

单侧声带麻痹为首发症状的甲状旁腺腺瘤 1 例并文献复习

王婷玉^{1,2}, 吕正华^{1,2}, 韩茜茜³, 孙臻³, 张海燕^{1,3}, 徐伟^{1,2,3}

1. 山东大学 齐鲁医学院, 山东 济南 250012
2. 山东省耳鼻喉医院 头颈外科, 山东 济南 250000
3. 山东省耳鼻喉医院 嗓音疾病科, 山东 济南 250000

摘要: **目的** 探讨以单侧声带麻痹为首发症状的甲状旁腺腺瘤 (parathyroid adenoma, PA) 的临床诊疗及预后, 为早期准确诊断及治疗提供依据。 **方法** 回顾性分析 1 例以单侧声带麻痹为首发症状的 PA 患者的临床资料, 并结合相关文献进行分析讨论。 **结果** 喉返神经损伤可由良性甲状旁腺腺瘤压迫引起, 而以单侧声带麻痹为首发症状的甲状旁腺腺瘤属实罕见且难以发现。当 PA 位于甲状腺背叶中下份并甲状腺下动脉分支入腺体的位置时, 喉返神经可被卡压在之间引起神经水肿, 导致声带麻痹。通过主客观嗓音评估及术前、术后喉肌电图证实, 准确的诊断与及时切除甲状旁腺腺瘤, 行喉返神经减压术可使神经功能及声带运动恢复正常。同时, 术后患者的甲状旁腺激素和血钙水平均可恢复正常。 **结论** PA 导致喉返神经功能异常较为少见, 因而当单侧声带麻痹为首发及唯一症状时, 易造成 PA 误诊或漏诊。单侧声带麻痹患者如发现甲状旁腺良性肿瘤, 尤其是肿瘤位于甲状腺背叶中下份并甲状腺下动脉分支入腺体位置时, 要考虑到良性肿瘤压迫喉返神经而使其功能受损的可能, 及时的手术切除并神经减压是最佳治疗方案。

关键词: 甲状旁腺腺瘤; 单侧声带麻痹; 嗓音评估; 喉返神经

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Unilateral vocal cord paralysis as the initial manifestation of parathyroid adenoma: a case report and literature review

WANG Tingyu^{1,2}, LÜ Zhenghua^{1,2}, HAN Qianqian³, SUN Zhen³, ZHANG Haiyan^{1,3}, XU Wei^{1,2,3}

1. Cheeloo College of Medicine, Shandong University, Jinan 250012, Shandong, China
2. Department of Head and Neck Surgery, Shandong Provincial ENT Hospital, Jinan 250000, Shandong, China
3. Department of Voice Center, Shandong Provincial ENT Hospital, Jinan 250000, Shandong, China

Abstract: Objective To investigate the clinical diagnosis, treatment, and prognosis of parathyroid adenoma (PA) with unilateral vocal cord paralysis as the first symptom and to facilitate accurate diagnosis and proper treatment. **Methods** The clinical data of one patient with unilateral vocal cord paralysis as the initial manifestation of PA were retrospectively analyzed, along with a review and discussion of the relevant literature. **Results** Recurrent laryngeal nerve injury can be caused by benign parathyroid adenoma compression. However, unilateral vocal cord paralysis as the initial and only manifestation of parathyroid adenoma is rare and difficult to detect. Parathyroid adenoma located in the middle-lower region of the dorsal thyroid lobe and the inferior thyroid artery may sandwich and pinch the recurrent laryngeal nerve, causing nerve swelling and, subsequently, vocal cord paralysis. Subjective and objective voice evaluation, in combination with laryngeal electromyography before and after the operation, revealed that accurate diagnosis, timely PA resection, and decompression of the recurrent laryngeal nerve can rescue nerve function and vocal cord movement. Additionally, these interventions can revert patient parathyroid hormone and blood calcium levels to normal. **Conclusion** PA rarely damage the recurrent laryngeal nerve. When unilateral vocal cord paralysis is its first and only symptom, PA can be easily misdiagnosed or remain undiagnosed. In patients with unilateral vocal cord paralysis, if a benign parathyroid tumor is found, the possibility of benign tumor compression and recurrent laryngeal nerve dysfunction should be considered, especially if the tumor is located in the

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通信作者: 张海燕. E-mail: hyzhang_ent@126.com; 徐伟. E-mail: xuwhns@126.com

middle-lower region of the dorsal thyroid lobe, where the inferior thyroid artery branches into the gland. Timely surgical resection and nerve decompression are the best choices of treatment.

Key words: Parathyroid adenoma; Unilateral vocal cord paralysis; Acoustic analysis; Recurrent laryngeal nerve

甲状旁腺腺瘤起病隐匿^[1], 发病率较低, 早期多无特定的临床症状和表现, 临床不易被发现。通常其体积较小^[2], 较难引起局部压迫的症状, 而引起声带麻痹的病例十分罕见。声带麻痹的病因复杂, 其中, 颈部占位性病变导致喉返或迷走神经功能异常多以甲状腺恶性肿瘤侵犯为主^[3-5], 良性肿瘤可因囊性变、内出血等原因对喉返神经造成机械压迫, 导致神经水肿, 从而出现声带运动不良, 但较为少见^[6-7]。本例甲状旁腺腺瘤患者无典型的甲状旁腺功能亢进的症状, 而是以单侧声带麻痹为首发和唯一症状。现回顾性分析该患者临床资料并复习相关文献, 探索甲状旁腺腺瘤与声带麻痹的关系, 为声带麻痹的病因学研究及甲状旁腺腺瘤诊疗提供新的思路。

1 资料与方法

1.1 一般资料

患者男, 50 岁, 2019 年 9 月 16 日因“声音嘶哑伴饮水呛咳 13 d”于山东省耳鼻喉医院嗓音疾病科就诊, 临床表现为声音嘶哑呈气息声, 伴有饮水呛咳及咳痰无力, 进食半流质、固体食物良好。从主、客观不同角度对嗓音质量进行评估。采用 GRBAS 分级对患者的嗓音质量进行主观评估, 其中 G (grade) 代表对嗓音异常的总体感知分级; R (roughness) 代表发音的不规则程度; B (breathiness) 代表气息声程度; A (asthenia) 代表发音无力程度; S (strain) 代表发音亢进程度。上述参数根据严重程度可分为 4 级: 0 正常; 1 轻度异常; 2 中度异常; 3 严重异常。采用嗓音障碍指数量表 (voice handicap index-10, VHI-10) 简化中文版对患者进行评分, VHI-10 可从功能、生理、情感 3 个方面量化嗓音疾病对患者生活质量的影响, 总分 40 分, 分值越高则患者嗓音质量越低。术前患者主观嗓音评估为 G3R2B3A2, VHI-10 评分为 37 分。采用嗓音声学分析软件 CSL4500 及设备 CSL model 4500 (KayPENTAX, 美国) 对患者的嗓音质量进行客观评估, 主要分析参数如下: 频率微扰 (Jitter)、振幅微扰 (Shimmer)、噪谱比 (noise to harmonic ratio, NHR)、最长发声时间 (maximum phonation time, MPT)。其中 Jitter、Shimmer 反映声带振动的稳定性, 数值越小则声带振动越稳定; NHR 反映噪声成分。术前患者 Jitter 为 11.19%, Shimmer 为 13.17%, NHR 为 0.462, MPT 为 2 s (表 1)。综上, 考虑该患者为中-重度声音嘶哑。临

床查体见软腭抬举良好, 伸舌不偏。动态喉镜检查发现双侧声带黏膜光滑, 右侧声带旁正中位固定, 左侧声带运动良好, 发音相呈梭形缝隙, 黏膜波明显减弱, 梨状窝分泌物潴留 (图 1)。喉肌电图检查示病变侧神经电位纤颤波及募集电位消失。患者既往糖尿病病史 5 年, 使用胰岛素治疗, 血糖控制欠佳。临床初步诊断为声带麻痹 (右, 原因待查); 2 型糖尿病。

1.2 方法

于我院完善检查, 甲状腺 B 超示甲状腺右侧叶后方见 1.8 cm×1.1 cm 低回声结节, 边界尚清, 内回声欠均, 提示甲状旁腺来源。随之进行颈部和胸部强化 CT 检查进一步明确占位性病变的来源及与周围器官和血管的毗邻关系, 结果示甲状腺右侧叶下份背侧见低密度结节, 与甲状腺分界不清, 病变向后突入右侧气管食管沟, 增强扫描呈明显强化 (图 2), 考虑甲状旁腺占位。进一步实验室检查示钙离子 2.92 mmol/L (正常范围 2.0~2.75 mmol/L), 甲状旁腺激素 72.73 pg/mL (正常范围 12.0~88.0 pg/mL), 血糖 19.1 mmol/L, 糖化血红蛋白 9.1%。颅底 MRI 及其余实验室检查未发现异常。综合以上检查考虑右侧甲状旁腺肿瘤致右侧喉返神经功能异常可能性大, 同时, 血钙升高, 甲状旁腺激素位于正常高值, 符合功能性甲状旁腺腺瘤临床特征, 因此, 需手术切除右侧甲状旁腺肿物并行右喉返神经探查术。调整胰岛素用量使空腹血糖和餐后 2 h 血糖分别降为 6~8 mmol/L 和 7~9 mmol/L, 后于 2019 年 9 月 29 日收入院于全麻下行右侧甲状旁腺肿物切除术+右喉返神经探查术, 术中发现右侧甲状腺下极背侧质韧肿物 (图 3), 约 2.0 cm×1.5 cm, 包膜完整, 向后压迫喉返神经, 与之关系密切。喉返神经卡压于甲状旁腺腺瘤与甲状腺下动脉之间, 明显肿胀, 无明显肿瘤侵犯表现。完整分离喉返神经并切除甲状旁腺腺瘤, 未见瘤体内出血改变。术中冰冻及术后常规病理 (图 4) 均提示为右侧甲状旁腺腺瘤, 并于术后 20 min 测定甲状旁腺激素 (15.23 pg/mL)。

2 结果

术后第 1 天复查血钙 (2.45 mmol/L) 及甲状旁腺激素 (9.34 pg/mL), 患者无手麻等低钙症状, 因此暂时不需要补充钙剂治疗, 继续监测甲状旁腺激素及血钙。术后 5 d, 患者颈部术区恢复良好, 动态喉镜检查可见右侧声带固定, 紧张度较前改善, 发音相梭形缝隙明显缩小, 梨状窝无分泌物潴留 (图 1),

患者自诉发声疲劳感减轻, VHI-10 量表评分为 30 分, 嗓音主观评估 G2R1B2A2。术后 36 d, 动态喉镜检查示右侧声带出现内收和外展运动的恢复, 双声带运动幅度对称, 右侧声带运动速度及黏膜波较左侧稍差, 发音相闭合可(图 1E、F); 嗓音主、客观评估较术前明显改善(表 1), 复查血钙 2.46 mmol/L, 甲状旁腺激素 35.64 pg/mL。术后 43 d, 电话随访, 患者自我感知音质恢复至既往正常水平。术后 49 d, 动态喉镜示右侧声带形态正常, 弓形改变

消失, 双声带活动好, 黏膜波对称、规律, 发音时声门闭合良好(图 1G、H), 喉肌电图示右侧甲杓肌、环甲肌及环杓后肌运动电位募集正常, 呈干扰相。主、客观嗓音评估音质正常(表 1), 复查血钙 2.49 mmol/L, 甲状旁腺激素 37.20 pg/mL。患者术后 3 年于我院复查, 此时音质正常, 喉镜检查示双侧声带活动好, 振动对称、规律, 发音时声门闭合良好, 颈部 B 超未见 PA 复发, 血钙及甲状旁腺激素均在正常范围内。

表 1 术前、术后主客观嗓音评估

Table 1 Subjective and objective acoustic analysis before and after surgery

评估参数	主观嗓音评估				VHI	客观嗓音评估			
	G	R	B	A		Jitter/%	Shimmer/%	NHR	MPT/s
术前	3	2	3	2	37	11.19	13.17	0.462	2
术后 36 d	1	1	0	1	10	1.09	5.11	0.102	10
术后 49 d	0	0	0	0	0	0.84	2.49	0.127	16

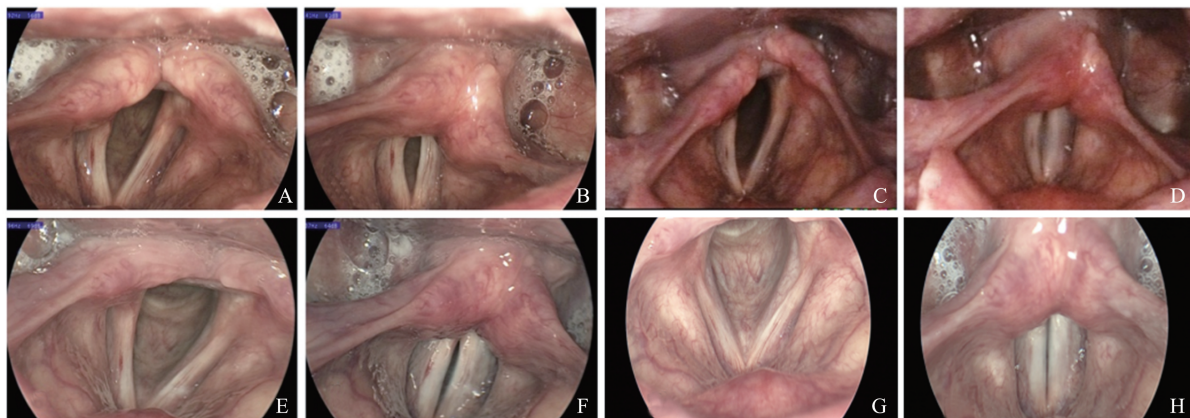


图 1 右声带动态喉镜检查

A: 术前呼吸相; B: 术前发音相; C: 术后 5 d 呼吸相; D: 术后 5 d 发音相; E: 术后 36 d 呼吸相; F: 术后 36 d 发音相; G: 术后 49 d 呼吸相; H: 术后 49 d 发音相

Figure 1 Video laryngostroboscopy of the right vocal cord

A: Preoperative respiratory phase; B: Preoperative phonation phase; C: Respiratory phase at 5 days after surgery; D: Phonation phase at 5 days after surgery; E: Respiratory phase at 36 days after surgery; F: Phonation phase at 36 days after surgery; G: Respiratory phase at 49 days after surgery; H: phonation phase at 49 days after surgery

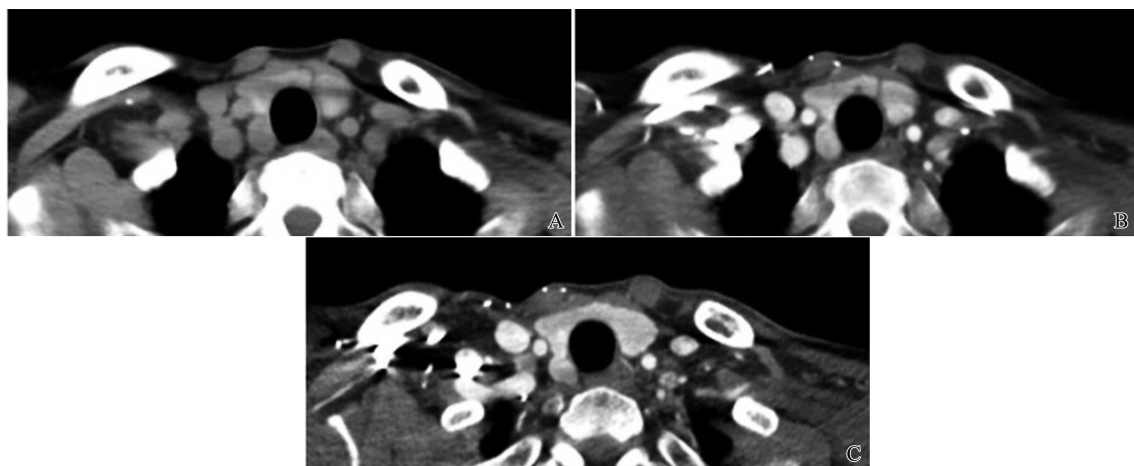


图 2 颈部强化 CT 表现(A-C)

Figure 2 Enhanced CT of the neck findings(A-C)

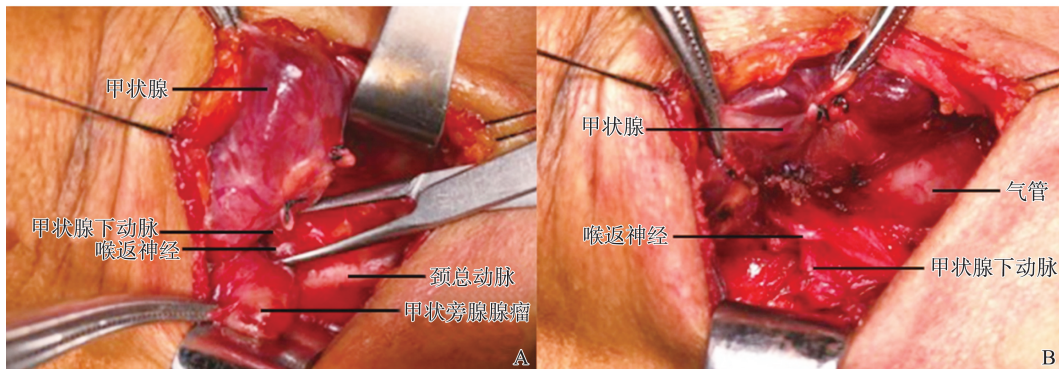


图 3 术中表现(A-B)
Figure 3 Intraoperative manifestation(A-B)

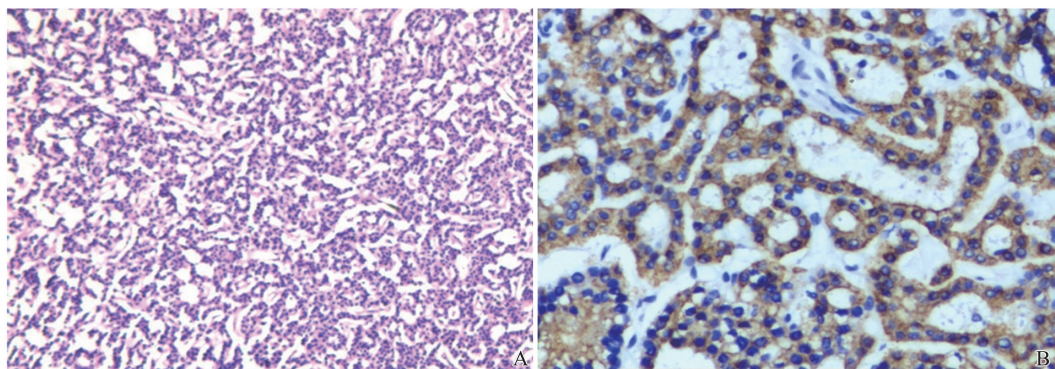


图 4 术后病理表现
A: 肿瘤细胞排列呈腺泡状、小梁状, 细胞大小较一致, 胞浆丰富、颗粒状, 部分胞浆嗜酸, 细胞核呈圆形(40×); B: 免疫组化标记肿瘤细胞甲状旁腺素弥漫强阳性(100×)

Figure 4 Postoperative pathological findings
A: Under low magnification, the tumor cells are arranged in acinar- and trabecular-like patterns, with round nuclei, uniform size, and abundant cytoplasm containing eosinophilic and partially eosinophilic granules (40×); B: Immunohistochemical labeling of tumor cells reveals diffuse and strongly positive staining for PTH under high magnification (100×)

3 讨论

甲状旁腺腺瘤患者多以甲状旁腺功能亢进的临床症状,即高钙血症引起的临床症候群于医院就诊^[8],本例甲状旁腺腺瘤患者以单侧声带麻痹为唯一的临床症状,具有特殊性及罕见性。诸多研究表明,导致喉返或迷走神经功能异常的甲状腺或甲状旁腺占位性病变多以恶性病变侵犯为主^[9-14],因此,喉返或迷走神经的功能异常通常被认为是恶性病变侵犯所致,易导致对甲状旁腺良性肿瘤的漏诊或误诊。Kamali 等^[15]曾报道 1 例首发并唯一症状为声带麻痹的无功能甲状旁腺占位,长径为 23 mm,因喉返神经功能出现异常,而误诊为恶性侵犯,遂切除左侧甲状腺、甲状旁腺及喉返神经,而术后病理示甲状旁腺腺瘤,证实为机械压迫致喉返神经功能异常。

既往关于甲状旁腺腺瘤引起声带麻痹的发病机制主要包括以下 3 种情况:甲状旁腺腺瘤内自发性内出血;甲状旁腺腺瘤内脓肿;位于迷走神经

鞘内的异位甲状旁腺腺瘤。甲状旁腺腺瘤可因自发性内出血导致肿瘤迅速肿大,从而压迫喉返神经,表现为突发性声带麻痹^[16-17]。Angelos 等^[18]报告了 1 例甲状旁腺腺瘤内脓肿的病例,考虑炎症引起喉返神经功能障碍。位于迷走神经鞘内的甲状旁腺腺瘤,可直接压迫迷走神经导致功能异常而出现暂时性声带麻痹,以往文献报道 14 例患者中有 4 例出现暂时性声带麻痹,1 例声带运动度最终未恢复^[19-21]。以往研究发现甲状腺良性结节致喉返神经麻痹的患者,结节往往位于甲状腺深叶尤其是背部下份,该位置是甲状腺下动脉分支入腺体的位置,若出现囊性变或出血,喉返神经走行于此夹角部位易受卡压,从而引起声带运动障碍^[20-24]。而本文所报道的 1 例由甲状旁腺腺瘤压迫同侧喉返神经致声带麻痹的病例具有一定的特殊性:①患者以单侧声带麻痹为首发症状就诊,术前并无甲状旁腺功能亢进及高钙血症引起的一系列临床表现,实验室血清钙水平升高,甲状旁腺激素水平在正常范围内的高值水平;②未发现甲状

旁腺腺瘤内出血或脓肿,而是由于瘤体位于喉返神经易受卡压的特殊位置,最终导致喉返神经水肿而出现同侧声带麻痹;③声带麻痹病程较短,及时的肿瘤切除并保护喉返神经使得声带运动度得以恢复。

3.1 甲状旁腺腺瘤导致声带麻痹的特殊性及发病机制

喉返神经或迷走神经损伤引起声带麻痹的病因复杂^[2,6,22,25],需通过详细的影像学及实验室检查进行排查,因颈部或甲状腺因素所致声带麻痹较常见,因此,可首先进行甲状腺及颈部超声检查。本例患者首先给予甲状腺及颈部 B 超检查,发现甲状旁腺结节,随之行颈部和胸部强化 CT 进一步了解肿物位置及与喉返神经走行区域的关系,发现占位性病变位于甲状腺背部下份,向后明显突入气管食管沟处。甲状旁腺腺瘤典型的实验室检查结果为甲状旁腺激素和血钙水平的明显升高^[26],研究表明血清钙水平升高及甲状旁腺激素水平在正常范围内的高值水平亦作为原发性甲状旁腺功能亢进的表现^[27],至少 10% 的经手术证实的原发性甲旁亢患者血清甲状旁腺激素水平位于正常高值^[28],本研究中患者表现出血钙轻度升高、甲状旁腺激素水平位于正常高值,使得患者术前并无高钙血症引起的一系列临床表现而导致病变隐匿,未以甲状旁腺功能亢进症状被发现。然而,由于腺瘤的特殊位置(即甲状腺下动脉分支入腺体的位置),喉返神经走行于此夹角部位易受卡压^[23-24,29-30],最终使患者以声带麻痹为首发和唯一症状就诊。综合考虑本例患者为功能性甲状旁腺占位致喉返神经功能异常可能性大,尽早手术切除甲状旁腺占位性病变并喉返神经探查术为首选,术中证实喉返神经位于甲状腺下动脉与甲状旁腺腺瘤之间,喉返神经受到卡压致其明显肿胀、充血,切除肿瘤的同时探查并完整分离喉返神经。

研究显示单侧功能性甲状旁腺腺瘤切除术后血清钙离子与甲状旁腺激素即刻下降,随访发现术后 6 个月内甲状旁腺激素及血清钙水平均可恢复正常^[16,31-33]。该例患者术后 20 min 甲状旁腺激素从术前 72.73 pg/mL 降至 15.23 pg/mL,术后第 1 天出现暂时性甲状旁腺激素下降,术后 36 d 时恢复至正常水平,经随访甲状旁腺激素及血钙均在正常值范围,与既往文献报道相符,并且,早期发现并及时切除功能性甲状旁腺腺瘤避免了可能会出现严重甲状旁腺功能亢进症状。

3.2 及时的甲状旁腺腺瘤切除并喉返神经减压可

使神经功能恢复

既往报道证实致喉返神经麻痹的甲状腺良性结节往往是甲状腺深叶结节囊性变或出血对喉返神经的急性压迫,从而引起声带运动障碍,良性甲状腺结节切除后可使声带运动度恢复,甲状腺良性结节致喉返神经麻痹减压术后 2 个月内神经功能可恢复^[25,29-30,34]。本例患者于症状出现后的第 26 天时进行了甲状旁腺占位切除和喉返神经减压,术中明确为甲状旁腺腺瘤压迫导致喉返神经水肿而出现单侧声带麻痹,术后通过主、客观嗓音分析及喉镜检查密切观察神经功能恢复情况,自术后第 5 天神经功能开始恢复,术后 49 d 通过嗓音评估、喉镜检查及喉肌电图证实喉返神经功能完全恢复,通过 3 年的随访,患者的嗓音功能恢复正常,以上结果表明及时的甲状旁腺腺瘤切除并喉返神经减压,可使喉返神经功能恢复正常,在解决患者甲状旁腺腺瘤器质性病变的基础上,还恢复了患者的嗓音功能,取得了满意的临床疗效。

4 小 结

综上所述,甲状旁腺腺瘤可导致喉返神经水肿,从而出现声带麻痹。因此,在单侧声带麻痹病因诊断过程中,若发现甲状旁腺占位性病变,尤其是占位位于甲状腺背叶中下份,甲状腺下动脉分支入腺体或结节的位置,纵然占位体积较小,也需要根据该位置解剖结构的紧密性及特殊性,考虑良性肿瘤压迫喉返神经而使其功能受损的可能,及时的手术切除并神经减压是最佳治疗方案,术后可使神经功能恢复,该例甲状旁腺腺瘤患者以单侧声带麻痹为首发症状,通过早期识别和干预,在解决器质性病变的同时恢复了患者的嗓音功能,对声带麻痹病因的诊断及手术决策的制定具有重要的参考意义。

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