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Case Report

Cystic fibrosis caused by homozygous *CFTR* gene mutation leading to pulmonary involvement: a case report

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Abstract: Cystic fibrosis (CF) is an autosomal recessive monogenic disorder caused by mutations in the CF transmembrane conductance regulator (*CFTR*) gene, resulting in impaired *CFTR* protein function. Predominantly affecting Caucasians, CF involves multiple organ systems, including the lungs, pancreas, liver, gastrointestinal tract, and reproductive system. In contrast, CF remains rare among Asian populations, particularly within the Chinese demographic. Reported cases in China predominantly feature heterozygous *CFTR* mutations, with no confirmed instances of homozygous mutations. A 15-year-old male presented with a 6-year history of recurrent cough and purulent yellow-green sputum production, without hemoptysis. Whole exome sequencing identified a homozygous *CFTR* mutation, NM_000492.4:c.2290C>T (p.Arg764*), confirming the diagnosis of CF complicated by pulmonary infection. The patient received intravenous cefoperazone/sulbactam (2.25 g every 12 hours) and moxifloxacin (400 mg once daily). Symptomatic improvement was achieved after 2 weeks, and azithromycin was prescribed (three times weekly) upon discharge. This case highlights the importance of considering *CFTR* gene mutations in patients with prolonged respiratory symptoms (recurrent cough and sputum production) and imaging findings indicative of pulmonary CF. Whole exome sequencing is recommended to determine the genetic etiology in such cases and guide targeted management.

Keywords: Cystic fibrosis, *CFTR* homozygous mutation, case report, pulmonary infection

Introduction

Cystic fibrosis (CF) is an autosomal recessive genetic disorder primarily impairing exocrine gland function. It is clinically defined by chronic obstructive pulmonary disease, pancreatic exocrine insufficiency, and elevated sweat electrolyte levels [1]. The condition manifests with diverse systemic complications, including respiratory tract involvement, hepatobiliary and gastrointestinal abnormalities, nasal polyposis, and male infertility [1]. First described by Davis in 1938 [2], CF exhibits significant ethnic and geographic variability in prevalence. In Caucasian populations across Europe and North America, the incidence is approximately 1 in 2,500, whereas it remains rare in Asian populations, with a reported incidence of 1 in 350,000 in Japan. In China, where the Han Chinese comprise the majority, CF prevalence is low, and comprehensive epidemiologic data remain unavailable [3]. Nevertheless, advancements in genetic testing and increasing clinical awareness have led to a steady rise in CF diagnoses within China in recent years [4, 5]. Li et al. [6] documented the first genetically confirmed case of CF in China in 2006. The patient, diagnosed at 14, exhibited persistent productive cough since birth. By age 7, bronchiectasis was identified alongside comorbidities including sinusitis, otitis media, steatorrhea, and cutaneous sodium chloride crystal deposits. Genetic analysis revealed compound heterozygous *CFTR* mutations inherited from both parents. Subsequent reports remained sporadic, with only limited case studies published [7, 8].

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In China, CF frequently fails to achieve timely diagnosis due to its low incidence and non-specific clinical presentation. The absence of diagnostic infrastructure - such as sweat chloride testing and comprehensive *CFTR* gene sequencing - combined with limited physician awareness, further impedes recognition. Misdiagnosis as bronchiectasis or recurrent pulmonary infections is common; although anti-infective therapies offer temporary symptom relief, disease recurrence is inevitable.

The CF transmembrane conductance regulator (*CFTR*) gene remains the sole gene implicated in CF pathogenesis. Located at 7q31, it spans approximately 250 kb and comprises 27 exons. To date, around 2000 mutations have been identified, including missense (39%), frameshift (16%), splice site (11%), nonsense (8%), and large deletions or insertions (2%) [6]. Globally, over 80% of CF patients carry at least one F508del allele, with approximately 40% being homozygous for this mutation. Apart from F508del, only five mutations - *G542X, G551D, N1303K, R117H*, and *W1282X* - exceed a 1% frequency, while roughly 50 others occur at frequencies above 0.1%. The remaining mutations are exceedingly rare [9]. Studies reveal that *CFTR* mutations among domestic CF patients present predominantly as heterozygous variants, with mutation spectra differing markedly from those observed in other populations [10]. Approximately 70%-90% of Caucasian CF patients carry at least one p.Phe508del allele [10], whereas this mutation is infrequent among Chinese CF patients [11]. Similar disparities are evident across age groups; adult CF patients rarely exhibit Phe508del mutations, while variants retaining residual function, such as p.Gly970Asp, are more prevalent [10]. In Western countries, the Phe508del homozygous mutation remains the most frequently identified genotype in CF patients regardless of age [10]. Its association with severe disease and early-onset clinical manifestations renders it a key diagnostic indicator in pediatric cases [10]. To date, the c.2290C>T (p.Arg764*) mutation, which contributes to pulmonary CF, has not been documented. This case demonstrates successful diagnosis and management, offering further insight into *CFTR* mutation-related CF and the supporting differential diagnosis, particularly when distinguishing CF caused by homozygous *CFTR* mutations. Additionally, the identified *CFTR* mutation enriches the genetic dataset for CF diagnosis in the Chinese population.

Patient information

The patient presented with a 6-year history of recurrent paroxysmal cough and sputum production without identifiable triggers. The cough produced yellow-green purulent sputum, predominantly worsening at night and in the early morning. Wheezing and exertional wheezing sounds were reported. Chest computed tomography (CT) revealed no evident infectious lesions, resulting in repeated misdiagnoses of "acute bronchitis". Although symptomatic relief was occasionally achieved with over-the-counter cough syrups, symptoms persisted. Two years prior, the patient sought evaluation at this hospital and was diagnosed with: "1. Diffuse panbronchiolitis, 2. Pan-sinusitis". The treatment regimen included cefotaxime and azithromycin for infection control, terbutaline and budesonide nebulization to relieve bronchospasm, and acetylcysteine for mucolysis. Symptomatic improvement was achieved following therapy, and long-term azithromycin (1 tablet daily) was recommended. However, the patient discontinued azithromycin after 6 months. Ten days before the current admission, the condition worsened, characterized by increased cough frequency and production of thick, greenish-white sputum that was difficult to expectorate. Additional symptoms included exertional wheezing, throat irritation, nasal congestion, left-sided frontal-temporal headache, and intermittent purulent nasal discharge. Intravenous treatment at a local clinic (details unavailable) yielded no significant improvement, prompting hospital admission for further management.

His parents and one younger sister were in good health. No familial history of infectious, neoplastic, or hereditary diseases was reported.

The patient presented a prior diagnosis of pansinusitis and mild bilateral inferior turbinate hypertrophy, although specific details remained unspecified. No history of chronic conditions, including hypertension, diabetes, or coronary artery disease, was documented. Infectious diseases such as tuberculosis, typhoid, or malaria, as well as relevant exposures, were denied. The patient reported no history of surgi-

cal procedures, blood transfusions, trauma, known food or drug allergies, or vaccinations. Occupational diseases, epidemic or endemic infections, and high-risk sexual behavior were also denied. Additionally, there was no reported exposure to toxic substances, occupational hazards, psychological trauma, or recent travel.

On physical examination, the following observations were recorded: (1) temperature 36.2°C, pulse 89 beats/min, respiratory rate 22 breaths/min, blood pressure 111/63 mmHg, height 165 cm, weight 42 kg, and BMI 15.4 kg/m^2; (2) general appearance marked by malnutrition, emaciation, and features of chronic illness, with normal developmental status; (3) absence of scleral or skin jaundice, no palpable superficial lymphadenopathy, and mild cyanosis of the lips; (4) tonsils not enlarged, no pharyngeal erythema, midline tongue positioning, and no jugular venous distention; (5) normal thoracic contour, no intercostal space widening, and symmetrical, regular respiratory movements; (6) no pleural friction rub or crepitus on palpation, clear lung fields with coarse breath sounds bilaterally, fine crackles auscultated in the left lower lung, and no dry rales or pleural friction rub detected; (7) cardiac percussion revealed no enlargement, with a regular heart rhythm; (8) abdomen soft with mild tenderness in the upper quadrant, without rebound tenderness or guarding, liver and spleen not palpable, no detectable masses, absence of costovertebral angle or ureteric pathway tenderness, no shifting dullness, and normal bowel sounds; (9) no peripheral edema observed in the lower extremities; and (10) physiological reflexes intact, with no pathological reflexes elicited.

Laboratory analysis yielded the following results: (1) complete blood count: white blood cell count 8.01 × 10^9/L, red blood cell count 5.80 × 10^{12}/L, hemoglobin 142 g/L, platelets 401 × 10^9/L (elevated), neutrophils 65.8%, lymphocytes 25.7%, and absolute neutrophil count 12.35 × 10^9/L; (2) inflammatory markers: C-reactive protein 75.0 mg/L, procalcitonin in 0.14 ng/L, NN-terminal pro-B-type natriuretic peptide 173.10 pg/mL; (3) alveolar lavage fluid (right upper lobe): no atypical cells identified, with neutrophils predominating, followed by lymphocytes, phagocytes, and squamous epithelial cells; (4) bronchial brush specimen (bronchoscopy): no atypical cells detected, primarily ciliated columnar epithelial cells with scattered neutrophils and minimal phagocyte presence; (5) additional evaluations: liver and kidney function, electrolytes, blood glucose, infection markers, myocardial enzyme profile, myoglobin, troponin, urinalysis, stool analysis, plasma D-dimer, antinuclear antibody profile, vasculitis-related autoantibodies, rheumatoid arthritis autoantibodies, complement components C3 and C4, and immunoglobulins (IgG, IgA, and IgM) all remained within normal limits.

The sinus CT performed at admission demonstrated complete sinusitis accompanied by mild inferior turbinate hypertrophy (**Figure 1**). Chest CT imaging revealed bilateral diffuse bronchiectasis with infectious changes, marked bronchial wall thickening, and mucus plugging within several airways. Small airway involvement was evident, along with lobular centrilobular nodules and air trapping (**Figure 2A-F**).

Bronchoscopy revealed diffuse mucosal erythema involving the right main bronchus, right upper, middle, and lower basal segments, with smooth surfaces and unobstructed lumens. Profuse viscous secretions accumulated at the orifices of each lobe, without evidence of neoplasms or hemorrhage (**Figure 3**). Comparable changes were identified in the left main bronchus, left upper lobe, lingula, and left lower basal segments, characterized by intact mucosal surfaces, patent lumens, and excessive viscous secretions at the lobar openings. No neoplastic lesions or active bleeding were detected (**Figure 3**). Bronchoalveolar lavage was conducted in the right upper lobe, and samples were submitted for pathologic assessment and microbiological culture. Pulmonary function testing demonstrated normal ventilatory and diffusing capacities, with total respiratory impedance, total airway resistance, central airway resistance, and peripheral elastic resistance all within normal limits. The bronchial provocation test yielded negative results.

Genetic analysis identified the c.2290C>T (p.Arg764*) nonsense mutation within the *CFTR* coding region (**Figure 4**), which induced mRNA degradation by nonsense-mediated decay (NMD) or triggered premature translational termination, ultimately abolishing normal protein function. Sanger sequencing verified biparental inheritance of this mutation (**Figure 5**).

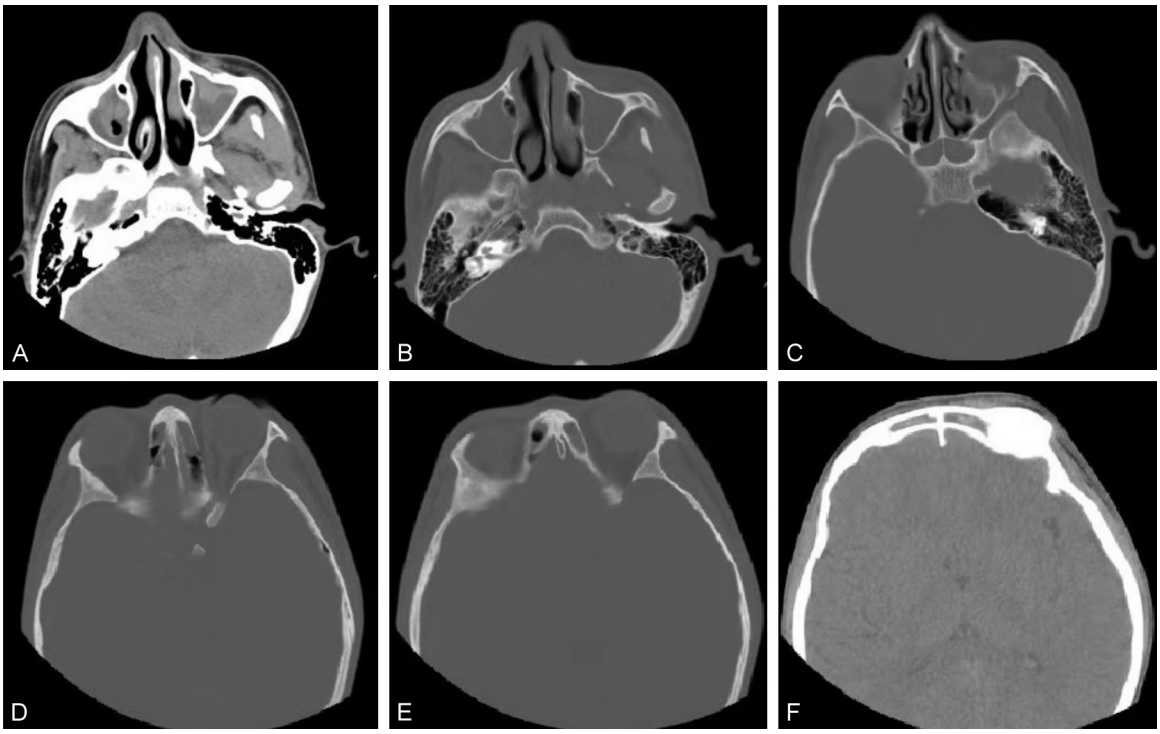

Figure 1. Nasal sinus CT findings at admission. A: Bilateral maxillary sinus CT (soft tissue window); B: Bilateral maxillary sinus CT (bone window); C: Bilateral sphenoid sinus CT (bone window); D: Bilateral ethmoid sinus CT (bone window); E: Bilateral ethmoid sinus CT (bone window); F: Bilateral frontal sinus CT (soft tissue window).

Based on clinical presentation, imaging, and genetic analysis, the patient was diagnosed with CF caused by a homozygous *CFTR* mutation, manifesting as pulmonary infection. Treatment included intravenous piperacillin-tazobactam and nebulized tobramycin for antimicrobial therapy, alongside nebulized acetylcysteine as a mucolytic agent. Daily positional drainage and sputum clearance were prescribed, supplemented by bronchoscopic sputum aspiration over two weeks. Symptomatic improvement was observed, with reduced cough and sputum production, and follow-up chest CT demonstrated marked lesion resolution (**Figure 2G-L**). Upon discharge, the patient was prescribed oral azithromycin 500 mg three times weekly for six months. Additionally, inhalation of 4 ml hypertonic saline (3%-7%) twice daily was recommended. Daily airway clearance through positional drainage and expectoration, along with oral acetylcysteine, continued as maintenance therapy. Follow-up evaluations every 3-6 months were advised, including respiratory assessment and pulmonary function tests. High-resolution chest CT should be repeated if indicated. Routine monitoring of steatorrhea symptoms, growth parameters, complete blood count, liver function, amylase, lipase, and upper abdominal ultrasound was recommended. Fasting glucose levels should be monitored regularly, with postprandial glucose and glucose tolerance tests performed as clinically indicated.

Three months post-discharge, the patient remained clinically stable without reported discomfort. Follow-up assessments, including liver and renal function tests, blood glucose levels, and abdominal ultrasound, revealed no abnormalities. Chest CT imaging indicated no evidence of infection. Regular physical activity was recommended, along with precautions against cold exposure and respiratory pathogens. Monthly follow-up evaluations were scheduled for a minimum of six months.

Discussion

Cystic fibrosis (CF) results from mutations in the *CFTR* gene, first cloned and isolated by Riordan et al. in 1989 [12]. The *CFTR* gene encodes a cAMP-regulated chloride channel

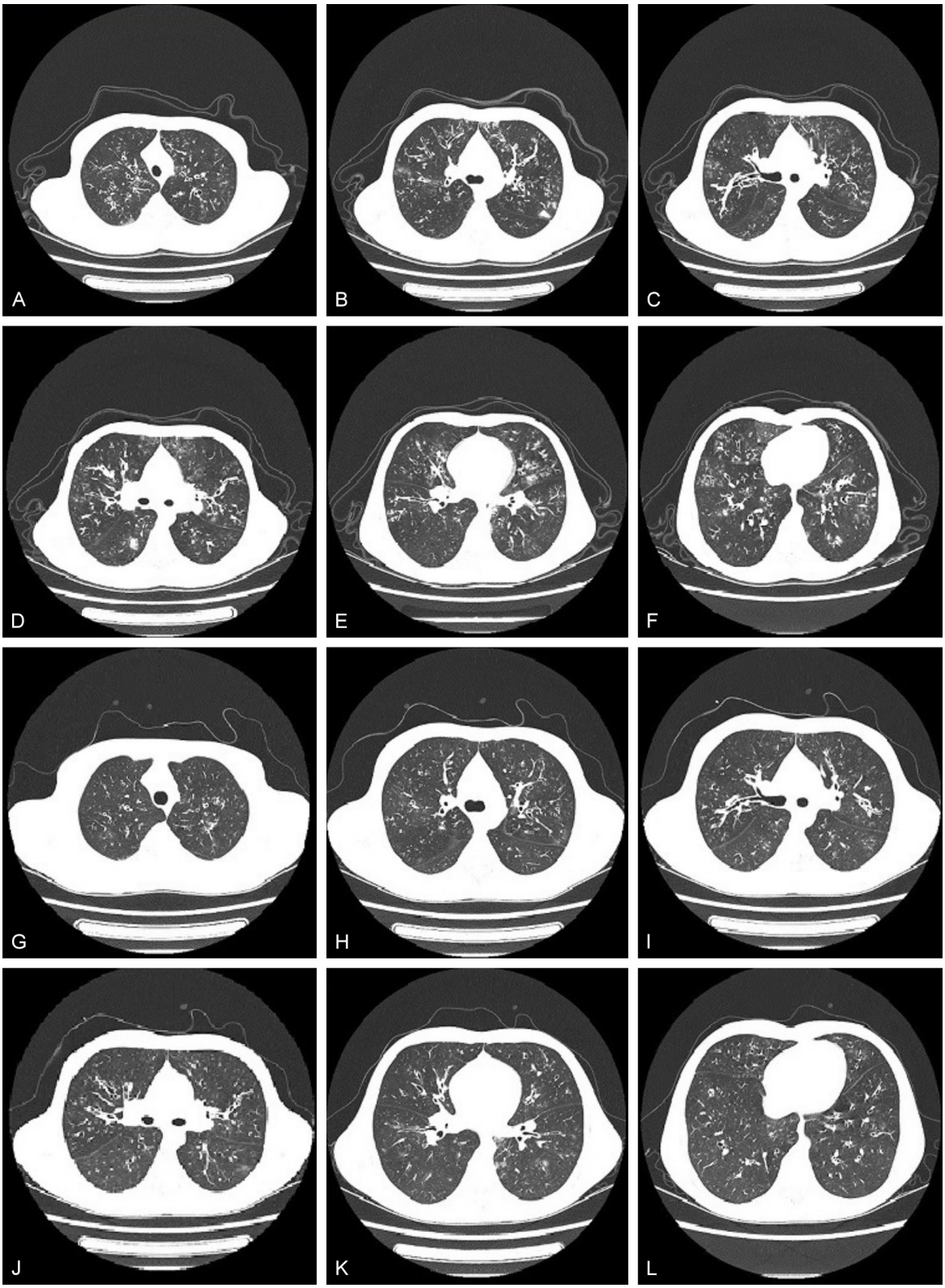

Figure 2. Chest CT findings before and after treatment. A-F: Chest CT before treatment. A: Upper lobe layer of both lungs; B: Tracheal prominence layer; C: Bifurcation layer of the anterior and posterior segments of the upper lobe of the right lung; D: Middle lobe of right lung; E: Bifurcation layer of left lower lung basal ganglia; F: Basal layer of both lungs. G-L: Chest CT after treatment. G: The upper lobe level of both lungs; H: The level of tracheal prominence; I: Bifurcation layer of the anterior and posterior segments of the upper lobe of the right lung; J: Middle lobe level of the right lung; K: Bifurcation level of the basal trunk of the left lower lung; L: Lower lobes of both lungs.

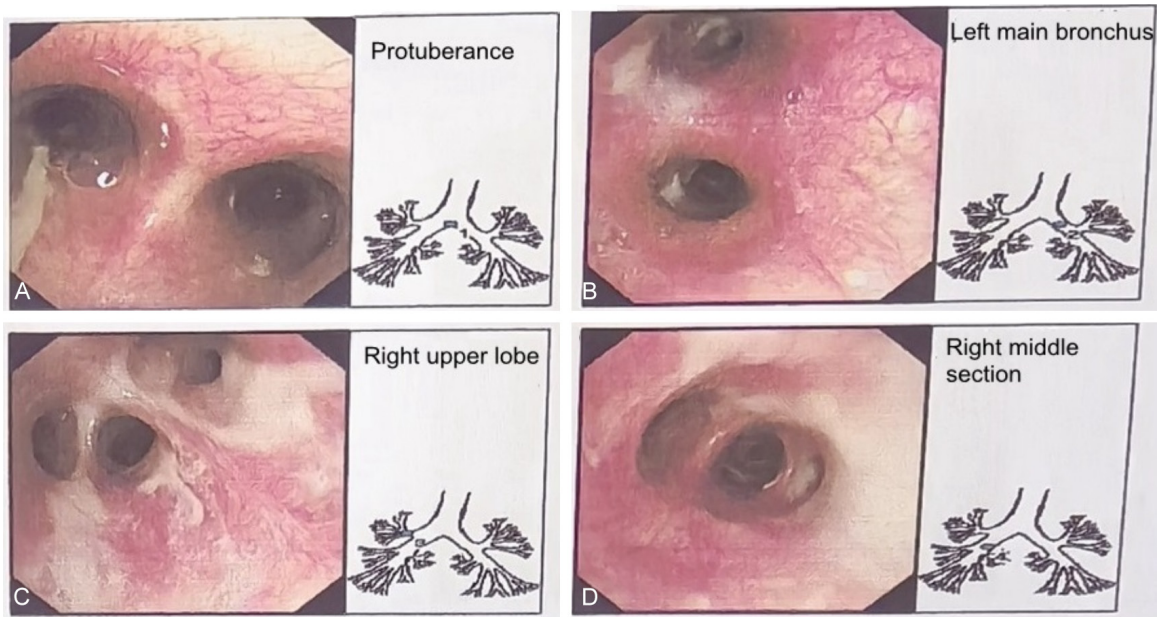

Figure 3. Bronchoscopic findings of the lungs. A: Protuberance; B: Left main bronchus; C: Right upper lobe; D: Right middle section.

located on the long arm of chromosome 7, essential for maintaining epithelial ion transport and fluid homeostasis. Mutations impair channel function, disrupting chloride and sodium ion balance in epithelial secretions and causing exocrine fluid dehydration. Accumulated viscous secretions obstruct airways, triggering persistent infection, inflammation, chronic airflow limitation, bronchiectasis, and progressive pulmonary parenchymal injury. In the pancreas and bile ducts, luminal obstruction from inspissated secretions induces bile duct blockage. In sweat glands, excessive chloride and sodium loss elevate electrolyte concentrations on the skin surface, occasionally producing visible sodium chloride crystals during perspiration.

In clinical settings, CF commonly presents with multisystem involvement, predominantly affecting the respiratory tract, particularly when pulmonary CF is present. Respiratory manifestations typically include recurrent infections, viscous sputum, impaired sputum clearance, wheezing, and chronic sinusitis. Sputum cultures frequently isolate *Pseudomonas aeruginosa* and *Staphylococcus aureus*. Radiologic findings often reveal bronchiectasis, pulmonary infiltrates, and atelectasis. Gastrointestinal involvement may manifest as neonatal meconium ileus, pancreatic insufficiency, recurrent pancreatitis, and malnutrition [13]. In China, pulmonary involvement remains the primary presentation, with limited digestive tract involvement and preserved pancreatic function in most cases [14]. By contrast, in Western populations, over 98% of male CF patients exhibit infertility secondary to congenital bilateral absence of the vas deferens [13]. Additional clinical features may include digital clubbing and the presence of white, powdery sweat crystals on the skin. This patient primarily exhibited pulmonary complications, with a six-year history of recurrent bronchial infections, airway obstruction, mild cough, and pneumonia. Chest CT scans identified bronchiectasis and pulmonary infection, suggestive of CF. However, symptom overlap with common bronchiectasis and recurrent pulmonary infections contributed to diagnostic delays. The patient was repeatedly misdiagnosed over six years with “diffuse pan-bronchiolitis”, “pan-sinusitis”, and “bronchiectasis with pulmonary infection”, leading to antibiotic and antitussive therapy. Although initial symptom relief was achieved, frequent relapses ensued.

Advancements in molecular biology and expanded access to genetic testing have substantially enhanced the diagnostic use of genetic analysis for CF. By 2017, over 2,000 *CFTR* gene mutations had been identified; how-

Molecular Genetic Testing Report

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Table1 Explain the (pathogenic/suspected pathogenic) variations in the phenotype of the test subject:

1.1 Single nucleotide variations and small fragment insertion/deletion variations (SNV/Indel)

Gene	Chromosomal location	Variation information	zygotic type	Disease name	Genetic pattern	Source of variation	Variation classification
CFTR	chr7: 117232511	NM_000492.4:c.2290C>T(p.Arg764*)	Homozygous	cystic fibrosis [MIM:219700]	AR	Father /Mother	Pathogenic variation

1.2 Large Segment Copy Number Variation (CNV)

Chromosome banding	Variation type	Related genes within the region	Related diseases	Source of variation	Variation classification
None					

Table2 Variants that are consistent with the main clinical phenotype of the subject, but cannot be clearly correlated with their onset or disease progression:

2.1 Single nucleotide variations and small fragment insertion/deletion variations (SNV/Indel)

Gene	Chromosomal location	Variation information	zygotic type	Disease name	Genetic pattern	Source of variation	Variation classification
None							

2.2 Large Segment Copy Number Variation (CNV)

Chromosome banding	Variation type	Related genes within the region	Related diseases	Source of variation	Variation classification
None					

Table3 Other variations that are only partially related to the clinical phenotype of the subject:

Gene	Chromosomal location	Variation information	zygotic type	Disease name	Genetic pattern	Source of variation	Variation classification
None							

Table4 Minor findings recommended by the American Society of Medical Genetics (ACMG):

Gene	Chromosomal location	Variation information	zygotic type	Disease name	Genetic pattern	Variation classification
TNNI3	chr19: 55665462	NM_000363.5:c.485G>A(p.Arg162Gln)	Heterozygous	Familial hypertrophic cardiomyopathy type 7 [MIM:613690]	AD	Suspected pathogenic variant

Figure 4. Report of molecular genetic testing.

ever, not all variants are pathogenic, and the mechanisms underlying this variability remain incompletely understood, with research efforts continuing to address these complexities [15]. In 2006, Li et al. [6] documented the first genetically confirmed CF case in China. The patient, diagnosed at 14 years of age, presented with lifelong recurrent sputum production, bronchiectasis diagnosed at 7, and comorbid sinusitis, otitis media, steatorrhea, and skin sodium chloride crystallization. Genetic analysis revealed compound heterozygous *CFTR* mutations inherited from both parents.

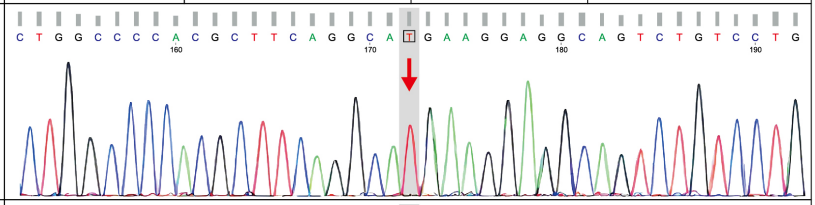
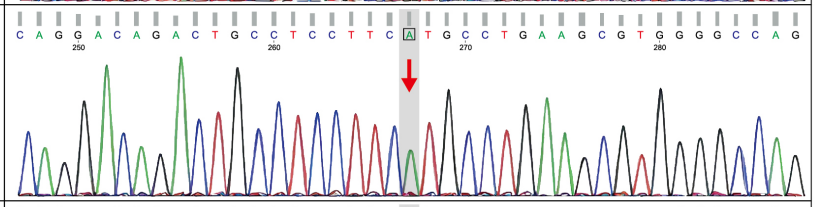
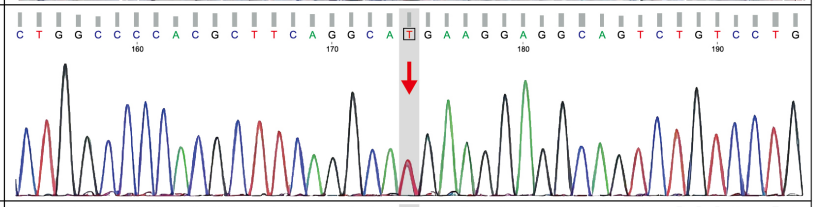
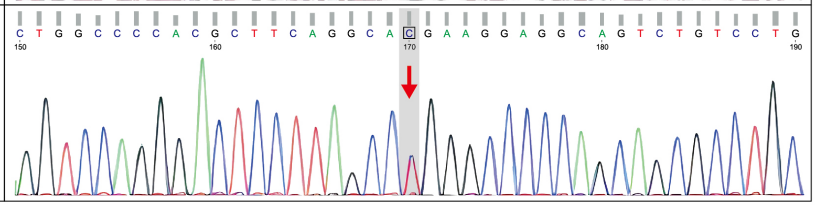
Substantial disparities in *CFTR* gene mutation spectra have been documented between Asian

Sanger Sequencing Diagram

A

Sanger verification results			
Verify site information	Relationship	Sample number	Verification results
CFTR chr7:117232511 Exon:14/27 NM_000492.4: c.2290c>T (p.Arg764*)	Proband	NP26S01408	Homozygous
	Father	VP26D02924	Heterozygous
	Mother	VP26D02923	Heterozygous
TNNI3 chr19:55665462 Exon:7/8 NM_000363.5: c.485G>A (p.Arg162Gln:)	Proband	NP26S01408	Heterozygous

B

Peak plot results					
Gene	*CFTR*	Chromosomal location	chr7:117232511	Variation information	c. 2290C>T (p. Arg764*)
NP26S01408 Proband Forward sequencing Homozygous					
NP26S01408 Proband Reverse sequencing Homozygous					
VP26D02924 Father Forward sequencing Heterozygous					
VP26D02923 Mother Forward sequencing Heterozygous					

C

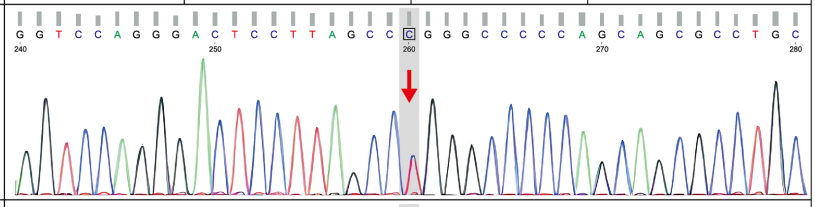
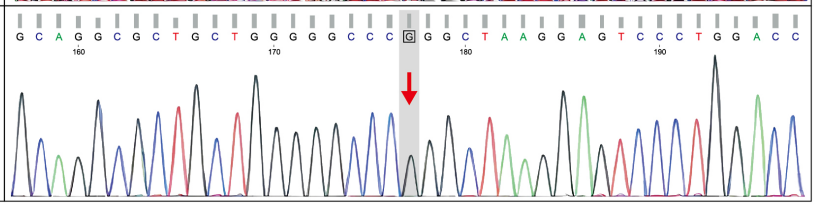
Peak plot results					
Gene	*TNNI3*	Chromosomal location	chr19:55665462	Variation information	c. 485G>A (p. Arg162Gln)
NP26S01408 Proband Forward sequencing Heterozygous					
NP26S01408 Proband Reverse sequencing Heterozygous					

Figure 5. Sanger sequencing chromatogram. A: Sanger verification results; B: Peak plot results of *CFTR* mutation gene for patient and his parents; C: Peak plot results of *TNNI3* mutation gene for patient.

and Western populations. F508del remains the predominant mutation among Caucasians, accounting for approximately 70% of cases [16]. In contrast, c.2909G>A (G970D) represents the most frequent variant in Chinese CF patients, while remaining rare in Western cohorts [17]. Additionally, mutations such as c.1766+5G>T and c.1898+5G>T have been identified in six cases in China but are absent in European and American CF populations [18, 19]. In this case, the patient harbors a homozygous nonsense mutation, c.2290C>T (p.Arg764*), which remains unreported in the existing literature. This variant converts the codon for arginine (Arg) to a premature stop codon, truncating *CFTR* protein synthesis at amino acid 764 and severely disrupting its structural integrity and functional capacity. The resulting truncated protein undergoes misfolding and fails to translocate to the cell membrane, abolishing chloride channel activity. Impaired *CFTR* function disrupts chloride and water transport, leading to viscous respiratory secretions with impaired clearance. Subsequent mucus accumulation predisposes to recurrent bacterial infection, persistent inflammation, bronchiectasis, and progressive pulmonary damage. Sanger sequencing identified biparental inheritance of the mutation. Although two heterozygous carriers are recorded in the gnomAD database, no homozygous cases have been documented.

The c.2290C>T (p.Arg764*) mutation is classified as pathogenic according to current evidence. For patients exhibiting clinical manifestations suggestive of CF, whole exome sequencing is recommended to identify rare or novel mutations, thereby expanding the known *CFTR* mutation spectrum and supporting precise diagnosis and targeted therapeutic strategies. Management of CF focuses on symptomatic control, including infection prevention, airway clearance, optimization of pulmonary function, and nutritional support to mitigate malnutrition.

Recent advances in molecular biology have driven substantial progress in CF therapeutics [20]. Given its monogenic nature, gene therapy offers a direct approach to correcting *CFTR* protein dysfunction [20]. Initial strategies employed viral and nonviral vectors to deliver functional *CFTR* genes into affected cells, though clinical trials demonstrated limited efficacy. In 2012, the FDA approved ivacaftor, a *CFTR* potentiator that enhances channel gating by prolonging *CFTR* channel opening, thereby improving chloride transport across epithelial membranes and reducing sodium chloride accumulation in secretions [21]. Clinical responses typically emerge within two weeks and may persist for up to 48 weeks without significant adverse effects. Current pharmacotherapy primarily includes ivacaftor and lumacaftor. However, effective targeted treatments for CF-related genetic variants prevalent among Chinese patients remain unavailable, highlighting a need for continued research into gene-based therapies for this population.

Gene therapy remains an area requiring further investigation for this patient population. Long-term azithromycin administration has demonstrated efficacy in enhancing pulmonary function, particularly in individuals with *Pseudomonas aeruginosa* infections. Severe infections necessitate intravenous β-lactam antibiotics combined with aminoglycosides for optimal management [22]. In the absence of intervention, CF carries a poor prognosis, with approximately half of affected children succumbing to complications before age 10, and survival into adulthood being rare. Nonetheless, early diagnosis and intervention substantially improve outcomes, enabling survival into adulthood. Advances in genetic testing and multidisciplinary care have markedly reduced pediatric mortality, with median life expectancy now exceeding 40 years [23]. Given the profound effect of CF on both quality of life and survival, along with the significant socioeconomic burden, families may consider third-generation *in vitro* fertilization (IVF) during reproductive planning to mitigate the risk of birth defects.

Genetic implications

Mutations in the *CFTR* gene are the primary cause of pulmonary CF. Genetic analysis in this case identified a homozygous nonsense mutation, c.2290C>T (p.Arg764*), which has not

been previously documented in the literature. Currently, CF remains incurable, with management centered on symptomatic treatment aimed at controlling infections, enhancing airway clearance, preserving respiratory function, and maintaining nutritional status to prevent malnutrition. While gene therapy has entered clinical application, genotype-specific targeted treatments remain inaccessible for Chinese patients. According to the American College of Medical Genetics and Genomics (ACMG) guidelines, incidental findings involving serious conditions unrelated to the current clinical presentation but potentially benefiting from early intervention should also be reported. In this case, a*TNNI3* gene mutation (NM_000363.5: c.485G>A, p.Arg162Gln) was detected, commonly associated with hypertrophic cardiomyopathy. Given its irrelevance to the present condition, further discussion is omitted, and cardiology follow-up is recommended.

Conclusion

In patients presenting with chronic, recurrent cough and sputum production alongside imaging suggestive of pulmonary CF, whole-exome sequencing is recommended to assess for *CFTR* gene mutations. *CFTR* mutations contribute directly to pulmonary CF pathogenesis. In this case, genetic analysis identified a homozygous c.2290C>T (p.Arg764*) variant, which has not been previously reported in the *CFTR* coding region. Within China, *CFTR* mutation-induced cystic pulmonary fibrosis remains uncommon and is frequently characterized by persistent respiratory symptoms, leading to repeated misdiagnosis as bronchitis, bronchiectasis, or pulmonary infection. Additionally, in some regions, indiscriminate use of *CFTR* genetic testing and sweat chloride analysis without appropriate clinical correlation results in prolonged diagnostic delays and improper management. This case highlights the need for heightened clinical vigilance to enhance diagnostic accuracy and optimize treatment strategies for CF driven by *CFTR* mutations.

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

Disclosure of conflict of interest

None.

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