CASE REPORT

Reconsidering isolated FEV_1 reduction: A case report of early-stage asthma with bronchial hyperreactivity and literature review

Reconsidération de la baisse isolée du VEMS: Un cas d'asthme débutant avec hyperréactivité bronchique et revue de la littérature

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Abstract

Introduction: Isolated low forced expiratory volume in one second (FEV_1) spirometric impairment (ILFSI) is characterized by a decreased FEV_1 while both forced vital capacity (FVC) and the FEV_1/FVC ratio remain within normal ranges. This pattern may hide an underlying respiratory disorder that warrants further examination. Notably, the 2022 European respiratory society/American thoracic society (2022-ERS/ATS) guidelines do not classify ILFSI as pathological, a stance that has sparked some controversy. This teaching report discussed the case of a woman with ILFSI who developed mild bronchial hyperreactivity after undergoing a methacholine bronchial challenge test (MBCT) and exhibited positive skin prick tests (SPTs) for dust mites.

Observation: A 28-year-old professional interior designer, who has no history of smoking or exposure to wood smoke and allergens, and who previously experienced a mild case of coronavirus disease-2019, consulted a pulmonologist for chronic cough, sputum production, and recurrent sneezing episodes. Asthma was suspected, leading to the performance of SPTs, spirometry, and either a bronchodilator test (in case of an obstructive ventilatory impairment) or MBCT (in case of a normal spirometry) as requested in the pulmonologist referral letter. The spirometry results indicated ILFSI, with a low FEV_1 (z-score = -1.74, 79%) while FVC (z-score = -0.97, 88%) and the FEV_1/FVC ratio (z-score = -1.35) remained normal. According to the 2022-ERS/ATS guidelines, these findings are considered normal spirometry because of the maintained FVC and FEV_1/FVC ratio. The MBCT confirmed mild bronchial hyperreactivity, showing a 20% drop in FEV_1 at a dose of 96 µg. Furthermore, SPTs were positive for dust mites (Dermatophagoides pteronyssinus and farinae).

Conclusion: The results of this report suggested a possible association between ILFSI and early allergic asthma, indicating that ILFSI should be re-examined in future revisions of the 2022-ERS/ATS guidelines for interpreting spirometric tests.

Keywords: Algorithm; Bronchial Provocation Tests; Case Report ; Cough; Guideline; Nonspecific Pattern; Pulmonary Function Tests; Respiratory Hypersensitivity

Résumé

Introduction: Le déficit spirométrique caractérisé par une baisse isolée du volume expiratoire maximal en une seconde (VEMS) (BI-VEMS) est défini par une baisse du VEMS alors que la capacité vitale forcée (CVF) et le rapport VEMS/CVF restent dans les normes. La BI-VEMS peut masquer une pathologie respiratoire sous-jacente nécessitant des investigations complémentaires. Notamment, les recommandations 2022 de la Société Européenne de Pneumologie et de la Société Américaine de Pneumologie (2022-ERS/ATS) ne considèrent pas la BI-VEMS comme pathologique, ce qui a suscité une certaine controverse. Ce rapport clinique à visée pédagogique présente le cas d'une femme avec une BI-VEMS, ayant développé une hyperréactivité bronchique légère lors d'un test de provocation bronchique à la méthacholine (TPBM) et présentant des tests cutanés positifs aux acariens.

Observation: Une designer d'intérieur professionnelle de 28 ans, sans antécédents de tabagisme ni d'exposition à la fumée de bois ou aux allergènes, et ayant contracté une forme légère de la COVID-19, a consulté un pneumologue pour une toux chronique, des expectorations et des épisodes répétés d'éternuements. L'hypothèse d'un asthme a été évoquée, conduisant à la réalisation de tests cutanés, d'une spirométrie et d'un test au bronchodilatateur (en cas de présence d'un déficit ventilatoire obstructif) ou un TPBM (en cas d'une spirométrie normale) comme demandé dans la lettre de liaison du pneumologue. Les résultats spirométriques ont révélé une BI-VEMS, avec un VEMS bas (z-score = -1,74 ; 79%), tandis que la CVF (z-score = -0,97 ; 88%) et le rapport VEMS/CVF (z-score = -1,35) étaient normaux. Selon les recommandations 2022-ERS/ATS, la spirométrie est considérée comme normale du fait de la préservation de la CVF et du rapport VEMS/CVF. Le TPBM a confirmé une hyperréactivité bronchique légère avec une chute de 20% du VEMS à une dose de 96 µg. Par ailleurs, les tests cutanés étaient positifs aux acariens (Dermatophagoides pteronyssinus et farinae).

Conclusion: Les résultats de ce rapport ont suggéré une association possible entre la BI-VEMS et un asthme allergique débutant, ce qui indique que la BI-VEMS devrait être reconsidérée lors des prochaines révisions des recommandations 2022-ERS/ATS pour l'interprétation des tests spirométriques.

Mots-clés: Algorithme ; Cas Clinique; Épreuves Fonctionnelles Respiratoires ; Hypersensibilité Respiratoire ; Profil Non Spécifique ; Recommandation ; Tests de Provocation Bronchique ; Toux

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Introduction

Isolated low forced expiratory volume in one second (FEV_1) spirometric impairment (ILFSI) is a pattern characterized by a decreased FEV_1 while forced vital capacity (FVC) and FEV_1/FVC ratio remain normal (1-5). ILFSI is so referred to as "non-restrictive" preserved ratio impaired spirometry (PRISm) (6). Its prevalence in adults varies between 2% and 9%, and in pediatric populations, it ranges from 2.15% to 2.65% (1-4). In clinical practice, and in line with the most recent European respiratory society/American thoracic society (2022-ERS/ATS) technical standard on interpretive strategies for routine lung function, including spirometry (7) , ILFSI is interpreted as a normal spirometric pattern, thereby excluding any pulmonary disease (Figure 1). This discrepancy highlights a challenge, as there is a divergence between international guidelines (ie, 2022-ERS/ATS (7)) and clinical practice (1-5).

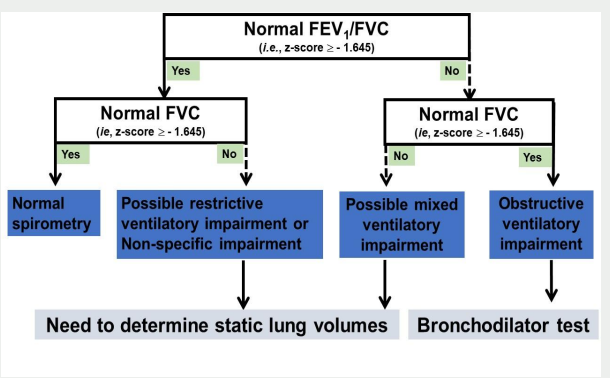

Figure 1. Algorithm recommended by the 2022- European respiratory society/American thoracic society technical standard on interpretive strategies for spirometry (7).

FEV_1: Forced expiratory volume in one second. **FVC**: Forced vital capacity.

In real-world settings, identifying ILFSI can affect clinical decisions by prompting further diagnostic testing, the initiation or adjustment of therapy, and patient counseling (1, 3). Recognizing ILFSI enables healthcare providers to promptly address potential underlying conditions, potentially leading to better patient outcomes (1, 3).
This teaching report presented the case of a woman with ILFSI who exhibited mild bronchial hyperreactivity following a methacholine bronchial challenge test (MBCT) and demonstrated positive skin prick tests (SPTs) reactions to dust mites. This case report with a literature review was prepared in accordance with the CAse REports guidelines (8).

Patient information

A 28.38-year-old woman consulted her private pulmonologist for a suspected respiratory allergy. The patient had been experiencing symptoms for nine years, including chronic cough, sputum production, morning bronchorrhea, and recurrent sneezing. The patient is a non-smoker with no known exposure to wood smoke or allergens and works professionally as an interior designer. Her medical history is notable for a mild case of coronavirus disease-2019 infection two years ago.

Clinical findings

Upon clinical examination, the patient was found to be eupneic. Pulmonary auscultation was normal, with ambient oxygen hemoglobin saturation at 97%, and blood pressure within normal limits (systolic: 120 mmHg and diastolic: 80 mmHg). Due to the suspicion of allergic asthma, the patient was referred to a private international center for functional explorations to undergo SPTs, spirometry, a bronchodilator test (in case of an obstructive ventilatory impairment) or MBCT (in case of a normal spirometry), as indicated in the pulmonologist referral letter.

Timeline

The patient's medical history is summarized in Box 1.

Box 1. Medical history timeline.

Time	Information
2015	Complaints: chronic cough, sputum production and recurrent episodes of sneezing
15.11.2024	1st visit of the private pulmonologist: clinical exam and request of lung function explorations.
30.11.2024	Spirometry test, methacholine bronchial challenge test, skin prick tests
02.12.2024	2nd visit of the private pulmonologist: treatments' initiation
17.12.2024	3rd visit of the private pulmonologist: control

Diagnostic assessment

The patient's age and anthropometric measurements [height: 171 cm, weight: 71.3 kg, body mass index: 24.38 kg/m²] were recorded following the center's protocol. Spirometry was conducted in accordance with the 2019-ERS/ATS standards (9) using a calibrated spirometer (MIR Spirodoc, Langlade, France) with a nose clip. The four phases of the FVC maneuver—maximal inspiration, an explosive expiration, sustained complete forced exhalation until either a plateau is reached or for a maximum of 15 seconds if no plateau occurs, and rapid inspiration to full lung capacity—were explained and demonstrated by an experienced technician (9). The following spirometric parameters were collected: FEV_1 (l, % predicted), FVC (l, % predicted), and FEV_1/FVC (absolute value). Since we adhered to the 2019-ERS/ATS standards, which guarantee that effort and completeness are appropriately evaluated, the possibility of an incomplete expiratory effort was eliminated (9). First, our main measures of completeness have been forced expiratory time (= 5.78 s) and curve plateaus (9). Second, we evaluated beginning effort using peak expiratory flow (PEF) (9). Third, we have provided ongoing coaching to make sure patients blow consistently and fully until expiration is actually complete (9).
Spirometry was interpreted based on the 2022-ERS/

ATS technical standard on interpretive strategies for spirometry, primarily using z-scores (ie, considered abnormally low when < -1.645) (7). The global lung function initiative 2012 spirometric norms for Caucasians were used to determine z-scores and predicted values (10). The expiratory limb's distinctive concave shape on the flow-volume curve (Figure 2) indicated airflow limitation in the tiny airways (7). The results revealed an ILFSI, with a low FEV_1 (z-score = -1.74, 79%) while FVC (z-score = -0.97, 88%), PEF (7.12 l/s, 103%, z-score = 0.11), and FEV1/FVC (z-score = -1.35) remained within normal limits (Figure 2). In light of the pulmonologist's explicit request and the fact that the 2022-ERS/ATS guide (7) views the aforementioned circumstance as a "normal spirometry," we have chosen to perform an MBCT instead of a bronchodilator test.

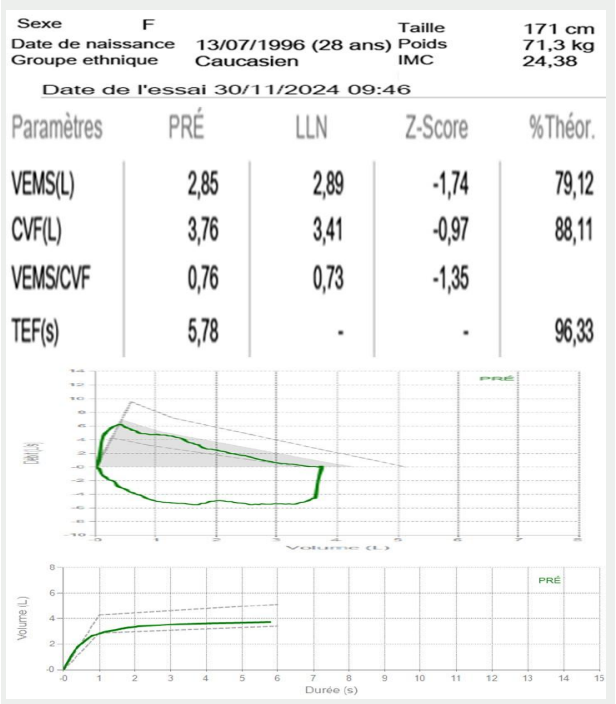

Figure 2. Basal spirometric data and flow-volume curve.

Note: The text inside the figure is in French. Below are the French-English translations of the main terms classified in alphabetical order:

ans: Years. **Caucasien**: Caucasian. **CVF**: FVC (Forced vital capacity). **Date de l'essai**: Test date. **Date de naissance**: Birth date. **Débit**: Flow. **Durée**: Duration. **F**: Female. **Groupe ethnique**: Ethnic group. **IMC**: BMI (body mass index). **LLN**: Lower limit of normal. **Paramètres**: Parameters. **Poids**: Weight. **Pré**: Pre-bronchodilation. **Sexe**: Sex. **Taille**: Height. **TEF(s)**: FET (Forced expiratory time). **Théorique**: Predicted. **VEMS**: FEV_1 (Forced expiratory volume in one second). %Théo: %Predicted.

After ruling out all medical and functional contraindications, an MBCT was performed following international guidelines (11), via a calibrated spirometer (Vyntus PNEUMO APS, JAEGER, Belgium). The patient was informed of the five-step procedure: [i) Inhalation of a small dose of methacholine via a nebulizer; ii) Spirometry after each dose to determine if there was a significant decline in FEV_1 (ie, 20% or more compared to the baseline); iii) Administration of increasing doses (if no significant reduction in FEV_1 is observed, higher doses of methacholine are given incrementally); iv) Administration of 400 µg of a short-acting bronchodilator at the end of the test; and v) A repeat spirometry 15-20 minutes later if the decline in FEV_1 was ≥ 10% relative to the baseline value]. The patient received a cumulative dose of 240 µg of methacholine, resulting in a 32.9% decline in FEV_1 [ie, from 2.86 l (79%) to 1.92 l (53%), Figure 3], which exceeded the recommended 20% threshold (11). The calculated provocative dose causing a 20% decline in FEV_1 (PD20) was 96 µg, indicating mild bronchial hyperreactivity (PD20 between 25 and 100 µg) (11). As recommended, the MBCT was halted, a 400 µg dose of a short-acting bronchodilator was administered, and spirometry was repeated after 15-20 minutes, revealing a recovery of FEV_1 to 2.76 l (77%), which represented only a 3.5% decline from baseline (ie, below the 10% threshold (11)).

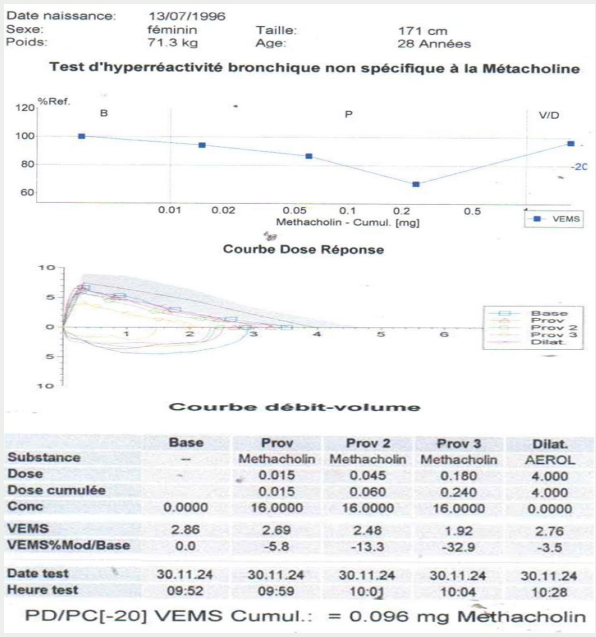

Figure 3. Methacholine bronchial challenge test.

Notes:

1. The 24-minute interval between the "Dilat." and "Prov 3" (ie; 10:28 minus 10:04), which is higher than the recommended threshold of 15-20 minutes, reflects the time taken for the technician to explain the maneuver of administrating 400 µg of a short-acting bronchodilator to the patient after taking the approval of the physician. The measurement at 10:28 corresponds to the time of final acceptance of the test.

2. The text inside the figure is in French. Below are the French-English translations of the main terms classified in alphabetical order:

Années: Years. **Base**: Basal. **Classification de la réponse**= Categorisation of airway response. **Conc**: Concentration. **Courbe débit-volume**: Flow-volume curve. **Courbe Dose Réponse**: Dose-response curve. **Cumul**: Cumulated. **Date de naissance**: Birth date. **Date test**: Test date. **Dilat**: Dilatation. **Dose cumulée**: Cumulative dose. **Féminin**: Female. **Heure test**: Test hour. **PC20**: Provocative concentration causing a 20% fall in FEV_1. **PD20**: Provocative dose causing a 20% fall in FEV_1. **Poids**: Weight. **Prov**: Provocation. **Sexe**: Sex. **Taille**: Height. **Test d'hyperréactivité bronchique non spécifique à la métacholine**: Non-specific bronchial hyperreactivity test with methacholine. **VEMS%Mod/Base**: FEV_1 percentage change compared to basal value. **VEMS**: FEV_1 (Forced expiratory volume in one second). %Ref: Percent of predicted

After performing the MBCT, followed by the administration of a short-acting bronchodilator, and after ruling out all SPTs' contraindications, the SPTs were performed in accordance with the international recommendations (12) [ie, i) Skin preparation; ii) Application of potential allergens [eg, 5 grasses, cupressaceous, dust mites (Dermatophagoides pteronyssinus and Dermatophagoides farinae), olive tree, pellitory, cat dander, negative control, and positive control (Histamine)] on marked sites; iii) Using small, sterile needles to lightly prick the skin through each allergen drop, allowing the allergens to penetrate without drawing blood; and iv) Waiting 15-20 minutes for the allergens to react with the skin]. The SPTs yielded a positive reaction to dust mites

(Figure 4).

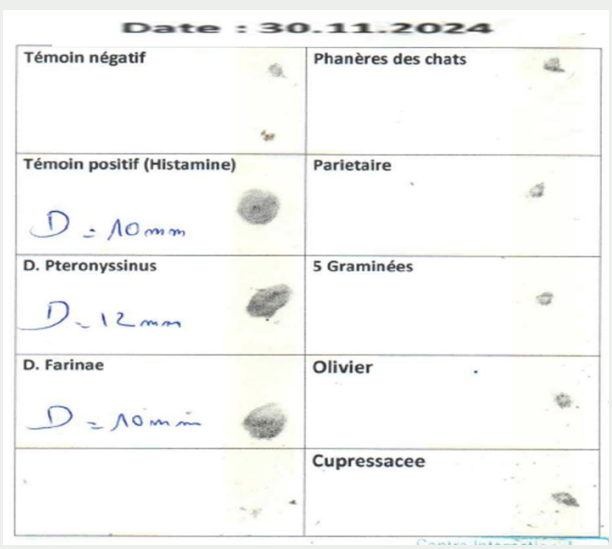

Figure 4. Results of the skin prick tests.

Note: The text inside the figure is in French. **Below are the French-English translations of the main terms classified in alphabetical order**: 5 graminées: 5 grasses. **Cupressacées**: Cupressaceae. **D. Farinae**: Dermatophagoides Farina. **D. Pteronyssinus**: Dermatophagoides pteronyssinus. **Olivier**: Olive tree. **Pariétaires**: Pellitory. **Phanères de chat**: Cat dander. **Témoin négatif**: Negative control. **Témoin positif (Histamine)**: Positive control (Histamine).

Therapeutic intervention

The patient was referred back to her pulmonologist, who confirmed the diagnosis of allergic asthma. A chest computed tomography scan was performed to rule out any associated pathology particularly bronchial dilation due to morning bronchorrhea. The chest computed tomography scan was normal. Due to a clinical suspicion of bacterial superinfection, the patient was prescribed an antibiotic (Amoxiclav, 1 gram, three times daily for seven days), an oral corticoid (40 mg per day for four days), and a combination of inhaled corticosteroids (ICS, 400 µg , twice daily) with a long-acting β-agonist (LABA; 12 micrograms, twice daily) for 15 days.

Follow-up and outcome

After 15 days without improvement, the pulmonologist adjusted the treatment regimen. The patient was subsequently prescribed an antihistamine (levocetirizine, one tablet per day) and an anti-leukotriene (10 mg per day) in addition to the 'LABA+ICS' combination.

Discussion

This case report highlighted a critical point: In symptomatic individuals, an ILFSI should not automatically be considered normal spirometry, contrary to the current 2022-ERS/ATS technical standard (7). Identifying ILFSI can have significant clinical implications, such as prompting additional diagnostic tests (eg, bronchodilator test, MBCT, or SPTs), modifying therapy, and guiding patient counseling (1, 3).

The 2022-ERS/ATS guidelines suggest that ILFSI should not be deemed clinically significant if it does not alter the FEV_1/FVC ratio (7). Indeed, in figure 8 on page 17 of the latter guidelines (7), ILFSI is not classified as abnormal spirometry, meaning that spirometry is considered normal in these cases. This perspective does not fully consider the complexity of early-stage asthma or allergic conditions, where airway hyperreactivity and subtle declines in FEV_1 may occur before more pronounced changes in lung volumes or the FEV_1/FVC ratio become apparent (13-16).

Identifying ILFSI during spirometric testing is crucial for several reasons (1, 3). First, ILFSI may indicate underlying respiratory diseases (1). A study analyzing 15,192 individuals reported that 2.1% exhibited an ILFSI (1). Compared to individuals with normal spirometry, those with ILFSI had higher incidences of smoking history (45.4% vs. 63.2%, respectively), radiological abnormalities such as bronchiectasis, emphysematous changes, pleural thickening, and inactive tuberculosis (4.3% vs. 15.5%, respectively), and respiratory disease history such as asthma, chronic bronchitis, and tuberculosis (3.0% vs. 8.4%) (1). These findings suggest that ILFSI is linked with abnormal spirometry and requires further evaluation to determine whether the cases are obstructive or restrictive in nature (1). Second, tracking FEV_1 over time provides insights into the stability or progression of lung diseases (3). Research has shown that ILFSI can recur over time and often reverts to a normal pattern, emphasizing that it is not merely a result of poor spirometry technique but an important clinical indicator for disease monitoring and management (3). Third, recognizing ILFSI ensures that healthcare providers can promptly address any underlying conditions, potentially leading to better patient outcomes (1, 3). ILFSI differs from other spirometric impairments where the FEV_1/FVC ratio remains normal (7). On one hand, a possible restrictive impairment or non-specific pattern is characterized by a normal FEV_1/FVC ratio with a low FVC (Figure 1) (7). On the other hand, PRISm is defined by simultaneous decreases in FVC and FEV_1 while the FEV_1/FVC ratio remains normal (7). Although our case report's ILFSI formally satisfies PRISm criteria, the clinical setting is very different from the group most frequently linked to PRISm in the 2022-ERS/ATS guideline (7), which is current or former smokers who have early airflow limitation or who may develop chronic obstructive pulmonary disease. The term PRISm was used just three times in the 2022-ERS/ATS guidelines, and it was primarily associated with phenotypes connected to smoking (7). We feel that our case highlights the existence of a unique clinical environment that may be underrepresented in current guideline frameworks because it encompasses a non-smoking individual with characteristics suggestive of early-stage asthma and ILFSI. In adults, only a few studies have reported ILFSI (1, 4-6, 17). The frequency of radiological abnormalities was comparable between adults with ILFSI and those with an obstructive ventilatory impairment (1). In a separate study involving roughly 11,000 adults attending an annual health check-up, Miura et al. (6) reported that a history of asthma or smoking served as independent risk factors for ILFSI, and that ILFSI was independently linked with an increased risk of developing airflow obstruction.

A distinctive concavity on the expiratory limb of our patient's flow-volume curve (Figure 2) indicated airflow limitation in the tiny airways (7). Therefore, it was preferable to use a bronchodilator test instead of the MBCT in the early evaluation phases, as advised by the Global Initiative for Asthma (GINA) (18). Nevertheless, we chose to respond to the pulmonologist's explicit request as stated in her referral letter, and we conducted an MBCT. The latter can uncover airway hyperreactivity even when FEV_1 values are not markedly reduced (11). The mild bronchial hyperreactivity provided evidence of abnormal airway responsiveness despite the absence of overt airway obstruction (19). Therefore, ILFSI should be re-evaluated in light of this reactivity, as it may represent a subclinical phase of asthma or allergic airway disease where inflammation is present without a significant reduction in the FEV_1/FVC ratio (13, 14, 20). The positive SPTs to dust mites in this case further reinforce the notion that allergic asthma can lead to bronchial hyperreactivity even when spirometry appears normal or exhibits ILFSI. Dust mites are a well-known allergen, and sensitization to them can trigger inflammation and bronchoconstriction without causing a marked drop in FEV_1 (13). This implies that allergic sensitization can induce airway changes that may not be detected by conventional spirometric measures, further challenging the view that ILFSI is clinically insignificant (4, 5).

The clinical course of this patient questions the 2022-ERS/ATS guidelines (7), which primarily rely on spirometric data—particularly the FEV_1/FVC ratio—for diagnosing asthma and other obstructive lung diseases. By focusing heavily on these parameters, the guidelines may underestimate the importance of an isolated decrease in FEV_1, potentially missing early-phase asthma or airway hyperreactivity in patients at the onset of allergic sensitization (13, 14, 16). This case underscores the need for a broader diagnostic approach—one that incorporates allergic sensitization, bronchial hyperreactivity, and early airway inflammation. While spirometry is essential, it should be considered alongside other diagnostic tools such as MBCT and SPTs (15, 21). Airway reactivity and allergen exposure should form key components of the asthma diagnostic pathway, particularly in atopic patients who do not yet meet the criteria for established obstructive lung disease.

Recognizing the clinical relevance of ILFSI is vital for the early diagnosis and management of asthma (6). In this case, the patient, despite having ILFSI, showed bronchial hyperreactivity on MBCT and positive sensitization to dust mites—both of which indicate a need for early therapeutic intervention. Early treatment, along with allergen avoidance strategies, may help prevent the progression of asthma and improve the quality of life for patients with allergic asthma, even when spirometry only shows mild abnormalities (such as ILFSI).

This case report's failure to take into account the most widely used international guidelines for managing asthma, including the GINA, is one "confusion point" (18). In cases where asthma is suspected, GINA suggested a bronchodilator test as the initial objective evaluation (18). Additionally, GINA recommended other measures for variable expiratory airflow, like response to an inhaled corticosteroid trial or variability in diurnal PEF (18). The MBCT for GINA is usually saved for situations in which preliminary testing yields conflicting results (18). The diagnostic strategy in private clinical practice is based on clinical judgments made by the treating pulmonologist for time and cost savings. This explains why the MBCT was used instead of the bronchodilator test. While some spirometric mid-expiratory indices, such as forced expiratory flow at 50% and maximal mid-expiratory flow, are frequently used to measure mid-range airflow, we did not analyze them because they are known to be highly variable, poorly reproducible, and lack specificity for small airway disease in individual patients (7). They also frequently do not add much to clinical decision-making beyond what FEV_1, FVC, and the FEV_1/FVC ratio already provide (7).

Implications for clinical care

ILFSI, especially when considered in the context of airway hyperreactivity and allergen sensitization, should not be dismissed as clinically insignificant. This case demonstrates that early-phase asthma or allergic airway disease can present with mild spirometric abnormalities that, when combined with bronchial hyperreactivity and positive SPTs, provide critical insights into the underlying pathology. A more comprehensive diagnostic strategy—including spirometry, MBCT, and SPTs—is necessary to ensure that patients with early-stage asthma are accurately diagnosed and effectively managed. Ultimately, detecting ILFSI is crucial for uncovering underlying respiratory conditions, monitoring disease progression, and guiding clinical management. We must move beyond simply classifying patients based on current guidelines, as continuous inquiry is essential (17).

In conclusion, the results of this case suggest a possible association between ILFSI and early allergic asthma, indicating that ILFSI should be re-examined in future revisions of the 2022-ERS/ATS guidelines for interpreting spirometric tests.

Patient perspectives

The patient expressed satisfaction with her care, reported significant clinical progress, and planned a trip to an Asian country.

Informed consent

Written consent was obtained from the patient for the publication of this case report.

ABREVIATIONS' LIST
ATS: American thoracic society
ERS: European respiratory society
FEV_1: Forced expiratory volume in one second
FVC: Forced vital capacity
ICS: Inhaled corticosteroids
ILFSI: Isolated low forced expiratory volume in one second spirometric impairment
LABA: Long-acting beta-agonist
MBCT: Methacholine bronchial challenge test
PD20: Provocative dose causing a 20% fall in FEV_1
PEF: Peak expiratory flow
PRISm: Preserved ratio impaired spirometry
SPTs: Skin prick tests

DECLARATION. The authors wish to disclose that an artificial intelligence tool (ChatGPT ephemeral) was used to enhance the clarity and coherence of the manuscript writing. The tool was employed solely for language refinement purposes, ensuring that the text was clear and coherent without altering the scientific content or generating new text (22).

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