (such as round face, drooping eyelids, strabismus, flat nose, protruding large ears, short philtrum, and small jaw). 18p deletion syndrome, first described by de Grouchy and colleagues, is now recognized as a long-standing chromosomal disorder, occurring in about 1/50,000 live births and the female/male ratio is 3:2. More than 300 cases have been reported in the medical literature since 1693, including the first case published in.

II. CASE REPORT

A 7-month-old female patient was admitted to the hospital due to fever and dyspnea, the disease lasted for 3 days. On the first 2 days, she had a productive cough, clear white mucus, coughing more at night, and had to wake up, the cough gradually increased to about 6-7 times a day, accompanied by a mild fever of about 38°C. She went to a private clinic for examination was

diagnosed with a viral infection, and was given medication to take home, but the drug was unknown. By the third day, she still had a lot of coughing with similar characteristics, fever, and dyspnea, and was taken to the hospital and admitted to Children's Hospital 1. The patient can eat and drink, and her bowel movements are normal. Regarding her medical history, the patient has had severe pneumonia twice and had to be hospitalized for treatment for at least 14 days:

- *The first time (01/29/2023 - 03/02/2023)* at 4 months old, treated for 30 days with unknown medication at Children's Hospital 2. The laboratory test results at this time:

+ Transcranial Doppler ultrasound showed that the patient had bilateral ventricular dilation with a ventricles height of about 8 mm;

+ Abdominal ultrasound did not record images of gastroesophageal reflux, monitoring multiple abscesses in the spleen;

+ The analysis of T, B, and Natural Killer Cells (T-B-NK) populations showed that the T cell population was normal range (CD3+: 2972.88 TB/µL, CD4+: 1621.52 TB/µL, CD8+: 1203.48 TB/µL), however, the

NK and B cell populations were reduced (CD56+CD16+: 109.77 TB/µL, and CD19+: 67.11 TB/µL) compared to the normal range according to age.

- *The second time (03/14/2023 - 03/30/2023)* at 6 months old, treated for 14 days with unknown medication at Pham Ngoc Thach Hospital.

+ AFB 2 samples test: negative, GeneXpert MTB/RIF: negative;

+ Tried treating for pulmonary tuberculosis for 1 month but did not respond.

Regarding obstetric history, the patient was born full-term by cesarean section, weighing 3 kg at birth, currently developing normally, fully vaccinated according to the vaccination schedule, no allergies recorded and the patient has chronic malnutrition (current weight 6.5 kg; height 60 cm). Family history has not recorded related diseases or genetic diseases.

The condition upon hospital admission: the patient is conscious, not feverish, SpO2 98%, breathing evenly, frequency 45 times/minute, has chest retraction, lungs have moist rales on both sides, and other organs have not recorded abnormalities. The discomfort symptoms are only related to respiration which are cough and dyspnea. With a history of multiple pneumonia, the patient was carefully examined and tested to assess the disease condition as well as find the cause. The results of the tests recorded are:

- Chest X-ray upon admission and CT scan: scattered interstitial damage on both lung fields;

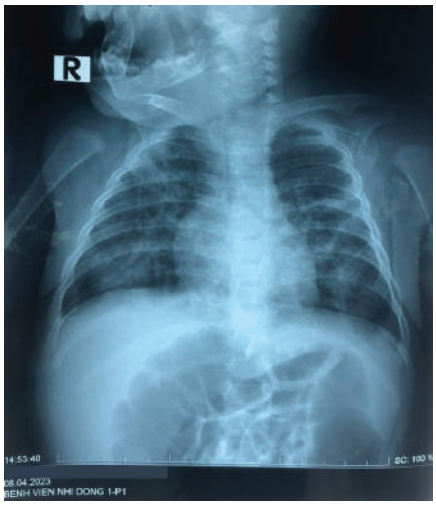

Figure 3. Chest X-ray image upon admission

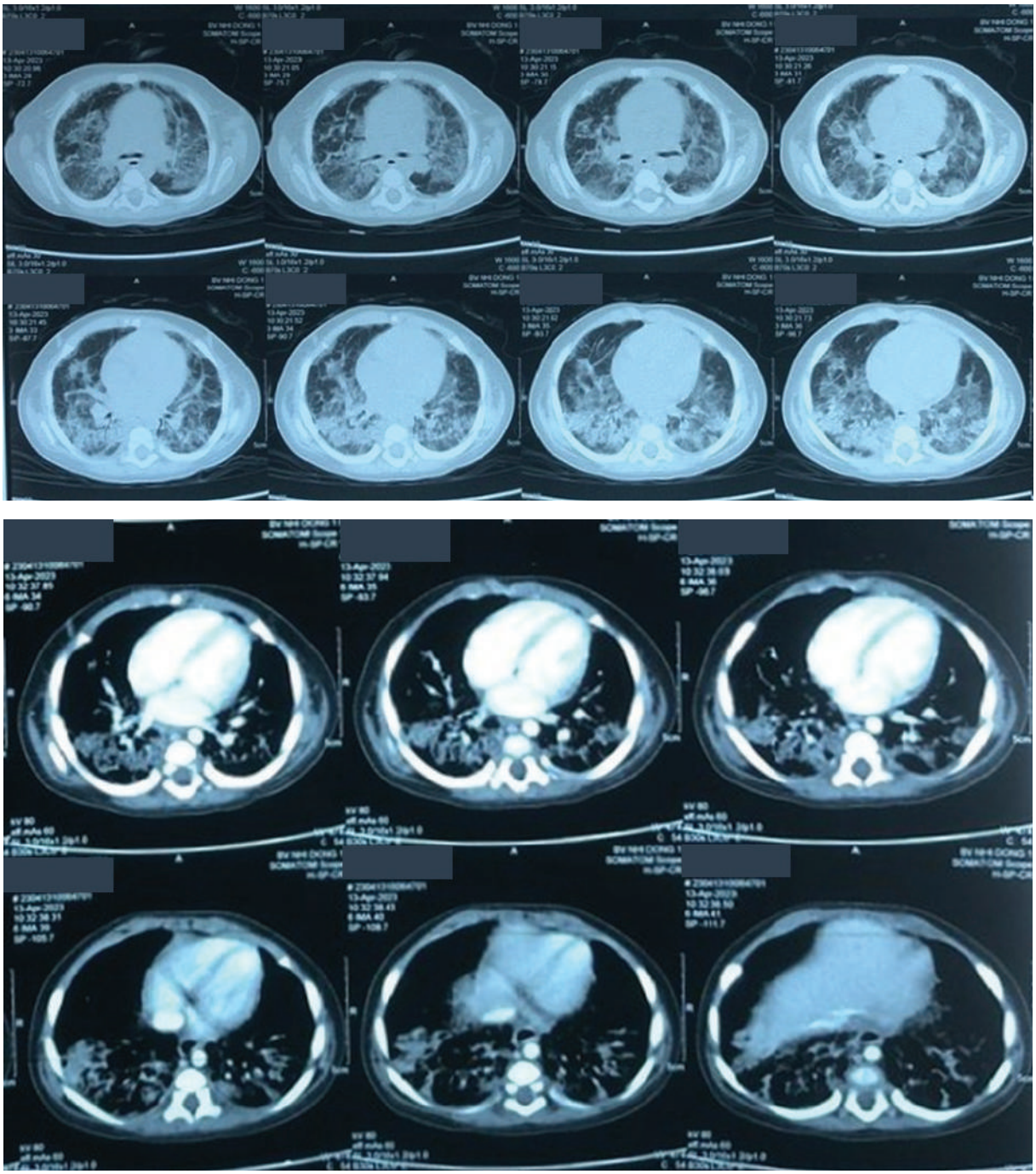

Figure 4. CT scan image

- The complete blood cell analysis showed that the number of white blood cells was normal range, however, in each component of the white blood cell line, the number of Lympho cells was severely reduced compared to the normal range according to age and only 23.5% remained (WBC: 10.96 x 103/µL, LYMPH: 2.58 x 103/µL, NEU: 8.12 x 103/µL), the number of platelets was normal range according to age and there was no anemia;

- C-reactive protein quantification increased to 39.84 mg/L; liver and kidney function tests were normal range;

- Immunological tests showed that the patient had a deep decrease in all 3 lines of Immunoglobulin A, G, and M compared to the age (IgA: 0.57 mg/dL, IgG: 13.8 mg/dL and IgM: 0.71 mg/dL); and the quantification of complement C3, C4 both increased (C3: 187.76 mg/dL, C4: 148.07 mg/dL);

- The results of protein electrophoresis showed that Albumin and Beta were normal range; Alpha increased, in which alpha-1: 0.31 g/dL, alpha-2: 1.2 g/dL; and Gamma decreased: 6.46 g/dL.

The patient was diagnosed with Recurrent Pneumonia - Bilateral ventricular dilation, after 17 days of treatment, the patient had a chest X-ray taken again and some necessary tests were done to monitor and evaluate:

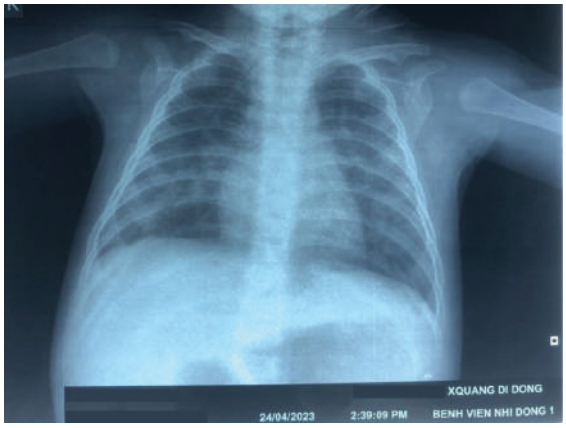

Figure 5. Chest X-ray image shows interstitial damage on both lungs and opacity on the left lung

The abnormal chromosome test result recorded the detection of deletion on chromosome 17 (del(17)(q12)) and deletion on chromosome 18 (del(18)(p11.32- p11.21)).

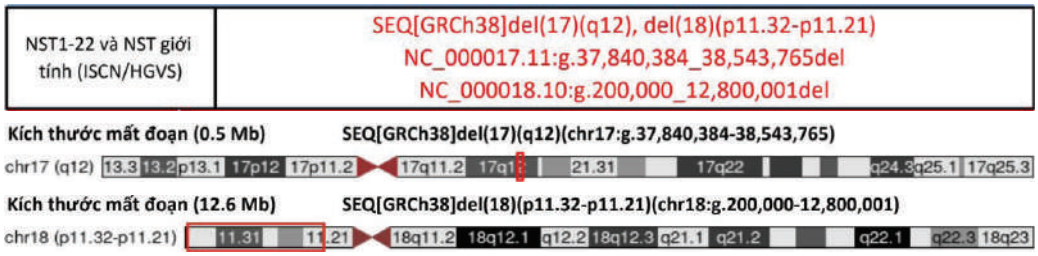

Figure 6. Abnormal chromosome test results

The mutation analysis results related to clinical information recorded the detection of 01 variant classified as pathogenic on the IKZF1 gene.

Gene	Modes of Inheritance	Homo/ Heterozygous	Position	Nucleotide/ Amino Acid Change	Consequence	Phenotype	Variant classification
IKZF1	Dominant	Heterozygous	chr7: 50382594	NM_00606 0.6: c.476A>G (NP_00605 1.1: p.Asn159S er)	Missense mutation	Immunodeficiency, common variable	Pathogenic

In addition, no variants classified as pathogenic/likely pathogenic were detected on hereditary cancer genes and genes recommended for reporting by the American College of Medical Genetics and Genomics (ACMG). Initially, the patient was given CPAP oxygen, antibiotics, and aggressive treatment during the treatment process. Since detecting the related genetic abnormality, the patient has been treated for congenital immunodeficiency by administering IVIg. As a result, the patient's life was saved, the respiratory failure and infection status were quickly improved, and there was no need to use antitubercular medications.

Currently, the patient has been treated for 5 months, the patient is still developing and is being closely monitored and managed, and every 1-2 months the patient needs IVIg transfusion along with prophylactic antibiotics.

III. DISCUSSION

The results of the abnormal chromosome analysis recorded a deletion on chromosome number 17 (del(17)(q12)), and a deletion on chromosome number 18 (del(18)(p11.32-p11.21)). A disease-causing variant was detected on the IKZF1 gene (dominant inheritance, heterozygous). This variant has been observed in patients with immunodeficiency.

From the results of genetic testing in the patient, the authors found a close relationship between congenital immunodeficiency and genetics, causing the condition of recurrent pneumonia in the reported case. Notably, in this patient, there is a mutation in the IKZF1 gene, which encodes Ikaros - a transcription factor with an important regulatory function in lymphocyte formation [14,15]. Based on the distinct functions of the Ikaros family members, it is suggested that mutations in the IKZF1 gene will greatly affect the process of forming blood cell populations, especially lymphocyte populations. For this case, IKZF1 has a dominant, heterozygous gene mutation form, and recent studies have shown changes in IKZF1 in somatic cells related to an increased risk of acute lymphoblastic leukemia B (B- ALL), while dominant heterozygous germ line mutations on normal chromosomes in IKZF1 are related to immunodeficiency. IKZF1 germ line heterozygous mutations can be classified into three allelic variants operating by haploinsufficiency (HI), dominant negative (DN) or hypomorphic defect (DD) mechanisms. Among them, DN mutations have an early-onset CID phenotype (<2 years old) with severe clinical and immune manifestations including opportunistic infections and an increased risk of leukemia [25,26]. Therefore, based on the age of onset of the disease along with the current clinical and paraclinical characteristics, it can support the DN mutation causing the phenotype of recurrent pneumonia.

The discovery of the main cause of the condition of recurrent pneumonia in the reported case, which is due to the IKZF1 gene mutation, has helped doctors to appropriately treat with Immunoglobulin, dramatically improving the clinical condition of the patient. The results of the analysis using WES technique show that the IKZF1 gene mutation in this patient is located at the position of chromosome number 07 (chr7:50382594), which has not been studied and published in the Vietnamese population. This study will be an important premise for larger sample studies in the future to determine the correlation between IKZF1 gene mutation and recurrent pneumonia in children. This plays a very large role in helping clinicians have appropriate treatment and management strategies for pediatric pneumonia recurrence cases related to genetic mutations, in order to reduce the prognosis of severe disease and mortality rate.

Figure 7. The mutation is located at position chr7:50382594 on the IKZF1 gene, on chromosome number 07.

The results recorded a mutation c.476 A>G due to A being replaced by G at nucleotide position 476 on the IKZF1 gene, leading to the change from asparagine to serine at amino acid 159 (p.N159S). This mutation is located in exon 5 containing ZF2, ZF3 responsible for DNA binding. According to the analysis in Figure 2.8, all patients carrying the heterozygous missense mutation IKZF1 N159S had early symptoms in life and all had onset symptoms under 15 months of age. Pneumonia caused by Pneumocystis jirovecii was diagnosed in all patients aged 6 to 24 months.

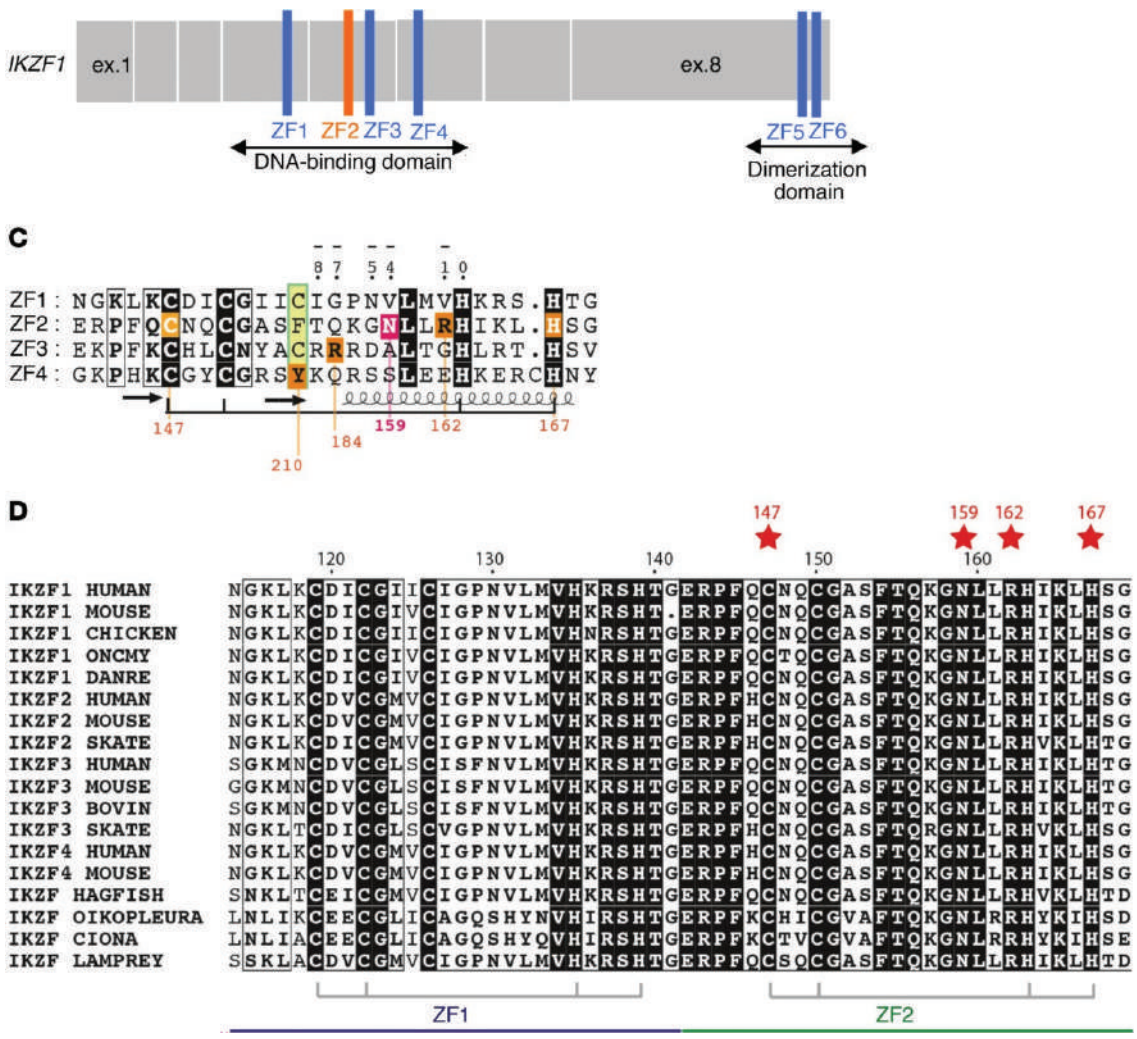

Figure 8. The mutation position of the nucleotide on the gene (c.476A>G) and the corresponding change on the encoded protein (p.N159S)

The deletion mutation on chromosome 17 is often associated with an increased risk of cancer. For 17p (short arm), it is mainly related to deletions, while on 17q (long arm), there is a complex combination of overlapping increases and decreases. Recent findings at 17q12-q21 are of interest because it corresponds to the amplification of ERBB2, so the deletion mutation on chromosome 17q in this patient may increase the risk of cancer, especially since this is a female patient, it may be closely related to an increased risk of breast cancer [21].

In addition to the deletion mutation on chromosome 17, the patient is also associated with a deletion mutation on chromosome 18p (18p-), also known as monosomy 18, which is a rare chromosomal abnormality with many phenotypes. Common clinical features include short stature; mild to moderate intellectual disability, especially clear speech delay; and facial dysmorphia. In addition to these clinical manifestations, bone deformities and eye complications are also often observed. Heart abnormalities, growth hormone deficiency, and neurological disorders such as motor disorders and seizures have also been reported, but are less common. Brain malformation, the most severe phenotype of this syndrome, which is part

of the spectrum of holoprosencephaly (HPE), has also been reported [22]. For this patient, the ultrasound results showed that the patient had bilateral ventricular dilation. Based on the relationship between the 18p deletion syndrome and the possible phenotypes, the authors think that ventricular dilation in the patient may be a consequence of this type of mutation.

IV. CONLUSION

Early identification of IKZF1 mutations in children with recurrent pneumonia allows for tailored immunological therapy such as IVIg, leading to improved outcomes. This case emphasizes the clinical utility of genetic screening and the importance of considering underlying immunodeficiency in recurrent pediatric infections.

V. ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Written informed consent was obtained from the patient's parents for publication of this case report and any accompanying images.

REFERENCES

1. **Global Burden of Disease Collaborative Network**. Global Burden of Disease Study 2019 (GBD 2019) Results. Seattle, United States: Institute for Health Metrics and Evaluation (IHME), 2021.
2. **Patria F, Longhi B, Tagliabue C,** *et al*. Clinical profile of recurrent community- acquired pneumonia in children. BMC Pulm Med. 2013;13:60.
3. **Schnabel E, Sausenthaler S, Brockow I,** *et al*. Burden of otitis media and pneumonia in children up to 6 years of age: results of the LISA birth cohort. Eur J Pediatr. 2009;168(10):1251-1257.
4. **GBD 2015 LRI Collaborators**. Estimates of the global, regional, and national morbidity, mortality, and aetiologies of lower respiratory tract infections in 195 countries: a systematic analysis for the Global Burden of Disease Study 2015. Lancet Infect Dis. 2017;17(11):1133-1161.
5. **Koh JWJC, Wong JJ, Sultana R** *et al*. Risk factors for mortality in children with pneumonia admitted to the pediatric intensive care unit. Pediatr Pulmonol. 2017;52(8):1076-1084.
6. **Owayed AF, Campbell DM, Wang EE**. Underlying causes of recurrent pneumonia in children. Arch Pediatr Adolesc Med. 2000;154(2):190-194.
7. **Belessis Y, Doyle K, Jaffe A**. Investigation of the Child with Recurrent Pneumonia. 2008.
8. **Montella S., Corcione A., Santamaria F**. Recurrent pneumonia in children: a reasoned diagnostic approach and a single centre experience. Int. J. Mol. Sci. 2017;18.
9. **Bolursaz MR, Lotfian F, Ghaffaripour HA, Hassanzad M**. Underlying Causes of Persistent and Recurrent Pneumonia in Children at a Pulmonary Referral Hospital in Tehran, Iran. Arch Iran Med. 2017;20(5):266-269.
10. **Ciftçi E, Güneş M, Köksal Y, Ince E, Doğru U**. Underlying causes of recurrent pneumonia in Turkish children in a university hospital. J Trop Pediatr. 2003;49(4):212-215.
11. **Hoang KL, Ta AT, Pham VT**. Severe recurrent pneumonia in children: Underlying causes and clinical profile in Vietnam. Ann Med Surg (Lond). 2021;67:102476.
12. **National Library of Medicine (NIH)**. How do geneticists indicate the location of a gene?
13. **Iacobucci I, Iraci N, Messina M** *et al*. IKAROS deletions dictate a unique gene expression signature in patients with adult B-cell acute lymphoblastic leukemia. PLoS One. 2012;7(7):e40934.
14. **Powell MD, Read KA, Sreekumar BK, Oestreich KJ**. Ikaros Zinc Finger Transcription Factors: Regulators of Cytokine Signaling Pathways and CD4+ T Helper Cell Differentiation. Front Immunol. 2019 Jun 6;10:1299.
15. **Read KA, Jones DM, Freud AG, Oestreich KJ.** Established and emergent roles for Ikaros transcription factors in lymphoid cell

development and function. Immunol Rev. 2021;300(1):82-99.

16. **Georgopoulos K, Bigby M, Wang JH,** *et al*. The Ikaros gene is required for the development of all lymphoid lineages. Cell. 1994;79(1):143-156.
17. **Molnár A, Wu P, Largaespada DA,** *et al*. The Ikaros gene encodes a family of lymphocyte-restricted zinc finger DNA binding proteins, highly conserved in human and mouse. J Immunol. 1996;156(2):585-592.
18. **Read KA, Jones DM, Freud AG, Oestreich KJ**. Established and emergent roles for Ikaros transcription factors in lymphoid cell development and function. Immunol Rev. 2021;300(1):82-99.
19. **Kuehn HS, Nunes-Santos CJ, Rosenzweig SD**. Germline IKZF1 mutations and their impact on immunity: IKAROS-associated diseases and pathophysiology. Expert Rev Clin Immunol. 2021;17(4):407-416.
20. **Boutboul D, Kuehn HS, Van de Wyngaert Z,** *et al*. Dominant-negative IKZF1 mutations cause a T, B, and myeloid cell combined immunodeficiency. J Clin Invest. 2018;128(7):3071-3087.
21. **Orsetti B, Nugoli M, Cervera N,** *et al*. Genomic and expression profiling of chromosome 17 in breast cancer reveals complex patterns of alterations and novel candidate genes. Cancer Res. 2004;64(18):6453-6460.
22. **Choi JY, Moon JU, Yoon DH,** *et al*. 18p Deletion Syndrome Originating from Rare Unbalanced Whole-Arm Translocation between Chromosomes 13 and 18: A Case Report and Literature Review. Children (Basel). 2022;9(7):987.