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家族性三叉神经痛*

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摘要: 三叉神经痛是一种临床常见疾病,典型的三叉神经痛主要表现为阵发性、闪电样的疼痛发作,疼痛剧烈,常无法忍受,呈电灼、针刺、撕裂样,每次发作持续时间数秒至数分钟不等。疼痛多发生于单侧,常有扳机点表现,其多表现为散发,而家族性三叉神经痛报道罕见,至今世界范围内报道仅 50 余个家系,其临床表现及发病特点与散发性三叉神经痛存在明显差别,尽管散发三叉神经痛患者的病因为责任血管压迫三叉神经 REZ 区已被普遍接受,但关于家族性三叉神经痛的病因是否为血管压迫存在争议,其遗传模式也没有达成一致的意見,文章复习了相关文献,并通过对这些文献进行分析综合,结合我们治疗三叉神经痛的经验,对其病因、发病机制、诊断和治疗原则、遗传模式等作了系统综述。

关键词: 家族性三叉神经痛;遗传模式;病因;发病机制;治疗

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Familial Trigeminal Neuralgia*

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ABSTRACT: Trigeminal neuralgia is a common disorder characterized by unilateral, paroxysmal, and shock-like facial pain attacks lasting a few seconds with remissions and recurrences, often triggered by sensory stimulation. However, familial trigeminal neuralgia is rare, until now, only about 50 families were reported in the literature. There are distinct differences in clinical manifestations and characteristics between familial and sporadic trigeminal neuralgia patients. The mechanism and inheritance pattern of the disease has not been understood by now. In this paper, with the literature reviewed, we analyzed familial trigeminal neuralgia comprehensively in aspects of etiology, mechanism, and inheritance pattern as well as treatment.

Key words: Familial trigeminal neuralgia; Inheritance pattern; Etiology; Mechanism; Treatment

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引言

三叉神经痛是指发生于三叉神经所支配区域的神经病理性疼痛。典型的三叉神经痛主要表现为阵发性、短暂的疼痛发作,疼痛严重,常无法忍受,呈电灼、针刺、撕裂样,每次发作持续时间数秒至数分钟不等。疼痛多发生于单侧,常有扳机点表现,洗脸、刷牙、说话、剃须等可诱发^[1]。其通常发生于中老年人,目前认为三叉神经痛主要由于随年龄增大,高血压、动脉粥样硬化等疾病导致血管扭曲而形成血管袢压迫三叉神经所致^[2]。三叉神经痛一般为散发,但在文献中可见家族性三叉神经痛的报道,在世界范围内至今为止已有 50 余个家系报道,但一般为个案报道,其遗传特性不明,其临床特点、与散发性三叉神经痛的鉴别及病因是否不同等尚待研究,本文综述家族性三叉神经痛的家系报道,并对其临床发病特点、诊断、遗传特性及治疗等进行讨论。

1 流行病学及临床特点

三叉神经痛是一种常见的颅神经疾病,目前为止其发病率

缺乏确切流行病学的统计数据支持,现有的统计数据认为患病率约为 10-20/100,000,其多发于老年人,60 岁之后的老年人发病率约为每年 4-5/100 000-20/100 000。其多发于女性,男女之比为 2:3^[3],疼痛多发于右侧^[4],家族性三叉神经痛最早的报道见于上世纪初,1914 年 Patrick^[5]首次报道 8 例家族性三叉神经痛患者,其后世界各地均有报道,据报道其发病率约占三叉神经痛的 1-2%^[6]。其发病时临床表现与散发的三叉神经痛患者相比,有不同特点。首先一般家族性三叉神经痛患者的疼痛常发生在同一神经分支分布区,多数位于右侧。其首次发病时间早于单发三叉神经痛患者,单发三叉神经痛一般 60 岁左右为发病高峰期^[3],而家族性三叉神经痛患者明显较早,根据附表中统计的数据,其发病初次年龄在 40 岁最多,Braga FM^[7]等报道其发病年龄在 30 岁左右,而且其岁后代延续,发病年龄逐步提前的趋势,1914 年 Harris W^[8]就曾指出其在家族中呈现随着遗传后代延续,其发病年龄逐步提前,其报道的一个家族中,外祖母发病年龄 43 岁,母亲与姨妈则 40 岁与 32 岁,而第三代首发年龄未 16 与 17 岁。这在多个学者的报道中得到证实^[9-11],在家族性三叉神经痛患者中,双侧三叉神经痛发病率比单发病例高^[8]

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^[10]。同时在家族性三叉神经痛患者中,患者可并发其他疾病,如 CMT 即遗传性运动和感觉神经性疾病^[11],而且在文献中有数个此类报道,尽管其具体关系尚不明确,但可能两者可能相关性^[12]。

2 发病机制

关于三叉神经痛病因的研究始于上世纪,1934 年 Dandy^[13]首次提出三叉神经痛由血管压迫所引起,其后 Jannetta P^[14]等采用微血管减压术治疗面肌痉挛及三叉神经痛获得显著成效,但血管压迫三叉神经导致三叉神经痛的具体病因不明,其病因自发现以来就备受争论,而且文献中报道有患者未发现血管压迫三叉神经,而其他病因如血管畸形^[15]、肿瘤^[16,17]、蛛网膜囊肿^[18]等也可引起三叉神经痛。对于家族性三叉神经痛病因的研究更少,因家族性三叉神经痛患者与散发患者临床特点等存在一定差异,所以其病因也尚不明确,多数学者在文献中报道发现血管压迫^[9,19],但也有未发现异常的情况^[11,20],且根据三叉神经痛的发病原因,一般由于患者的年龄增大,从而导致血管扭曲,压迫三叉神经根部导致,但家族性三叉神经痛患者的发病年龄普遍较年轻,甚至很多家系的患者少年就发病,有些患者甚至并发其他疾病^[11]。

目前关于家族性三叉神经痛的病因主要两种观点,一种观点认为其由于血管压迫导致,不管其发病年龄,根据我们整个统计数据来看,确实大部分患者,尤其是近年来随着影像学的发展,头颅 MRI 的广泛引用及微血管减压术的推广,发现血管

压迫患者的概率大大增加。据此推断:与散发患者相同,家族性三叉神经痛患者也是由于血管压迫三叉神经引起。但目前为止没有关于血管压迫类型的统计,在家族性面肌痉挛患者中,有椎动脉扭曲变异导致压迫的报道^[21],但没有关于家族性三叉神经痛患者血管变异类型的报道。后颅窝的畸形被认为是另一种可能的原因,但缺乏相关证据。

我们的观点认为家族性三叉神经痛与单发患者的病因相同,都是由于血管压迫引起,但不排除后颅窝畸形及其它后颅窝占位也可引起本病,不过决定家族性三叉神经痛的遗传因素可能是前者。

3 治疗方案

对于其治疗,在明确病因后,我们认为其治疗原则与散发三叉神经痛患者相似,首先建议采用卡马西平等药物治疗,在药物无法控制情况下,患者可耐受手术情况下,可采取微血管减压术进行治疗,在青少年患者^[22]及老年患者中^[23]都发现微血管减压术疗效显著及随访复发概率小。对于部分老年患者及身体状况差的患者,若无法耐受手术,可采用射频治疗。

4 遗传模式

根据我们的统计,其显著呈现常染色体显性遗传的特点,表明家族性三叉神经痛是一种常染色体显性遗传病,既然现在已经确定家族性三叉神经痛是一种显性遗传,但其呈现家族性

表 1 家族性三叉神经痛病例报道汇总

Table 1 Summary of familial trigeminal neuralgia cases in the literature

Year	Author	Family	Age at onset/year	Family tree	Etiology	Pathogenesis	Treatment
1936	Harris W ^[18]	10	< 40	1GM,2 DA, 1 GD in a family; other 9 families were N/A	N/A	N/A	Alcohol injection of trigeminal ganglion
1940	Harris W ^[6]	30	N/A	STG	N/A	N/A	Alcohol injection of trigeminal ganglion
1981	Testa D ^[11]	1	< 40	1FA, 1SO, 1DA	CMT	N/A	Trigeminal rhizotomy
1982	Bracale C ^[24]	1	53	2 SI	NC	NC	MVD
1985	DiCorato MP ^[10]	1	< 50	1GM, 1DA, 1 GS	N/A	N/A	Carbamazepine
1986	Braga FM ^[7]	1	24-31	2BR, 2SI	N/A	N/A	Trigeminal rhizotomy
1989	KirkpatrickDB ^[25]	1	Early middle age	1AU, 3NI	N/A	N/A	N/A
1991	Coffey RJ ^[12]	2	-	-	CMT	Demyelination of trigeminal nerve	blockage of Semilunar ganglion
1999	Duff JM ^[26]	1	-	1 MO 1DA 1NI	N/A	N/A	N/A
2001	Fleetwood IG ^[27]	1	-	-	-	-	Trigeminal rhizotomy
2003	Smyth P ^[9]	1	36.5	1GF 2DAs 1GD	N/A	NC	MVD
2007	Savica R ^[20]	1	66.5	1FA 1SO 1DA 1NW	normal	N/A	Carbamazepine
2008	El Otmani H ^[28]	1	-	STG		NC	Carbamazepine
2010	Ebner FH ^[19]	1	< 40	1MO 2DAs 1SO	Compression by SCA	NC	MVD

STG: successive three generations(连续三代); GF: grandfather(祖父 / 外祖父); GA: grandmother(祖母 / 外祖母); FA: father(父亲); MO: mother(母亲); AU: aunt(姑妈 / 姨妈); DA: daughter(女儿); NW: nephew(侄子); NI: niece(侄女); SI: sister(姐妹); GD: granddaughter(孙女 / 外孙女); BR: Brother(哥 / 弟); SO: son(儿子); MVD: microvascular decompression(微血管减压术); CMT: Charcot-Marie-Tooth disease(进行性神经性肌萎缩); SCA: superior cerebellar artery(小脑上动脉); NC: neurovascular conflict(血管神经冲突); N/A: not available (未获得)。

的决定性因素是什么呢? 是什么基因的异常导致家族性三叉神经痛的发病呢,不少患者进行了研究,有作者认为既然家族性三叉神经痛的发病原因与血管扭曲异常有很大关系,因而有学者找寻与血管变异类疾病有关基因并比较其与家族性三叉神经痛患者相关性,未发现其必然的联系。还有学者通过对同时患有家族性三叉神经痛及 CMT 的患者进行研究后提出是一种同时作用于中枢神经系统与周围神经的异常所致^[12],但也为发现相关的异常分子。

5 小结与展望

家族性三叉神经痛临床特点与散发患者不同,但大部分仍由血管压迫三叉神经引起,目前已普遍被认为是常染色体显性遗传病,但其具体遗传变异基因尚未发现。其治疗与散发三叉神经痛患者相似,在药物无法控制疼痛时,推荐应用 MVD 治疗。

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