

喉部感觉神经性疾病的诊疗进展*

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[关键词] 喉部感觉神经性疾病;病因;诊断;治疗

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Advances of the treatments and diagnosis for sensory laryngeal neuropathy

Summary Sensory laryngeal neuropathy(SLN) is a kind of peripheral neuropathy presenting globus pharyngeus, chronic cough, increased mucus, dry throat, sore throat, frequent clearing of the throat, etc. When the sensory nerve of the larynx is affected by chemical, biological, mechanical or nutritional factors. Because of its nonspecific signs and symptoms, SLN is easy to be misdiagnosed as chronic pharyngitis or laryngopharyngeal reflux disease. SLN was came up to ENT physician in recent years and there are rare systematic reports currently, therefore, this review aims to summarize the etiology, clinical manifestations, diagnosis and treatment of SLN, to raise awareness of this disease among our colleagues.

Key words sensory laryngeal neuropathy; pathogeny; diagnosis; therapy

咽喉的基本功能有呼吸、吞咽、发声和咳嗽等^[1],这些功能离不开分布于咽喉部的神经支配(迷走神经、舌咽神经)。当炎症刺激、胃酸反流等外界因素或病毒感染、营养、代谢等内在因素影响咽喉部时,该区域感觉神经的功能或结构可能出现异常,从而出现咽喉部异物感、慢性咳嗽、黏液增多、干燥、灼痛、频繁清嗓等症状^[2-3]。喉部感觉神经性疾病是咽喉部感觉神经过敏的外周神经性疾病,最早于 2005 年由 Lee 等提出^[4],他研究招募了 28 例感染后或未知因素触发后突发咳嗽、清嗓及喉痉挛等的患者,行质子泵抑制剂(PPI)、雾化等治疗后效果欠佳,喉部肌电图等检查提示神经病变,尝试使用加巴喷丁反而得到肯定的疗效,遂提出此

病的存在。其后 Halum 等^[3,5-6]报道发现类似病例。该类疾病在临床上极易被单纯诊断为“慢性咽炎”而疗效欠佳。本文通过复习国内外相关文献,对喉部感觉神经性疾病的发病机制、临床表现、诊断原则、诊治方案等进行综述。

1 主要病因及可能发病机制

1.1 内在因素

1.1.1 病毒感染 急性上呼吸道感染迁延不愈后,喉部黏膜的病毒感染喉部感觉性神经纤维,可表现为喉感觉过敏及感觉异常等^[2,7-9]。喉感觉过敏为喉黏膜对普通刺激特别敏感,当有食物、唾液等触及喉部时,常引起呛咳甚至喉痉挛^[10]。喉感觉异常是指喉部发生不正常感觉,如刺痛、瘙痒、烧灼、干燥或异物感等。部分文献将病毒感染影响迷走神经感觉支后引起一系列咽喉部症状的疾病称为病毒感染后迷走神经性疾病(postviral vagal neuropathy)^[7]。

1.1.2 锌、铁等微量元素缺乏 微量元素虽然在体内含量很少,但是发挥重要的生理、生化等功能。

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比如:锌通过锌转运体 3 被固定在突触小泡中,动作电位来临后,它从突触前小泡释放到突触间隙,参与神经相关的信号通路的激活^[11]。此外,锌还参与突触的重塑。锌缺乏时不仅影响神经冲动的传导,还影响突触的形成。因此,硫酸锌常被用来治疗周围神经病变^[12],耳鼻喉医生也常使用甘草锌缓解咽喉异物感等症状。有报道认为缺铁也可能导致咽部异物感。其机制可能有:铁是许多细胞酶不可缺少的辅助因子,是氧转运、DNA 合成和修复、呼吸活动、髓鞘形成维持和神经递质合成等重要功能的辅助因子,并参与轴突的可塑^[13],铁缺乏可致脱髓鞘等外周神经病变,表现出感觉异常等不适,部分呈现不可逆损害^[14-15]。

1.1.3 糖尿病等全身疾病影响 外周神经疾病是糖尿病最常见的并发症,通过皮肤和神经活检等研究表明在诊断糖尿病时甚至更早时已出现外周神经纤维脱髓鞘或逐渐减少,感觉症状比运动症状更为突出,如疼痛、麻木等^[16-18],同时糖尿病患者可以“咽干咽痛、咽喉部异物感、吞咽困难^[19]、咳嗽”等为首发症状。有研究认为,喉部感觉神经性疾病在糖尿病患者中的发生率显著高于健康人群^[5]。此外,甲状腺功能低下者也可能与喉部感觉神经性疾病有关^[6]。

1.2 外界刺激

1.2.1 咽喉反流 咽喉反流性疾病与喉部感觉神经性疾病不仅在临床症状上非常相似,而且在发病机制上也可能相辅相成。咽喉反流作为喉部感觉神经性疾病的病因之一,一方面胃内容物反流直接刺激咽喉部黏膜,引起局部损伤及咽喉不适^[20],当声门区化学受体被激活时可引起喉异物感、痉挛等不适^[21],同时反流的物质可松弛颈段食管括约肌,使反流物更易进入到咽喉部引起进一步的损伤^[22];另一方面喉部感觉神经性疾病可能通过迷走神经导致胃轻瘫、肠道消化吸收差等,进一步加重胃酸反流至咽喉部^[23]。咽喉部如长期暴露于酸性环境中可加重喉部感觉神经性疾病的症状^[24]。因此,合并咽喉反流和喉部感觉神经性疾病的患者可同时使用 PPI 和神经调节类药物^[25]。

1.2.2 不良因素的吸入或摄入 日常生活中吸入有害气体(如工业气体、烟味、化学粉尘)、刺激性气味(香水、洗手液、清洁液散发的气味)^[20]、质量较差的空气(如 PM_{2.5} 超标)或经口摄入辛辣刺激性食物均可能损害喉部黏膜或感觉神经,导致咽喉部不适或慢性咳嗽。神经系统的可塑性可在这之后发生,刺激物直接引起上皮损伤并潜在损伤传入性感受器,促进局部炎症递质的产生,增强感觉性神经对咽喉部刺激的敏感度,从而导致中枢调控的慢性咳嗽和频发清嗓。

2 诊断与鉴别诊断

2.1 临床症状与体征

喉部感觉神经性疾病^[3-6,8,26-28]常见的临床表现有咽喉部异物感、慢性咳嗽、黏液增多、干燥、灼痛、频繁清嗓,极少数患者可合并运动神经功能障碍出现喉痉挛、发声障碍、吞咽障碍,严重者可出现呼吸困难,可急性或慢性起病。喉部感觉神经性疾病通常无特异性体征。

2.2 辅助检查

喉镜检查可提示咽喉部黏膜的异常^[21]。不过,多数患者的内镜检查无明显异常发现。有学者认为,基于表面激发的喉感觉性神经肌电图(Surface evoked laryngeal sensory action potential, SELSAP)有助于喉部感觉神经性疾病的诊断^[1,5,26,28-30]。SELSAP 是一种采用无创表面电极定位来检测喉上神经复合感觉动作电位的方法,可直接分析喉上神经的感觉支功能情况。其操作方法为在甲状软骨板双侧及颈下各放置一枚电极,在耳后进行电位刺激,通过记录波形变化来评估喉部感觉神经的病变情况。

2.3 诊断与鉴别诊断

SELSAP 是喉部感觉神经性疾病最重要的确诊依据之一,需与鼻后滴漏综合征^[31]、慢性咽炎、变应性咽炎、咽喉反流、咽异感症、咳嗽变异性哮喘^[32]等相鉴别。

根据详细的病史、症状、体查及辅助检查(pH 监测/变应原检测/SELSAP 等),喉部感觉神经性疾病与上述疾病鉴别不难(如:pH 监测评估咽喉反流的可能,依发病规律与变应原检测考虑是否为变应性咽炎,根据精神心理评估量表与咽异感症相鉴别^[33])。上述疾病的 SELSAP 检查应表现为阴性,此可进一步与喉部感觉神经性疾病相鉴别。

值得注意的是,由于咽喉反流是喉部感觉神经性疾病的可能病因之一,当咽喉反流病程较长或反复迁延时,其可能同时合并喉部感觉神经性疾病。部分确诊为咽喉反流性疾病的患者如行 PPI 等治疗效果欠佳,则需考虑是否合并喉部感觉神经性疾病。

3 治疗

喉部感觉神经性疾病的病因及临床表现复杂多样,基于不同的病因和临床表现应采取不同的治疗方式。如清嗓、黏液增多、干燥、灼痛、咽喉部异物感和咳嗽明显需注意饮食习惯并辅以药物治疗、行为治疗,必要时行手术治疗。

3.1 患者教育

对于存在危险因素的患者应改变生活环境、生活方式及饮食习惯等^[34-35]。生活环境:避免吸入刺激性气体,保持空气流通等;生活方式:戒烟戒酒,减肥,避免穿紧身衣服,忌做弯腰俯身等增加腹内压的动作,睡时垫高床头,宽松衣着入睡等;改变饮

食习惯:避免浓茶、咖啡、碳酸类饮料等的刺激,避免微量元素缺乏,忌高脂类、油炸辛辣食物,少食柑橘类水果,少食多餐,睡前3 h 禁饮禁食;其他:避免感冒,治疗鼻窦炎和变应性鼻炎的相关问题等^[36]。

3.2 一般药物治疗

常用药物为加巴喷丁和阿米替林。国内外的数项研究均证实加巴喷丁和阿米替林治疗喉部神经性病变的有效性及其安全性^[2,4,21,27,37-39]。加巴喷丁消除频发清嗓和减轻灼痛的机制可能与其抑制中枢反应性致敏、气道高反应性及气道炎症有关^[3,37],对于慢性咳嗽及胃食管反流性咳嗽亦有效^[4,9,27,35,40]。阿米替林是一种三环抗抑郁药,通过阻断外周传入神经的激活及抑制中枢来发挥作用,对于喉部神经病变引起的慢性咳嗽及慢性疼痛均有一定疗效^[2-3,35,38,40]。如患者合并咽喉反流性疾病,可同时使用PPI治疗。PPI对缓解反流性咽喉炎的咽喉部症状有效,但在改善咳嗽和声嘶症状方面疗效不显著^[21]。

3.3 局部注射曲安奈德+利多卡因

曲安奈德是糖皮质激素,局部注射曲安奈德已被用于治疗尺神经病变^[41]。其作用机制可能有以下几点:①减轻神经干周围组织炎症^[41],消除神经组织水肿,改善神经血液循环,促进病变神经组织恢复;②减少血管壁的通透性,抑制巨噬细胞和中性粒细胞对神经纤维组织的破坏;③抑制局部免疫反应,减少有害物质的产生,有利于神经纤维病变的恢复;④抑制神经递质中P物质的释放。局部注射利多卡因已被用于治疗喉部神经病变和尺神经病变等^[41-42]。利多卡因与神经组织有较强的亲和力,与神经组织接触后被吸收,并可在短时间内阻断来自末梢的触觉刺激,抑制假突触的传递及舌咽神经节神经元的易兴奋性,导致自然的不应期产生,减弱其传导功能,松解神经压迫。因此,曲安奈德和利多卡因对神经病变引起的疼痛和异常感觉的缓解均有一定的疗效^[43]。

3.4 行为治疗

据相关研究报道,经验丰富的言语病理学家通过行为治疗可以使喉部感觉神经性疾病得到显著改善。治疗的重点是通过识别需要改变的行为或呼吸模式来制定适宜策略^[44-45]。患者需要接受个体化的发声和呼吸训练^[20]。

4 总结

喉部感觉神经性疾病与突聋等非特异性疾病一样,发病机制尚不明确,临床表现无特异性,需谨慎地综合诱因、病史、喉镜、肌电图等做出排他性的诊断。该疾病主要治疗方法有:患者教育、神经调节类药物、局部注射曲安奈德+利多卡因等。目前喉部感觉神经性疾病尚处于被认识的阶段,其

诊断和治疗虽取得了一定的进展,但有关其发病机制、诊断标准、治疗原则等还需要进一步探索与证实。

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