



Letters

Drug-associated inducible laryngeal obstruction complicating penicillin allergy testing

We report a case of drug-associated vocal cord dysfunction (VCD) diagnosed during a drug challenge associated with penicillin allergy testing. A 48-year-old woman presented for an evaluation of penicillin allergy after receiving a positive treponemal antigen test result. She had a long history of atypical reactions to a variety of medications. In regard to her history of penicillin allergy, she recounted being told by her mother that she was given penicillin at the age of 6 years and later experienced shortness of breath and throat tightness. These symptoms were so severe that she was reportedly admitted to a hospital, received epinephrine, and was intubated for several days. She also reported a similar history of throat closure with a dose of baby aspirin at the age of 10 years for which she was hospitalized for several days. She recalls taking aspirin 10 years ago and had hives and nausea and received oxygen. Since then, she has not taken any nonsteroidal anti-inflammatory drugs. Her medical history was notable for a history of hypertension, breast cancer, psychogenic nonepileptic seizures, schizoaffective disorder, conversion disorder, and anxiety.

Penicillin allergy skin testing was performed with prick and intradermal skin tests to benzylpenicilloyl polylysine and penicillin G, and all skin test results were negative. After negative penicillin skin test results, she was administered 500 mg of amoxicillin orally per our usual protocol. Notably, 15 minutes after initiating an oral challenge, she experienced severe shortness of breath and throat tightness. She was noted to have coughing paroxysms and was gasping for air with audible inspiratory wheezing but without hypoxia. Rhinolaryngoscopy was performed within minutes of symptom onset and the results revealed paradoxical adduction of vocal cords during inspiration in association with wheezing. She received a diagnosis of VCD and was immediately counseled on open mouth and diaphragmatic rescue breathing, resulting in complete resolution of her symptoms within minutes without further need for medical intervention. Because of her reaction, she returned to our clinic for her first dose of intramuscular benzathine penicillin and tolerated this dose and her remaining doses without problem.

Vocal cord dysfunction is defined as paradoxical adduction of the vocal cords during inspiration. This condition has been called by many names, including paroxysmal vocal cord motion, episodic paroxysmal laryngospasm, and more recently inducible laryngeal dysfunction (ILO) which is now the preferred term.¹ The larynx is one of the most highly innervated structures of the body and is integral to the essential functions of swallowing, phonation, and protection of the airway. There are multiple theories to explain the pathophysiology of ILO, including mechanical insufficiency,

neural dysfunction, and psychological contributions.^{2,3} It is a well-documented mimicker of asthma in that the associated symptoms are largely indistinguishable. Dyspnea, chest pain, cough, and wheezing are noted in both conditions. ILO imitating anaphylaxis has not been as thoroughly reported, despite the 2 also sharing a near-identical symptom profile.^{4–6} As with anaphylaxis, chest tightness, tachypnea, dysphonia, and stridor can also be seen in ILO.^{6,7} These signs and symptoms can give the appearance of an upper airway obstruction. ILO misdiagnosed as anaphylaxis may lead to a multitude of poor outcomes. Inappropriate pharmacotherapy, cardiopulmonary resuscitation, intubation, and even emergency tracheostomy could all be inflicted on a patient who was misdiagnosed.^{1,7}

A variety of screening tools are available to assist in the diagnosis of VCD. The VCD screening checklist, the Newcastle laryngeal hypersensitivity questionnaire, and the dyspnea index assess for the presence of VCD.² The VCD questionnaire, VCD-5, and the Pittsburgh VCD Index can help differentiate between VCD and asthma. However, none of the existing questionnaires are designed to discriminate between VCD and anaphylaxis. Differentiation of VCD from anaphylaxis with laryngeal edema can be achieved primarily through a careful history, physical examination, and, if possible, laryngoscopy (Table 1). Patients with laryngeal obstruction from anaphylaxis frequently have concomitant visible oropharyngeal edema and may have other symptoms of airway edema, including the inability to control secretions and drooling. Hypoxia is common in laryngeal edema but rarely occurs with ILO.

ILO is more frequently seen in women, health care workers, and those with gastroesophageal reflux.^{3,8} Patients who have been diagnosed as having psychiatric illnesses are also more likely to have ILO. Emotional stressors are the primary trigger of psychogenic ILO.⁹ Anxiety disorder, panic disorder, history of sexual abuse, combat deployment of military personnel, and participation in competitive sports all increase the risk of a patient experiencing ILO as a physical expression of psychological hardships.^{3,9} The extent of psychopathologic conditions may possibly be correlated with the severity of psychogenic ILO. Environmental exposures, such as perfumes, chemical vapors, smoke, and other irritants, including gastric acid, have been implicated as triggers of ILO.^{3,8} Exercise may also aggravate a hyperkinetic larynx and induce ILO. In contrast to other triggers, drug-associated ILO (or VCD) has rarely been reported despite the relatively common occurrence in our experience.⁵ Cognizance of the similarities between ILO and anaphylaxis when patients report drug allergy symptoms or during drug allergy testing can help physicians make the correct diagnosis.

This patient's initial history as stated was more suggestive of a true allergic reaction given the young age and requirement for intubation and prolonged hospitalization. However, her history of

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Table 1
Differentiating Inducible Laryngeal Obstruction From Anaphylaxis With Laryngeal Edema

	ILO	Laryngeal edema
Historical features		
Isolated throat tightness	Frequent	Rare
Subjective report of facial or tongue swelling	Common	Common
Recurrent episodes	Common	Uncommon
Rapid onset	Frequent	Frequent
Physical findings		
Objective evidence of orofacial angioedema	Rare ^a	Frequent
Facial or upper chest flushing	May be present	May be present
Urticaria	Rare ^a	Common
Drooling or inability to control secretions	Not present	Common
Laryngoscopy	Intermittent contraction of laryngeal structures (eg, adduction of vocal cords)	Edema of larynx
Laboratory features		
Hypoxia	Rare	Common
Tryptase	Normal	May be elevated
Acute management	Rescue breathing (pursed lip, breathing through straw) or heliox	Airway management (intubation, if needed) or epinephrine

Abbreviation: ILO, inducible laryngeal obstruction.

^aPatients with acute urticaria or angioedema may also have ILO.

similar episodes with aspirin, history of schizoaffective disorder, conversion disorder, and psychogenic seizures are all clues that her history may not have been accurate and that drug-associated ILO may have been a factor in some of these previous reactions.

To the best of our knowledge, drug-associated ILO has not been reported in association with penicillin allergy testing. Penicillin is one of the most common drug allergies reported by patients and accounts for most in-office drug allergy tests. Because direct challenges to penicillin without preceding skin testing are becoming

more popular and are also being performed by non-allergy/immunology specialists, this potential complication is important to recognize.¹⁰ This case illustrates the importance of using a lack of objective findings supportive of anaphylaxis and fiberoptic laryngoscopy to confirm drug-associated ILO.

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