

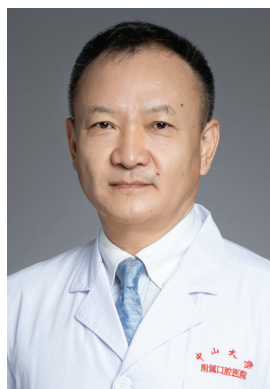
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• 专家论坛 •

腮腺慢性阻塞性疾病的再认识

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【摘要】 腮腺慢性阻塞性疾病(chronic obstructive diseases of parotid)在临床多见,病情反复,治疗效果欠佳。本文参阅“腮腺反复肿胀”相关文献,结合个人临床实践和研究成果,从病因学的角度将腮腺阻塞性疾病分为机械性阻塞、特异性阻塞和非特异性阻塞3大类,并引入流体力学的原理解释腮腺阻塞的机制,针对不同病因提出改变腮腺微流场中唾液流动状态,减少流动阻力以解除阻塞的治疗新思路:传统的结石取出可清除导管内机械性阻塞,药物促进唾液分泌以改变唾液粘滞度,内镜下扩张导管或放置支架以扩大管径,选择性栓塞侧支导管以减少流场中高压区和低速区等等,这些方法均能有效提高唾液流动速率,减少唾液滞留和腮腺阻塞的发生。

【关键词】 腮腺阻塞; 结石病; 慢性复发性腮腺炎; 舍格伦综合征; IgG4相关性腮腺炎; 放射性腮腺炎; 非特异性腮腺炎; 流体力学; 治疗策略

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Re-cognition of chronic obstructive diseases of the parotid gland TAO Qian, HUANG Yun. Department of Oral and Maxillofacial Surgery, Guanghua School of Stomatology, Hospital of Stomatology, Sun Yat-sen University, Guangdong Provincial Key Laboratory of Stomatology, Guangzhou 510055, China

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【Abstract】 Chronic obstructive diseases of the parotid gland are common clinically, with repeated swelling and a prolonged course and poor treatment outcomes. Based on the summarization of clinical practice and related literature, from the viewpoint of etiology, parotid obstructive diseases can be classified as mechanical obstructions, specific obstructions and non-specific obstructions. The principles of fluid mechanics are introduced to explain the formation of parotid obstructions. According to the different causes, the methods of changing the flow pattern of saliva in the parotid to reduce the resistance and relieve the obstruction, are proposed, such as mechanical factors removals, application of drugs that

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promote saliva secretion and lower saliva viscosity, ductal expansion under endoscopy and stent placement, and embolization of collateral ducts. These managements can effectively increase the salivary flow rate, reduce the occurrence of the saliva stranded and parotid gland obstructions.

【Key words】 obstruction of parotid gland; lithiasis; chronic recurrent parotitis; Sjögren's syndrome; IgG4-related parotitis; radiation-induced parotitis; non-specific parotitis; fluid mechanics; therapeutic strategy

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反复肿胀是腮腺非肿瘤性疾病最常见的一种临床症状,可累及单侧或双侧腺体,常与进食、咀嚼等刺激相关,持续时间不等,肿胀往往可自行消退,继发感染者则可见局部肿痛和导管口溢脓,既往又被称为“慢性腮腺炎”、“阻塞性腮腺炎”、“腮腺管炎”和“慢性阻塞性腮腺炎”等等,并认为导管内结石/异物是腮腺反复肿胀的主要原因^[1-3]。但是近年来越来越多的临床资料证明:很多的局部和全身因素都可能导致腮腺肿胀症状的反复发作,不同因素引起肿胀的特点也不尽相同^[4-6]。对这类以腮腺反复肿胀为主要表现的疾病进行再认识,一方面可以丰富和充实疾病的内涵,体现病因和机制的多样性;另一方面可扩大其外延,充分涵盖疾病复杂多样的临床表现,针对不同病因和机制精确指导临床诊断和治疗。在此思路指导下,笔者收集和总结临床诊治的“腮腺反复肿胀”患者资料,对这些患者的临床表现、腮腺造影的全景片和锥形束CT(cone beam computed tomography, CBCT)影像资料、唾液腺内镜探查的结果等加以分析归纳,参阅相关文献资料,认为“腮腺慢性阻塞性疾病(chronic obstructive diseases of parotid)”更能全面体现和覆盖这一类疾病,其实质和共性就是各种原因影响唾液在腮腺导管内流动和排空,唾液滞留引起腮腺肿胀;并尝试对“腮腺慢性阻塞性疾病”进行病因学分类,以期为临床诊治提供参考。同时,介绍“流场和流体理论”对腮腺慢性阻塞性疾病的病因和机制研究的新进展,从流体力学的角度分析和解释腮腺反复肿胀的可能成因。

1 腮腺慢性阻塞性疾病的病因

腺泡分泌的唾液经过腺体内导管汇流进入腮腺导管,由导管口流入口腔,在这个生理过程中影响唾液的分泌、导管内的流动以及排空过程的诸

多因素都可以引起唾液在导管和腺体内滞留,进而导致以腮腺反复肿胀为核心表现的一组临床疾病,统称为腮腺慢性阻塞性疾病。综合文献资料^[1-5,7-10],引起腮腺阻塞和肿胀的常见原因包括结石或异物等机械性因素,感染、创伤和放射线等物理性因素,抗SSA和IgG4相关的免疫性因素以及腮腺导管系统结构变异等解剖因素。

2 腮腺慢性阻塞性疾病的分类

从病变发生部位和发病机制的角度分析,可将腮腺慢性阻塞性疾病分为“腺泡型”、“导管型”和“混合型”等3种类型:①腺泡型主要指发生在腺泡的病变,引起唾液的分泌量、渗透压和粘度等性状改变^[11];②导管型主要指导管上皮炎症、瘢痕、息肉和扭转等改变导管的内径和弹性,进而影响唾液的排空效率^[12-13];③混合型是指病变同时累及腺泡和导管,共同改变唾液在导管内流动的状态^[14-15]。腮腺造影片有助于这3种类型的相互鉴别。

从病因学角度来讲,腮腺慢性阻塞性疾病可以分为机械性、特异性和非特异性3大类:①机械性阻塞指导管系统内结石或异物阻碍了唾液流动^[2-4],也称唾液腺结石病;②特异性阻塞指明确的局部或全身因素引起的唾液分泌和排出障碍,包括感染和创伤等引起的慢性化脓性腮腺炎、自身免疫性因素引起的舍格伦综合征、IgG4相关性腮腺炎以及头颈部放射治疗后的放射性腮腺炎等^[2,7-9];③非特异性阻塞主要指不能明确病因的腮腺反复肿胀,腺体肿胀与进食咀嚼等刺激因素的相关性不显著^[16]。

3 腮腺慢性阻塞性疾病的临床特点

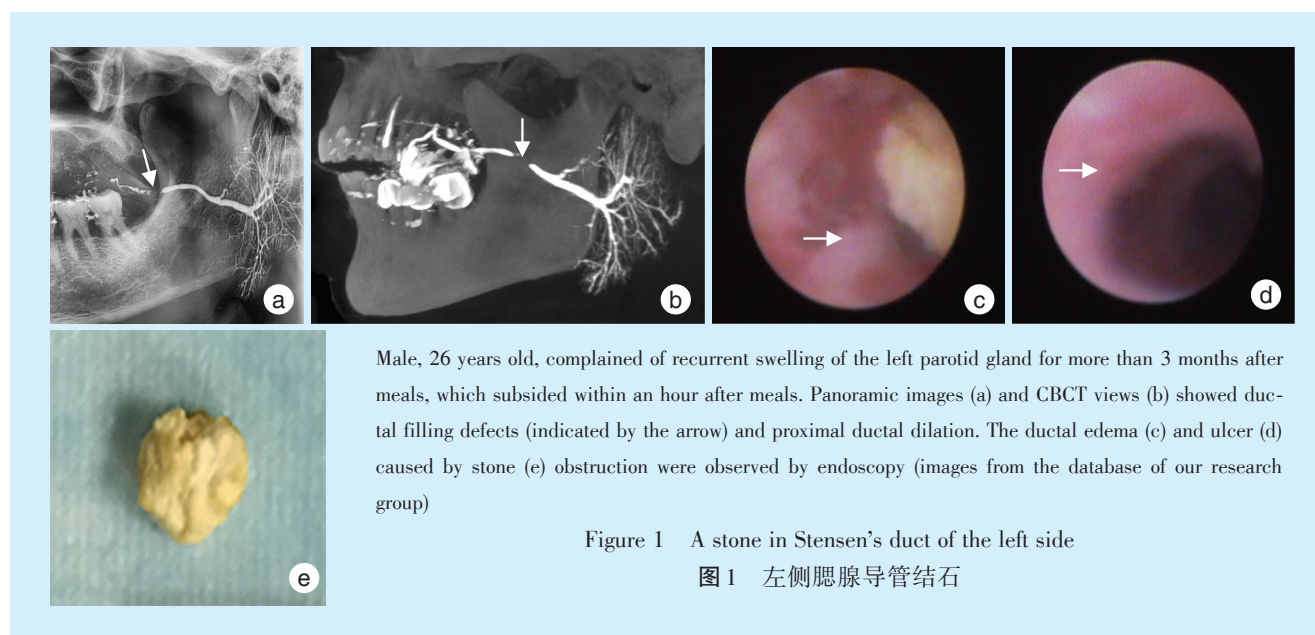
腮腺区肿胀是所有腮腺慢性阻塞性疾病的主要表现和共同症状,但是不同原因引起腮腺阻塞

的发作频率、时机、持续和消退时间以及伴随症状等不尽相同。

3.1 腮腺结石病

腮腺结石病也称结石性腮腺炎。腮腺结石多发生在单侧导管中,偶有双侧同时发生者,阻塞的发生与进食或咀嚼等促进唾液分泌的刺激因素关系密切,肿胀发生迅速,多在刺激消失后数小时内消退,常反复发作^[17-18]。腮腺造影常见导管节段性充盈缺损,近心端导管扩张,内镜下可见结石梗阻

处导管内壁充血及斑片状溃疡^[19-20](图1)。结石曾笼统地被认为是唾液腺阻塞肿胀的最常见原因,Huoh等^[19]报道唾液腺结石的发病率为1/30 000至1/10 000,2016年南卡罗来纳医科大学唾液中心^[12]报告了1 659例唾液腺阻塞病例,46.1%为结石性阻塞。值得指出的是,近年来唾液腺内镜以及CBCT等临床应用发现,与下颌下腺相比,腮腺结石的发生率较低^[21]。笔者数据库中,结石引起的腮腺阻塞的占比20%左右。



3.2 慢性复发性腮腺炎

患者多有儿童期复发性腮腺炎病史,病情迁延不愈,成年后腮腺肿胀发作频率降低,挤压腺体常可见胶冻状和/或脓性分泌物从导管口流出,有自发缓解的倾向^[22]。Zou等^[23]报道腮腺功能可在临床症状消失后3~5年内恢复。急性发作时表现出腮腺区红、肿、热、痛的症状,导管口可分泌脓性液。造影片显示末梢导管呈点状、球状扩张,可见散在的“碘池”,主导管走行僵硬,呈“腊肠样”改变^[20]。内镜下可见受累腮腺主导管壁苍白少血管,散在溃疡,管腔内可见纤维碎片或黏液栓(图2)。

3.3 舍格伦综合征

舍格伦综合征是以淋巴细胞浸润和破坏外分泌腺为基本病变的系统性自身免疫疾病,临床表现为口干、眼干和涎腺肿胀,腮腺为最常受累的唾液腺^[14]。患者表现出双侧腮腺交替、间歇性和弥漫性肿胀,与进食等刺激关系不密切,疼痛感不明显,可缓慢消退,后期逐渐出现双侧腮腺弥漫肥

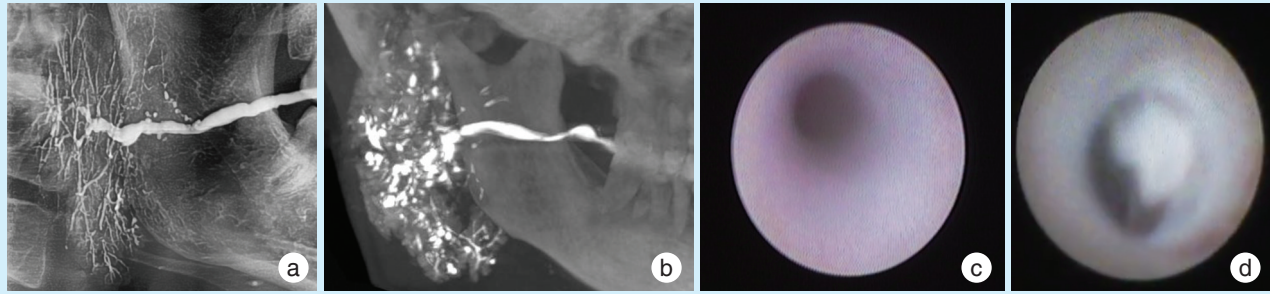
大。舍格伦综合征影响的腮腺腺泡表现为点状、球状、腔状或腺泡间隔破坏性的扩张和主导管狭窄,管壁苍白及弹性不足。挤压腮腺可见少量凝胶样液体从管口流出,造影检查可见末梢导管扩张呈“腊梅样”的典型特征,伴有排空功能迟缓。内镜下可见管腔内粘液栓子形成^[15](图3)。

3.4 IgG4相关性腮腺炎

IgG4相关性唾液腺炎多累及下颌下腺,其次为腮腺,主要表现双侧唾液腺和泪腺的无痛性、持续性和弥漫性肿大,质地中等。在此基础上可以伴发腮腺阻塞症状,腺体肿胀的发生、发展和消退均较缓慢^[9,24](图4)。

3.5 放射性腮腺炎

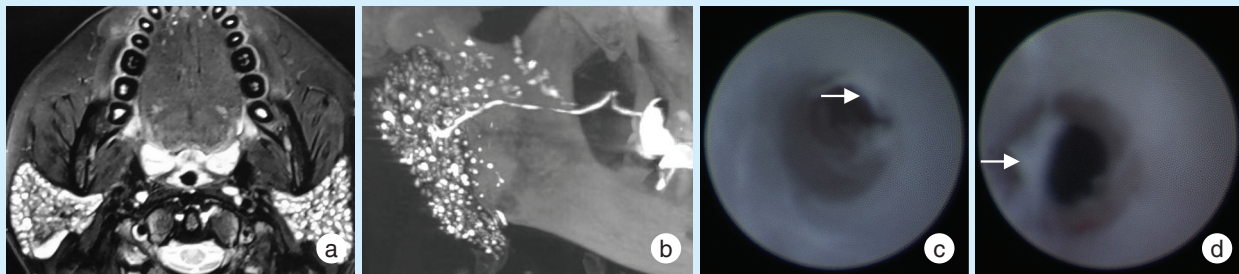
患者多有接受放射治疗的病史,常见于头颈癌的放射治疗和¹³¹I治疗甲状腺癌后。通常表现为双侧受累的腮腺肿胀和疼痛,唾液分泌量减少以及偶有脓性唾液分泌^[25]。造影检查可见主导管局段扩张,呈现出腊肠样外观^[8,20]。内镜探查可见苍



Patient A: female, 42 years old, complained of repeated swelling of the right parotid gland for more than 2 months, with ductal expansion in the panoramic images (a). Patient B: male, 57 years old, complained of repeated swelling of the right parotid gland for more than 1 year, ductal expansion and stenosis were observed after the 3-dimensional reconstruction of CBCT images, with scattered iodine dots inside the gland (b), under the endoscope, stenosis of the partial duct can be seen (c), mucus plugs are visible in the duct and the tube is pale in appearance (d). There was no relationship between the swelling and meals in these two patients, swelling lasted for several hours to several days, and both patients acknowledged a history of juvenile recurrent parotitis (images from the database of our research group)

Figure 2 Chronic recurrent parotitis of the right side

图2 右侧慢性复发性腮腺炎



Female, 36 years old, complained of swelling of the bilateral parotid glands for more than one year, accompanied by dryness of the mouth and eyes. Serological examination revealed positivity for the anti-SS-A and anti-SS-B antibodies. MRI showed the expansion of bilateral parotid glands (a). CBCT demonstrated expansion of the posterior duct (b). Under the endoscope, the wall is pale in appearance and mucus plugs (c & d) can be seen in the duct (images from the database of our research group)

Figure 3 Sjögren's syndrome

图3 舍格伦综合征



Male, 53 years old, complained of persistent swelling of the bilateral submandibular and parotid glands for more than half a year. Signal enhancement of the bilateral parotid glands was seen in the axial position of MRI under the T1 signal (a). Obvious swelling of the submandibular glands was observed (b). Coronal, enlargement of the submandibular gland was shown in MRI under the T1 signal (c) (images from the database of our research group)

Figure 4 IgG4-related sialadenitis

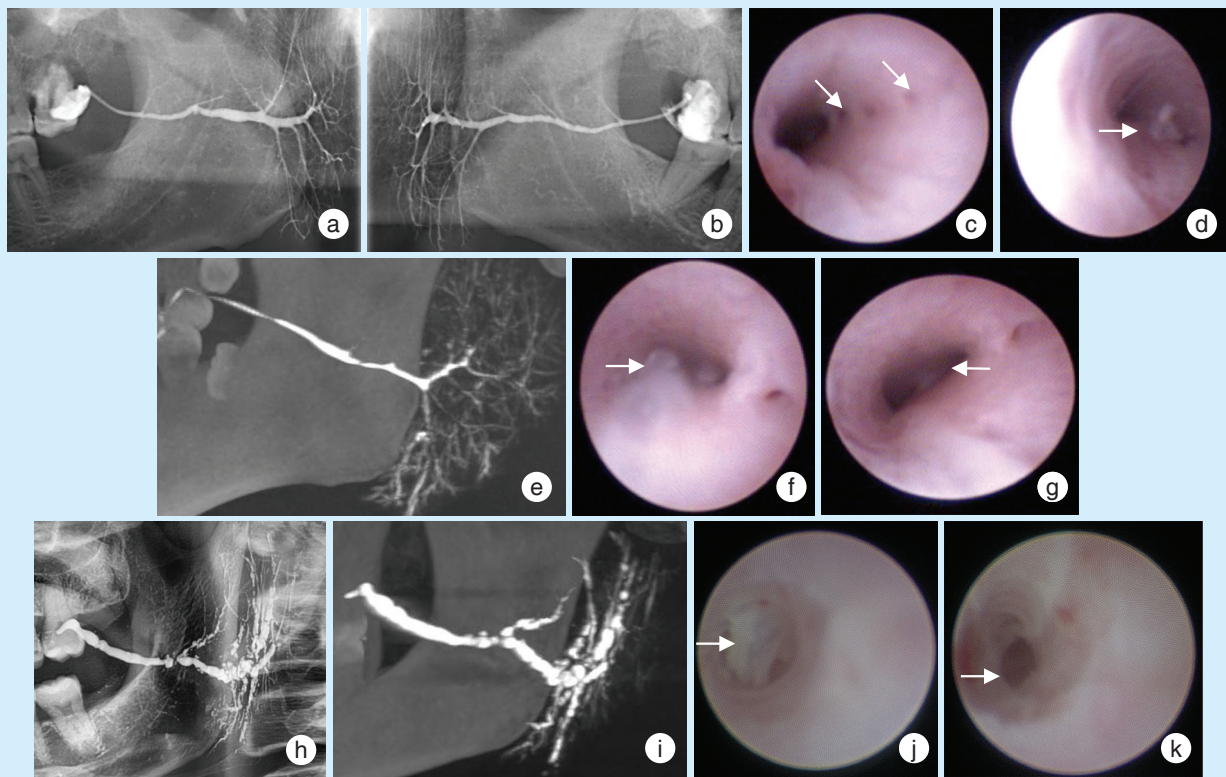
图4 IgG4相关性唾液腺炎

白的管壁,管腔内有粘液栓子以及纤维碎片阻塞,Vashishta等^[13]发现84%放射线唾液腺炎患者导管系统内可出现不同程度的狭窄。

3.6 非特异性腮腺阻塞

非特异性腮腺阻塞是指没有明确的局部或全身病因的腮腺阻塞和反复肿胀。1998年Bhatty等^[16]用慢性非特异性腮腺炎(chronic non-specific parotid sialadenitis)描述过19例腮腺间断性肿胀疼痛的患者,其中7例由结石引起,其余病因不明。Mahalakshmi等^[26]在2017年报道了一例非特异性腮腺炎,既往病史未见特殊,仅在造影检查提示腺体末梢导管点状扩张,造影剂于5 min后完全排

空,提示腺体排泄功能正常。笔者的临床实践中也观察到部分腮腺肿胀患者,既无儿童腮腺炎、外伤以及放疗史,血清学检查也未提示免疫学改变,超声或造影等影像学检查以及内镜探查等都没有结石。腮腺肿胀与进食等刺激存在一定的关联,但持续时间短,消退迅速。多见于中年,以单侧肿胀为常见。比较有意义的是,这类患者腮腺造影片上导管系统连续完整,多表现为导管系统呈树干状或末梢导管分叉角度大,以及主导管有多个侧支等特点。内镜下在侧支导管汇合或分支导管交汇处可见粘液栓子形成(图5)。



a-d: female, 36 years old, complained of recurrent swelling of bilateral parotid glands for 2 weeks, panoramic imaging revealed a large number of collateral ducts in the ductal system (a & b), and the openings of collateral ducts were seen under the endoscope (indicated by arrow) (c), with the formation of mucus plugs seen at the junctions (d)

e-g: male, 43 years old, complained of repeated swelling of the left parotid gland for half a month, three-dimensional reconstruction of CBCT images showed that the angle between the branches was relatively large (e), without obvious abnormalities found under the endoscope, and the formation of mucus plugs was seen at the junction of the branches (f & g)

h-k: female, 53 years old, complained of repeated swelling of the left parotid gland for more than 10 years. panoramic imaging and three-dimensional reconstruction of CBCT showed the trunk-like duct system of the patient, with beadlike expansion of Stensen's duct, and a filling defect at the junction of the collateral ducts, which was presumed to be the low-velocity region of the flow field (h & i); under the endoscope, mucous plugs were seen in the lumen of the duct at confluence (j). After washing the embolus, the confluence of the collateral duct was seen to have ductal stenosis (k) and expansion coexisting

Figure 5 Nonspecific parotid obstruction

图5 非特异性腮腺阻塞

4 腮腺阻塞的流体力学分析

腮腺导管分支末端与腺泡相连接,唾液逐级经过闰管、纹管和排泄管的各级管腔,最终在腮腺主导管内汇集,并通过导管口排出至口腔中发挥生理功能。腮腺内唾液正常流动过程受到影响后流速改变,引起导管内唾液滞留,大量滞留的唾液可导致腺体肿胀。腮腺分泌的唾液在导管内的流动方式,与长江黄河从源头逐步流归大海的方式十分相似,当来水超过河道排泄能力时,就会发生河水在上游淤积等现象。因此将腮腺导管和流动的唾液看成一个微小流场,用流体力学分析唾液在导管内流动的规律和影响因素,将有助阐明腮腺阻塞性疾病的反复肿胀的发生机制^[21]。

根据泊肃叶公式 $R = \frac{8\eta L}{\pi r^4}$ (R 、 r 、 L 、 η 分别为流阻、管道半径、管道长度及粘性系数),在唾液和导管系统构成的流动体系中,影响唾液流动的因素主要包括:①导管的解剖特点、管径以及长度等;②唾液的粘滞度等理化特性。在腮腺慢性阻塞性疾病中:结石或异物以及狭窄等对导管形成机械性阻塞,相当于河水流动体系中堰塞湖的形成,滞留的唾液逐渐导致腺体肿胀;Bhatty等^[16]分析非特异性腮腺炎的发生与唾液流量的减少和唾液粘滞度的增加导致唾液流动缓慢和机会性口腔菌群逆行感染等有关。舍格伦综合征等免疫性疾病可以破坏腺泡的分泌功能,改变唾液性状,如本研究团队用椎板式粘度测试仪检测发现这类阻塞患者的唾液粘滞度要高于正常人,Liang等^[27]在原发性舍格伦综合征小鼠模型中发现连环蛋白 α -3(catenin α -3, CTNNA3),酪氨酸蛋白磷酸酶非受体6型(tyrosine-protein phosphatase non-receptor type 6, PTPN6)及Ras相关的C3肉毒杆菌毒素底物(ras-related C3 botulinum toxin substrate, RAC2)等3个水离子通道蛋白的失调可能导致唾液分泌障碍,这些均证明流场理论可以合理解释机械性或特异性腮腺阻塞的肿胀形成原因。对于非特异性腮腺阻塞患者而言,课题组在前期证实患者侧支导管数量较多以及分支导管间的角度较大的基础上^[28],基于这类患者的CBCT资料三维重建了相应的导管模型,并进行计算流体力学分析:管壁的压强云图显示,侧支与主导管汇合处为流场的高压区;速度云图显示分支汇流处存在低速区,且低速区的范围随着夹角的增大而扩大。低速区和高压区都可以影响唾液流动速度,阻碍唾液排空并最终引起阻塞症状^[28-30]。

腮腺阻塞性疾病引起的腺体反复肿胀,病程迁延,结石病以外患者的治疗效果欠佳,常常给患者的正常工作和生活造成影响。从多个角度对腮腺慢性阻塞性疾病进行再认识,将有助于指导临床分类诊疗:如机械性阻塞应及时清除导管内结石或异物;舍格伦综合征和IgG4相关性唾液腺炎可在免疫调节等病因治疗的同时,配合药物促进唾液分泌、降低唾液粘滞度等改善唾液性状,减少流动和排空阻力;慢性复发性腮腺炎与放射性腮腺炎则可通过内镜下灌注导管系统、内镜下放置支架以及配合术后按摩等手段进行治疗。流场和流体力学分析和阐明阻塞成因的研究成果,为非特异性腮腺阻塞的治疗提供了新思路:将腮腺看成一个微型流场,着眼在减少唾液流动的阻力的发生,如内镜下扩张导管或者放置支架可以解除导管系统的狭窄,增大管径;选择性栓塞过多的侧支导管可以减少导管内的低速区或高压区,避免涡流或湍流的发生,维持唾液的正常流动和排空,解除引起腺体肿胀症状的病因。

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