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眼眶丛状神经纤维瘤合并腹膜后神经纤维瘤1例报告并文献复习

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摘　要

目的：探讨眼眶丛状神经纤维瘤的临床特征，以加深对该肿瘤的认识。方法：回顾性分析1例眼眶丛状神经纤维瘤患者的临床资料，并结合国内外文献进行复习探讨。结果：患者以发现左眼眼球突出2年为主要临床表现，眼科联合神经外科经颅开眶行眶内及颅内肿瘤切除术，术后病理学检查示肿瘤细胞排列松散，呈纺锤样，组织可见丰富小血管及绳索样的粗大神经，神经纤维束呈波浪状排列。免疫组化染色示S-100阳性、SOX10弱阳性，不表达SMA、EMA、CD34。随访1个月未见肿瘤复发、转移。结论：眼眶丛状神经纤维瘤临床较罕见，具有独特的病理学特征，手术治疗疗效确切。

关键词

丛状神经纤维瘤，眼眶肿瘤，免疫组织化学，诊断，病例报告

A Case Report and Literature Review of Orbital Plexiform Neurofibroma Complicated with Retroperitoneal Neurofibroma

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Abstract

Objective: To investigate the clinical features of plexiform neurofibroma (PNF) to improve understanding. Methods: The clinical data of a patient with orbital plexiform neurofibroma were retrospectively described, reviewed and discussed with domestic and international literature. Results: The patient presented with eye tubercle for 2 years as a main clinical manifestation. Ophthalmology combined with neurosurgery performed transcranial orbital and intracranial tumor resection. The tumor cells were loosely arranged and spindle-like, with abundant small blood vessels and rope-like thick nerves visible in the tissues. The nerve fiber bundles were arranged in a wavy pattern. Immunohistochemistry showed that the tumor cells were positive for S-100, weakly positive for SOX10, and didn't express SMA, EMA, CD34. No tumor recurrence or metastasis was observed in the 1-month follow-up after surgery. Conclusion: Orbital plexiform neurofibroma is rare clinically, and has unique clinical pathology features. The efficacy of surgical excision is definite.

Keywords

Plexiform Neurofibroma (PNF), Orbital Tumors, Immunohistochemistry, Diagnosis, Case Report

1. 引言

神经纤维瘤(Neurofibroma)是一种起源于周围神经的良性肿瘤，由神经鞘细胞及成纤维细胞两种主要成分组成，可以表现为孤立性病变，也可作为全身神经纤维瘤病(neurofibromatosis)的一部分[1]，临床上将其分为三型：局限型、丛状型、弥漫型，与局限型相比，丛状和弥散型神经纤维瘤更常见于眼眶和眼睑[2]。丛状神经纤维瘤(plexiform neurofibroma, PNF)常见于神经纤维瘤病 I 型(NF-1)患者，眶内单发者少见[3] [4]。本文报道 1 例眼眶丛状神经纤维瘤合并腹膜后神经纤维瘤患者，并结合相关文献探讨其临床特征，旨在提高临床对该肿瘤的认识和诊断能力。

2. 临床资料

患者男性，71 岁，因“发现左眼眼球突出 2 年”于眼科门诊就诊。追溯患者病史，患者诉 2 年前无明显诱因出现左眼眼球突出，伴视力障碍及左侧上睑下垂，无虹膜性状及颜色改变，无疼痛、畏光、流泪等不适，无恶心呕吐，无言语障碍及面部麻木，1 年前在当地医院诊断为“脑膜瘤”，未予诊治，眼突症状逐渐加重遂来我院就诊。患者既往无自身免疫病及肿瘤病史，40 年前行鼻息肉切除手术。

眼科检查：视力：右眼 0.8，矫正 1.0，左眼 0.2，矫正 1.0；眼压：右眼 15 mmHg，左眼 20 mmHg；左眶压增高，左眼向前下突出，眶上壁内侧可触及弥漫生长肿物 10 × 5 × 4 mm，质韧，边界不清，无明显触压痛。上睑遮盖角膜约 5 mm (见图 1)；左眼角膜透明，前房深度正常，房水清，瞳孔圆，对光反应正常，晶体不均匀混浊，眼底未见明显异常。眼球运动：上转部分受限，余各方向尚可。眼突度检查：右眼 13 mm，左眼 23 mm，眶距 100 mm。全身皮肤及黏膜未见牛奶咖啡斑。眼部 B 超(见图 2)：左眼眶

内占位性病变。眼眶 CT (见图 3)：左侧蝶骨体、翼腭窝、海绵窦区占位性病变并骨质改变。眼眶 MRI (见图 4)：左侧眶内、翼腭窝、海绵窦见多发病变。

Figure 1. The patient's facial appearance: Left eyeball was protruding and the left upper lid was drooping, covering the cornea by approximately 5 mm
图 1. 患者面部外观：左眼球突出，左上睑下垂，遮盖角膜约 5 mm

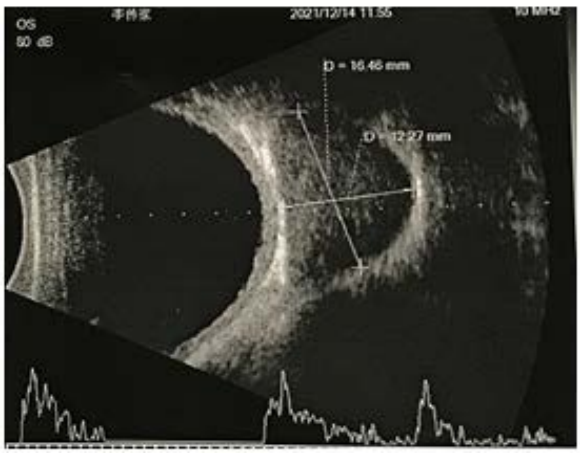

Figure 2. Ocular B-ultrasonography: An intraorbital occupying lesion in the left eye. A hypoechoic dark area with a size of about 17 × 13 mm was seen in the left superior medial orbit, with clear borders and relatively uniform internal echogenicity and signs of compression (−)
图 2. 眼部 B 超提示：左眼眶内占位性病变。左眼眶上内侧可见一低回声暗区，大小约 17 × 13 mm，边界清，内回声较均匀，压缩征象(−)

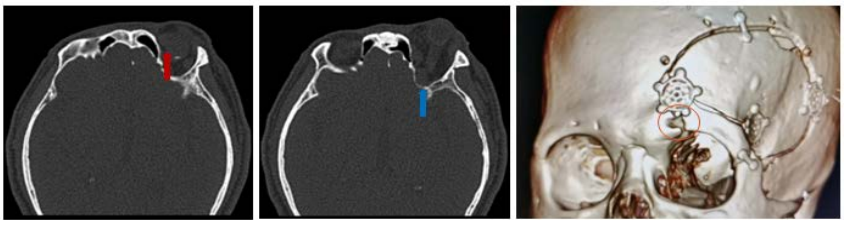

Figure 3. Orbital CT: Left superior rectus nodule with ophthalmic prominence (red arrow); left pterygoid body, pterygopalatine fossa, and cavernous sinus area with occupying lesions and bony changes (blue arrow); left supraorbital fissure enlarged (red circle), left supraocular vein tortuous
图 3. 眼眶 CT：左侧上直肌上方结节并眼球突(红色箭头)；左侧蝶骨体、翼腭窝、海绵窦区占位性病变并骨质改变(蓝色箭头)；左侧眶上裂扩大(红色圆圈)，左侧眼上静脉迂曲

考虑神经源性肿瘤，于全麻下经颅开眶，行眶内及颅内肿瘤切除术，术中见三处(额部皮下、眶内、海绵窦)多量肿瘤组织沿神经孔道行走，摘除标本送检病理(图 5)，诊断为左眼眶内多发丛状神经纤维瘤。

免疫组化染色示肿瘤细胞表达 S-100，SOX10 弱阳性，不表达 SMA、EMA、CD34。术后第 3 天眼科检查：视力左眼 0.2，眼压 Tn，左眼上转稍受限，眼突度：右眼 13 mm，左眼 17 mm。影像学检查显示眼眶内未见肿瘤组织残留。

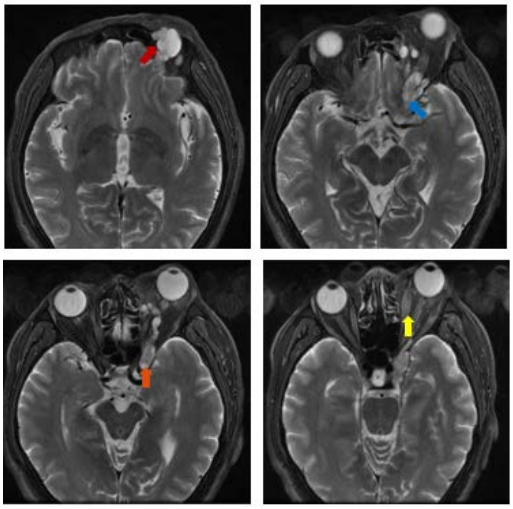

Figure 4. Orbital MRI: Multiple lesions are seen in the left intraorbital (red arrow), pterygopalatine fossa (blue arrow) and cavernous sinus (orange arrow), along the neuroforaminal tract, adjacent bone compression and resorption, thickening of the left extraocular muscle (yellow arrow)
图 4. 眼眶 MRI：左侧眶内(红色箭头)、翼腭窝(蓝色箭头)、海绵窦(橘色箭头)见多发病变，沿神经孔道走行，邻近骨质压迫吸收，左眼眼外肌增粗(黄色箭头)

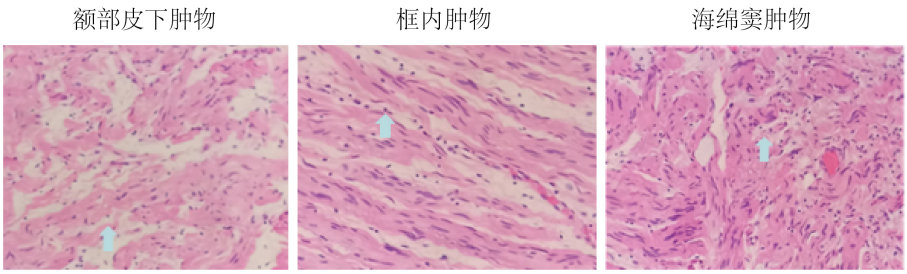

Figure 5. Pathological examination results: The microscopic structures of the 3 specimens were identical, with nodular growth of proliferating spindle-shaped nerve fibers, long, slender spindle-shaped tumor cells, loosely arranged cells, rod-shaped, slender and wavy twisted nuclei (blue arrow), and lightly stained chromatin (HE×200)
图 5. 患者组织病理学检查结果：3 处标本镜下结构相同，增生的梭形神经纤维呈结节状生长，瘤细胞呈纤细的长梭形，细胞疏松排列，细胞核呈杆状，纤细并呈波浪状扭曲(蓝箭头)，染色质淡染(HE×200)

3. 讨论

丛状神经纤维瘤是末梢神经肿瘤，具有遗传性[5]，好发于青、中年人，新生儿或幼儿期即可出现，生长缓慢，病程可达十余年。52%~53%的 PNF 发生于头颈部，多位单侧，肿瘤以“网状模式”生长，最常累及三叉神经、舌咽神经及舌下神经[6]。本例患者无家族史，全身检查未见异常，以慢性进展性眼球突出为主要症状，视力未受累、不伴眼痛。门诊行激素治疗无效。眼部 B 超提示左眼眶内占位性病变，

但由于其局限性，不能扫描到眶内肿物部分，不具有代表性。眼眶 CT 及 MRI 示左侧眶内、翼腭窝、海绵窦区多发性病变，沿神经孔道走行，伴骨质吸收。综合以上资料，初步诊断为神经源性肿瘤：神经纤维瘤或神经鞘瘤。

我们报道的是一例眼眶原发孤立性神经纤维瘤病例，而多数丛状神经纤维瘤病例与 1 型神经纤维瘤病(NF-1)有关，该病由德国病理学家 von Recklinghausen 于 1882 年首次报道，又称为 von Recklinghausen 病。这是一种常染色体显性神经皮肤综合征，临床表现多样，好发于皮肤、骨骼和神经系统[7] [8] [9]。目前临床常用的诊断标准为：1) 父母、同胞、子女中有 NF-1 患者；2) 全身皮肤牛奶咖啡斑数量 ≥6 个，成人咖啡斑直径 >15 mm，儿童需>5 mm；3) 腋窝或腹股沟区雀斑；4) 虹膜 Lisch 结节(错构瘤) ≥2 个；5) 视神经胶质瘤；6) 皮肤或皮下神经纤维瘤病灶 ≥2 个，或丛状神经纤维瘤 ≥1 个；7) 有骨发育不良，如蝶骨翼发育异常、骨皮质变薄和(或)假关节病。当存在以上≥2 项者，可诊断为 I 型神经纤维瘤病[10]。约 95%的 NF-1 患者 8 岁时即达到诊断标准，且在 20 岁之前符合全部标准[11]。NF-1 具有眼部特征性病变，其中一些表现，例如 Lisch 结节、视神经胶质瘤和丛状神经瘤，是 NF-1 的标志和诊断标准[12]。

丛状神经纤维瘤最常累及眼睑。早期即有肿块出现，随后眼睑下垂并肥大。肿瘤倾向于眼睑中外三分之一处，可扪及呈面团样和条索状肿物，类似一“囊袋蠕虫”结构。提上睑肌受累时，上睑下垂，睑裂呈“S”型[13]，或被遮盖。眼球突出，多向下移位。当眶骨缺损时会有搏动性突眼的表现[14]。眼外肌受累可出现眼球运动障碍及复视等。后期肿瘤可延伸至前额、太阳穴处，导致头颈部区域外观和功能畸形[15]。若伴有神经纤维瘤病，可有皮肤牛奶咖啡色斑、腋下雀斑、虹膜表面 Lisch 结节[16]等改变。本病例眼部表现较单纯，眼突为主要症状，余为继发表现，无特异性，根据临床表现不能确诊。

由于患者的临床表现和影像学检查无特异性，确诊主要依据术后组织病理学及免疫组化检查。目前文献报道丛状神经纤维瘤为分叶状、结节状的灰白或灰红色组织，质软，无明显包膜，多沿皮下脂肪间隙浸润性生长，与周围组织分界不清。若肿瘤累及整条神经干，可呈串珠状或条索状增粗。本病例病理学大体检查示肿瘤为多发病灶，额部皮下、眶内、海绵窦处肿瘤大小分别为 4 cm × 3 cm × 1.5 cm、4.5 cm × 3 cm × 1.5 cm、4.2 cm × 1.7 cm × 1 cm，切面分别呈灰白、灰黄、灰红色，质地韧，边界欠清；镜下见黏液样基质内有排列松散的纺锤样细胞，核呈杆状，组织可见丰富小血管及绳索样的粗大神经，神经纤维束呈波浪状排列。可以根据上述两项检查将神经鞘瘤和神经纤维瘤区分开。神经鞘瘤(neurilemoma)是由神经纤维周围的 Schwann 细胞增生形成的良性外周神经性肿瘤[17]，肿瘤具有完整包膜，由交替分布的束状区及网状区构成，结节周围厚神经鞘包绕，束状区可见施万细胞栅栏样排列，间质较少含有黏液。两者均表达 S-100，提示肿瘤起源于神经嵴。Schwann 细胞对 SOX10 呈阳性，而成纤维细胞和神经周围细胞则没有。本文患者 S-100 阳性、SOX10 弱阳性，不表达 SMA、EMA、CD34，提示本病例为神经纤维瘤，而非神经鞘瘤或平滑肌、上皮、血管源性肿瘤[18]，诊断明确。

对于良性神经源性肿瘤，包括神经鞘瘤和神经纤维瘤，放化疗不敏感，需早期手术切除，患者通常在切除后预后良好[19]。手术进路应根据影像学检查而定[20]。本例患者 CT 及 MRI 提示颅眶沟通良性肿瘤可能性大，选择全麻下经颅开眶，行眶内及颅内肿瘤切除术，整块彻底切除肿瘤。据报道，许多神经纤维瘤因其体积大、广泛浸润和血管丰富难以通过手术治疗[21]，这时外科医生可能仅会选择在肿瘤引起痛苦、神经功能缺陷或具有高度恶性潜能的情况下进行手术。手术切除始终为一线治疗，此外手术期间根据患者个体风险采取必要的预防措施也同样重要。术后我们的患者恢复良好，无并发症，随访无复发迹象。

4. 结论

综上所述，丛状神经纤维瘤是发病率较低的一种神经源性良性肿瘤，早期切除者预后较好。充分认识其临床、影像学检查、病理形态及免疫表型特征，对该病的临床诊断、治疗及预后评估具有重要价值。

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