The Characteristics of Upper Respiratory Tract in the Patients with Asthma and the Patients with Episodic Laryngeal Obstruction

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Abstract

Background. Asthma and some other diseases of the upper respiratory tract have similar symptoms and signs. The signs and symptoms of rhinitis and laryngitis are not unusual in patients with allergic asthma. Attacks of dyspnea are not characteristic only for asthma but also for some other diseases with pathogenesis in the larynx.

Methods. The recent papers on upper respiratory tract characteristics in the patients with asthma and the patients with episodic laryngeal obstruction were reviewed.

Results. The connections between the nasal signs and symptoms and asthma are well established what is not the case for laryngeal problems. The laryngeal symptoms and signs in patients with asthma can be caused by the same triggers as asthma. However, they can also be merely the consequences of the asthma signs and symptoms or the asthma treatment. The pathogenesis of the episodic laryngeal obstruction includes a variety of causes which dictate the mode of treatment. In some cases, asthma and episodic laryngeal obstruction can coexist.

Conclusions. In order to find the correct diagnosis and proper treatment of the upper respiratory tract problems in patients with dyspnea attacks, a team of different specialists is necessary.

Keywords: asthma, rhinitis, laryngitis, allergy, dyspnea, diagnostics, treatment

Upper Respiratory Tract Problems in the Patients with Asthma

Nasal Disorders

The upper and lower respiratory tract share the same anatomical, functional, pathogenic, clinical, and immunological features. The airborne allergens activate the similar effector cells in the respiratory tract. Therefore, a term »the united airway disease« was introduced[18]. It is well known that asthma and allergic rhinitis appear together in a considerable number of patients. In a large study in China, it was confirmed a 29.4% prevalence of allergic rhinitis in asthmatic patients, and a 20.6% prevalence of asthma in patients with allergic rhinitis[27]. The association between asthma and allergic rhinitis was extensively studied. It is very likely that it is a disease occurring simultaneously in both parts of the respiratory tract[11,24,17]. In a recent study on molecular mechanisms causing asthma, rhinitis and eczema, 15 pathways involved in this multi-morbidity were found[2]. There are limited studies on the risk factors responsible for the progression of allergic rhinitis to asthma. However, recent data suggest that it is possible to prevent asthma onset by allergen immunotherapy in the patients with allergic rhinitis[30].

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Laryngeal Disorders

In terms of unified respiratory path (nose, middle ear, larynx, lungs), a mediator response in one organ can trigger similar responses along the rest of respiratory tract. There is a paucity of research on allergic laryngitis. Some authors even doubt that such entity really exists. The diagnosis of allergic laryngitis is a diagnosis of exclusion after all other possible diagnoses (laryngopharyngeal reflux, retronasal drip as a consequence of sinusitis, laryngeal symptoms due to irritation at working place, etc) are ruled out[47]. Most patients with suspicion of allergic laryngitis complain because of cough, throat clearing, sensation of a foreign body and excessive mucous in the throat, postnasal drip, and different voice disorders. When the researchers studied reaction of laryngeal mucosa to various antigen exposures thick-viscous endolaryngeal mucous and transient or chronic reactive vocal folds oedema and hyperaemia was noticed in a great majority of the cases[39,6]. There are several studies showing a link between allergic rhinitis and vocal symptoms which can improve with increased duration of immunotherapy treatment[31,44].

Voice disorders are not unusual in the patients with asthma. Deteriorated voice quality was noticed in asthma patients when compared to healthy controls with the use of objective and subjective evaluation methods[14]. There are several different mechanisms through which the voice quality in asthma patients can be affected. According to the theory of the unified respiratory disease, the vocal fold mucosa may be affected by allergic inflammation thus altering the mass of the vocal folds and their vibrating characteristics. The mucous on the vocal folds can give the characteristic of »wet voice« but also forces the patient to cough. As a matter of fact, cough is one of the most prominent symptoms of asthma. During cough the vocal folds violently strike together causing mechanical trauma, oedema, erythema and even the occurrence of some benign laryngeal lesions[46]. The third possible way is though the reduction of air flow coming from the lungs of the asthmatic patient to the vocal folds. Consequently, the available subglottic pressure does not suffice for good voice quality and causes the speaker to change the activity of laryngeal muscles during phonation in order to compensate for the insufficient subglottic pressure[46].

The fourth possible mechanism of affecting voice quality is through the influence of asthma treatment on larynx. Dysphonia is the most common side effect of inhaled corticosteroids treatment. After inhaled steroids exposure the laryngeal findings range from vocal fold oedema, erythema, and atrophy to irregularities of the vocal fold edges, interarytenoid thickening, and supraglottic hyperactivity[19]. The vocal fold atrophy results in vocal folds' bowing and incomplete vocal folds closure during phonation. Ozbilen Acar et al. proved corticosteroid-associated myopathy after inhaled corticosteroids treatment by performing EMG and stroboscopy during therapy and after its cessation. The glottis gap and voice disorders improved in several weeks after the end of therapy[35].

Inhaled corticosteroids produce their affects mostly by local immunosuppression secondary to reduced mRNA synthesis[35]. Localized laryngopharyngeal candidiasis is the most frequently documented infection after the use of inhaled corticosteroids. The incidence of laryngeal candidiasis associated with dysphonia was estimated at 20% in those taking inhaled steroid therapy[50]. As a matter of fact, the entire microflora of the larynx changes after regular inhalation of corticosteroids, and potentially lead to the occurrence of rare opportunistic laryngeal infections[49].

Episodic Laryngeal Obstruction

Attacks of dyspnea and wheezing are not only the typical symptoms of asthma. Sudden airway obstruction at the level of the larynx was first described as a disturbance in the

functioning of the laryngeal muscles in 1842 and was called "hysterical croup"[15]. Since then, more than 70 different names have been used for the problem described. Recently, the terms periodic occurrence of laryngeal obstruction or episodic laryngeal obstruction (ELO) have been used, which include the possibility of pathological events both at the level of the vocal folds and at the level of the supraglottis[9].

Etiology

The etiology is not entirely clear. Among the possible causes for inducible laryngeal obstruction with breathing disorders many different factors and situations are mentioned: the aerodynamic principles possibly connected with age, gender and physical capacity[20,45,29,40]; alteration of the laryngeal sensibility after stimulation of the supraglottis mucosa or direct stimulation of the superior laryngeal nerve by laryngopharyngeal reflux, allergy, infections[36,25,40], irritants, temperature and humidity of the air in the surroundings[26]; and psychological aspects[42,23].

Morrison hypothesized that the cause for abnormal laryngeal obstruction during inspiration is a change in the central nervous system resulting in hyper-irritable state of the sensory and motor pathways. Various pathophysiological processes lead to chronic irritation of the laryngeal nerves, and due to the plasticity of the nervous system, the way the central neurons respond to an incoming stimulus may change. Thus, the event triggers a sensory stimulus, and airway obstruction occurs due to the hyperexcitable state of the neural network in the brainstem that controls the functioning of the larynx[32]. Ayres and Gabbott believe that the altered balance of the autonomic nervous system maintained by structures in the central nervous system plays a role in abnormal vocal folds movement in patients with ELO[5]. Frequent prevalence of symptoms of laryngopharyngeal reflux and decreased laryngeal sensitivity have been reported among individuals with ELO. The authors thought that sudden laryngeal closure could be triggered by poorer laryngeal sensitivity or inflammation of the laryngeal mucosa. Another possible explanation could be that the threshold of excitability is lowered, but when it is reached, it triggers a very strong reaction in the sense of "all or nothing"[13,22]. Some believe that the cause of mainly supraglottic approximation of structures is the negative inspiratory pressure during rapid deep breathing which attracts tissues into the lumen of the larynx. They call it „bottle neck" theory based on special laryngeal anatomy with narrow laryngeal inlet[41,40]. In the case of coexisting laryngopharyngeal reflux from the oesophagus, the characteristic oedema of the laryngeal inlet makes it even more pliable and the approximation of aryepiglottic folds is more likely[22].

Classification

The ELO is divided into three categories according to the triggering factor:

1. ELO due to irritation (substances from the environment, laryngopharyngeal reflux),
2. exercise-induced laryngeal obstruction (EILO),
3. psychogenic ELO.

In fact, all three forms of ELO can be intertwined. Airway obstruction can occur at the level of the vocal folds or supraglottis, or at both levels at the same time. In some patients, vocal folds' approach occurs not only during inspiration but also during expiration. Between dyspnea attacks, the patient has no breathing problems[9].

Epidemiology

There are no accurate data on the prevalence of ELO in the population. ELO is thought to be the real cause of breathing problems in 10% of patients who are unsuccessfully treated for asthma. It is often the cause of breathing

problems in patients with certain psychiatric disorders (e.g. depression, childhood sexual abuse, obsessive-compulsive disorders)[16,4]. Women predominate among ELO patients, with a 3:1 ratio in their favour as reported in the professional literature. Problems most commonly occur between the ages of 20 and 40, but patients aged 6 to 83 years have also been described[9,23].

More information is available for EILO, one of the subtypes of ELO. EILO occurs mostly in adolescent or young adult women, often top athletes at maximum exercise. Among randomly selected young people in Denmark, at least 7.5% of people with EILO were identified, and among adolescents with upper respiratory hyperexcitability, as many as 26.1% of people with EILO[42,8].

Symptoms and Signs

Especially in EILO, shortness of breath occurs and very often also inspiratory stridor during physical exertion, so these patients are initially treated for exercise-induced asthma[33,43]. Other symptoms include dysphonia, dysphagia, cough, and some patients also report a foreign body sensation in the throat or a feeling of discomfort in the chest and throat[9]. Problems can occur at rest or during physical exertion, either during the day or at night. Symptoms of shortness of breath and inspiratory stridor can be triggered by an identified trigger (e.g. strong odour, irritants in the air, emotional stress), or they can occur without any obvious reason. Problems usually pass within seconds, minutes rarely lasting longer[32]. Occlusion at the level of the supraglottis occurs more frequently. The arytenoids descend forward above the entrance to the larynx, the aryepiglottic folds approach the median line, leaving little room for breathing between them and the epiglottis. In the case of glottis closure, the vocal folds come very close together, they can even be practically compressed, leaving only a tiny space for breathing between the two vocal processes of the arytenoid cartilages[9,12].

Diagnostic Procedures

A group of different specialists should be involved in the diagnostics of ELO (otorhinolaryngologist, pulmonologist, gastroenterologist, neurologist, psychiatrist, psychologist, speech therapist and others according to the clinical picture). The gold standard in ELO diagnostics is a larynx examination using a flexible nasolaryngoscope during the attack of dyspnea. In most cases it is impossible to have the opportunity to perform the examination and to have the necessary equipment on site. Only in EILO, the diagnostic procedure can be planned and carried out. Flexible nasolaryngoscopy is performed during exercise on a bicycle or treadmill while monitoring ECG, lung function, blood oxygen saturation, and blood pressure fluctuations[21,48,40]. At rest or in the period without problems, the laryngoscopic picture is usually normal.

In the differential diagnosis of ELO, asthma, especially stress-induced asthma, anaphylactic and other allergic reactions, foreign body in the respiratory tract, angioedema, laryngospasm, epiglottitis, other upper respiratory infections, unilateral and bilateral paralysis of the larynx from other causes, adductor-respiratory congenital anomalies and benign and malignant changes in the larynx, stenosis of the larynx and upper trachea must be mentioned. To exclude other diseases that can also cause occasional breathing problems and audible breathing, it is advisable to take a measurement of lung function. The flow-volume curve shows a typical decrease in the curve during inspiration during an ELO attack. A methacholine test is required to rule out asthma. Positive allergy tests, detection of peripheral blood eosinophils, C1 inhibitor concentrations, and C4 levels distinguish ELO from allergic manifestations and angioedema[9]. It is possible that exercise-induced asthma and EILO coexist.

Among the youth with airway hyperresponsiveness, the prevalence of EILO was 26.1%[8].

Treatment

Team approach is necessary to treat patients with ELO problems. When the correct diagnosis is established with appropriate procedures, we can explain the events to the patient in the acute phase and calm him down. In some patients, rapid "dog breathing" is successful, in others a slow long breath through the nose, in others an attempt to smell or phonate a high voice / s / or a combination of these two manoeuvres. Some patients are helped by speaking quickly, loudly, coughing, or holding their breath[1]. Some authors report the success of diazepine therapy, while other authors are not in favour of this method of treating acute dyspnea[1,9]. Christopher and colleagues were the first to describe the immediate beneficial effect of inhaling a mixture of helium and oxygen during an attack, and the effect of the treatment was not only acute but also long-lasting[10]. Although ELO is benign in nature and difficulty breathing ceases after a period of time, cases have been described where intubation or even tracheotomy was required due to severe respiratory distress during the attack[9].

So far, quite a few methods have been used in the treatment of recurrent problems with varying degrees of success. Speech therapy treatment is based on breathing exercises, exhalation against resistance, strengthening of inspiratory muscles and relaxation of vocal cords[9,7]. Psychotherapy and counselling help in 30% to 90% of cases, greater successes are of course in the psychogenic form of ELO. There are some reports of successful use of hypnosis in the paediatric population[3,9].

Until a few years ago, experts believed that gastroesophageal reflux to the level of the larynx and pharynx was the main cause of ELO. This is the case in certain patients. There are studies that have demonstrated the presence of reflux in patients with ELO, so it was logical to use proton pump inhibitors, ranitidine, and antacids in those patients. The success of such treatment is very good in those patients in whom reflux has been demonstrated[38,34].

Surgical treatment also gives good results, but only in selected patients. The most commonly used method is to cut the aryepiglottic folds closer to the epiglottis and to remove the mucosa and cuneiform cartilage from the aryepiglottic fold with the help of a laser (supraglottoplasty). The use of a suture that pulls the epiglottis towards the root of the tongue and lateralization of one vocal cord with a suture is also described[28,51].

Pinder and co-workers used a questionnaire to determine the long-term course of the disease. After 15 years of ELO onset, none of the patients reported deterioration. The condition improved or completely recovered in 68% of included subjects[37].

Conclusions

Respiratory tract acts as a whole. The same causes can induce asthma, rhinitis and laryngitis in some individuals. Some of the laryngeal characteristics of the asthma patients can be just the result of asthma symptoms or asthma treatment. In others, there are different diseases manifesting the same symptoms of the upper respiratory tract. In some patients, different pathologies coexist. Therefore, a team of different specialists must be involved in the diagnostic procedures and the treatment of asthma, asthma – caused conditions, asthma-accompanying diseases, and asthma-like diseases of the upper respiratory tract.

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