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1例年轻患者视网膜分支静脉阻塞的10年随访

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[摘　要] 视网膜静脉阻塞(retinal vein occlusion，RVO)是发生率仅次于糖尿病性视网膜病变的视网膜血管病。RVO后导致视网膜血管损伤进而引起血管闭塞，造成视网膜缺血从而促进异常视网膜新生血管(retinal neovascularization，RNV)的增生，晚期发生玻璃体积血、新生血管性青光眼等并发症，积极治疗可以稳定患者的眼部情况，避免并发症的发生。本文报告了1例患有高血压病的23岁年轻女性患者发生视网膜分支静脉阻塞并发新生血管增殖膜的病例，给予病变区视网膜激光光凝治疗，10年后随访发现RNV膜机化萎缩。

[关键词] 视网膜分支静脉阻塞；视网膜新生血管；视网膜激光光凝；新生血管机化；年轻患者

A 10-year follow-up report of retinal branch vein occlusion in a young patient

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Abstract Retinal vein occlusion (RVO) is the second most common retinal vascular disease after diabetic retinopathy. Retinal vascular damage after RVO leads to venous occlusion, which further causes retinal ischemia and promotes abnormal retinal neovascularization (RNV). Later complications such as vitreous hemorrhage and neovascular glaucoma occur. Active treatment can stabilize the ocular condition of patients and avoid the occurrence of complications. This paper reports a case of a 23-year-old young female patient with hypertension who developed branch RVO complicated by neovascularization membrane. The lesion area was treated with laser photocoagulation. The RNV was found to be mechanized and atrophied after 10 years of follow-up.

Keywords retinal branch vein obstruction; retinal neovascularization; retinal laser photocoagulation; neovascularization mechanized; young patient

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视网膜静脉阻塞(retinal vein occlusion，RVO)是发生率仅次于糖尿病性视网膜病变的视网膜血管病[1]。按阻塞发生的部位不同，可以分为视网膜中央静脉阻塞与视网膜分支静脉阻塞，视网膜分支静脉阻塞多见于静脉第1~3分支的动静脉交叉处。其主要发病原因为动静脉交叉处增厚硬化的动脉壁对静脉的压迫，其次要原因为局部或全身炎症诱发。RVO后导致视网膜血管损伤进而引起血管闭塞，造成视网膜缺血从而促进异常视网膜新生血管(retinal neovascularization，RNV)的增生[2]，晚期发生玻璃体积血、新生血管性青光眼等并发症，积极治疗可以稳定患者的眼部情况，避免并发症的发生。本文报告了1例患有高血压病的23岁年轻女性患者发生视网膜分支静脉阻塞并发新生血管增殖膜的病例，给予病变区视网膜激光光凝治疗，10年后随访发现RNV膜机化萎缩。

1 临床资料

患者女，23岁，既往高血压病病史，因“左眼视物模糊13 d”于2011年4月15日就诊于济宁医学院附属医院眼科，眼科查体：右眼视力为0.6，左眼视力为0.08，双眼眼前节情况正常，右眼眼底动脉反光增强，静脉略迂曲(图1)，左眼眼底颞上方视网膜大片火焰状出血、棉绒斑、静脉迂曲、黄斑水肿(图2)。眼底荧光血管造影示：左眼颞上方网膜大片荧光遮蔽，微血管瘤，未见明显无灌注区(图3)，诊断“左眼视网膜分支静脉阻塞，双眼高血压视网膜病变”，给予随访观察，控制血压。发病36 d时，眼底检查见：左眼视盘新生血管(图4)；眼底血管造影检查见：左眼视盘荧光渗漏，颞上视网膜大片无灌注区(图5)，给予眼底病变区视网膜激光光凝治疗。发病75 d时，眼底检查见：左眼视盘新生血管增殖膜，颞上方视网膜血管闭塞，散在激光斑(图6，7)，补充病变区激光治疗。发病103 d时，眼底血管造影检查见：左眼视盘荧光渗漏，颞上方视网膜异常血管网(图8，9)，补充病变区激光治疗。发病138 d时，左眼视力为0.02，视盘形成新生血管膜，表面血管旺盛(图10，11)，再次补充病变区激光治疗。10年后因“右眼视力下降3 d”就诊，查体：右眼视力为0.4，左眼视力为0.4；眼底检查见：左眼视盘新生血管膜机化萎缩，表面无血管(图12)，右眼后极部颞下、颞上视网膜棉绒斑，鼻下和鼻侧视网膜浅层出血，鼻上视网膜少许硬性渗出(图13)。

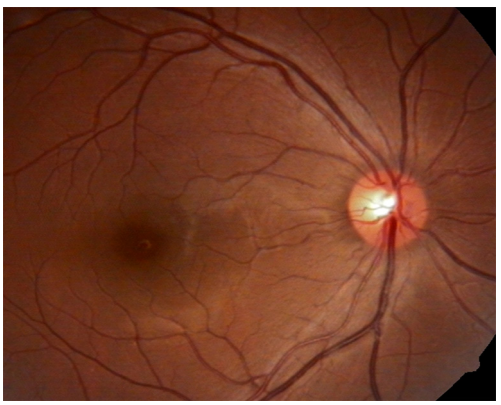

图1 右眼眼底彩照：动脉反光增强，静脉略迂曲(发病13 d)

Figure 1 Color fundus of the right eye showed enhanced arterial reflection and slightly tortuous veins (oneset of 13 d)

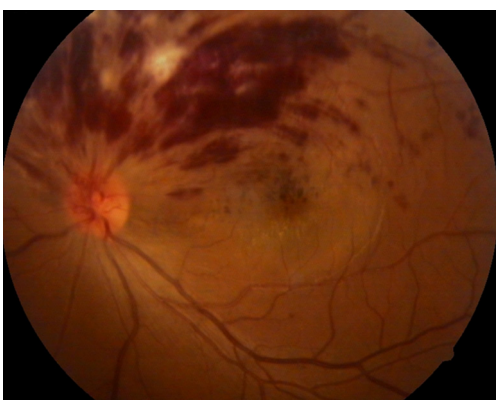

图2 左眼眼底彩照见颞上方视网膜大片火焰状出血，棉绒斑，静脉迂曲，黄斑水肿(发病13 d)

Figure 2 Color fundus of the left eye showed large flaming hemorrhage, cotton velvet spot, and tortuous veins of the supratemporal retina , macular edema (oneset of 13 d)

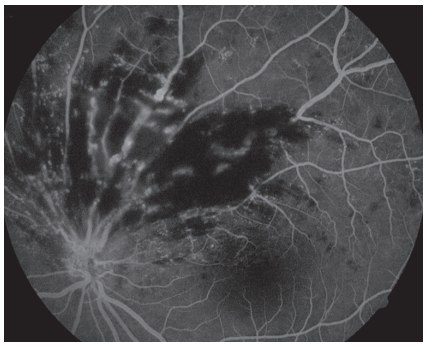

图3 左眼眼底荧光血管造影见颞上方网膜大片荧光遮蔽，微血管瘤，未见明显无灌注区(发病13 d)

Figure 3 Fluorescein fundus angiography of the left eye showed large fluorescent occlusion, microhemangioma, and no non-perfusion area of the supratemporal retina (oneset of 13 d)

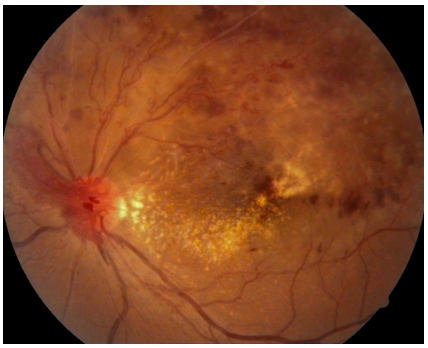

图6 左眼眼底彩照见视盘新生血管增殖膜(发病75 d)

Figure 6 Color fundus of the left eye showed the neovascularization membrane of the optic disc (oneset of 75 d)

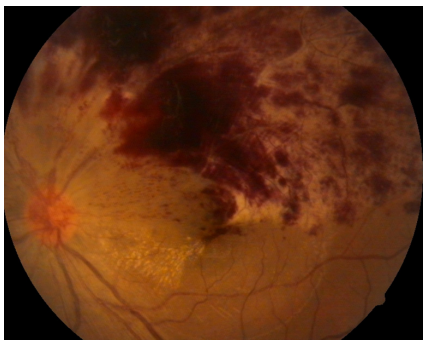

图4 左眼眼底彩照见颞上方网膜大片火焰状出血，静脉迂曲，黄斑区可见渗出，视盘新生血管(发病36 d)

Figure 4 Color fundus of the left eye showed large flaming hemorrhage and tortuous veins of the supratemporal retina, exudation of the macula, the neovascularization of the optic disc (oneset of 36 d)

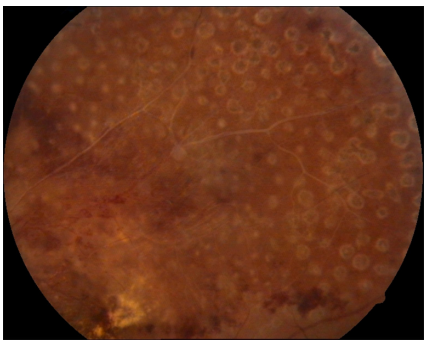

图7 左眼眼底彩照见颞上方视网膜血管闭塞，呈白线状，网膜部分出血吸收，散在激光斑(发病75 d)

Figure 7 Color fundus of the left eye showed the vessels were occluded and the retinal hemorrhage was partly absorbed by the supratemporal retina (oneset of 75 d)

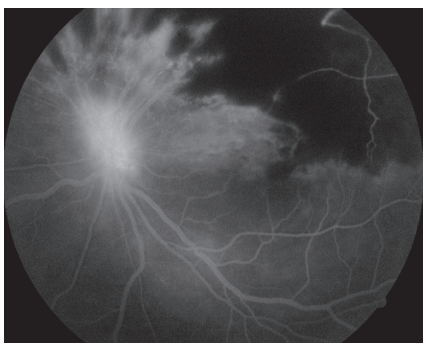

图5 左眼眼底荧光血管造影检查见左眼视盘荧光渗漏，颞上视网膜大片无灌注区(发病36 d)

Figure 5 Fluorescein fundus angiography of the left eye showed high fluorescence of the optic disc，non-perfusion area of the supratemporal retina (oneset of 36 d)

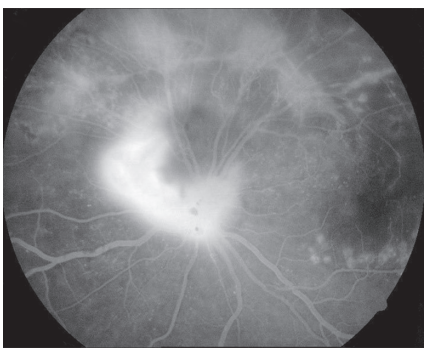

图8 左眼眼底荧光血管造影见视盘荧光渗漏(发病103 d)

Figure 8 Fluorescein fundus angiography of the left eye showed fluorescence leakage of optic disc (oneset of 103 d)

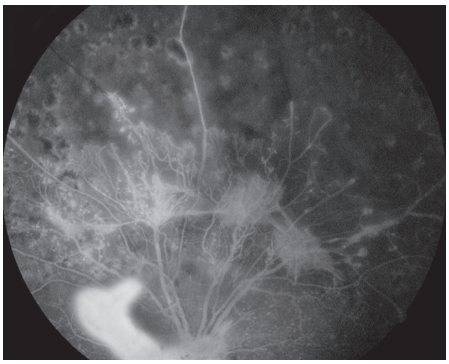

图9 左眼眼底荧光血管造影见颞上方网膜可见新生异常血管网(发病103 d)

Figure 9 Fluorescein fundus angiography of the left eye showed abnormal neovascularization network of the supratemporal retina (oneset of 103 d)

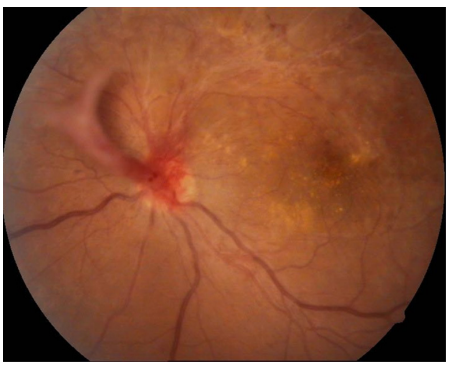

图10 左眼眼底彩照见视盘形成新生血管膜(发病138 d)

Figure 10 Color fundus of the left eye showed the optic disc forms a neovascularization membrane (oneset of 138 d)

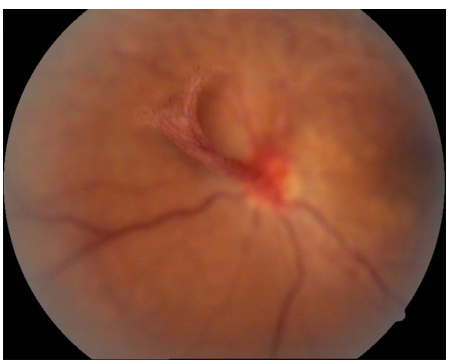

图11 左眼眼底彩照见视盘新生血管膜表面血管旺盛(发病138 d)

Figure 11 Color fundus of the left eye showed the optic disc neovascularization membrane with vigorous surface vessels (oneset of 138 d)

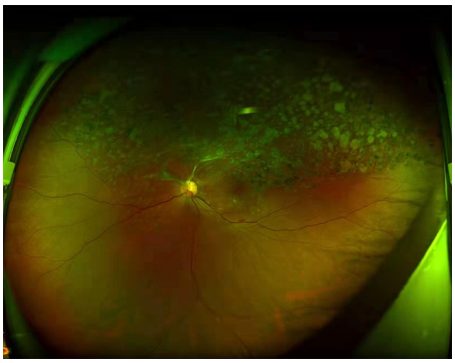

图12 左眼眼底彩照见视盘新生血管膜机化萎缩，表面无血管(发病10年)

Figure 12 Color fundus of the left eye showed the neovascularization membrane of the optic disc were mechanized and atrophied, and there were no vessels on the surface (oneset of 10 years)

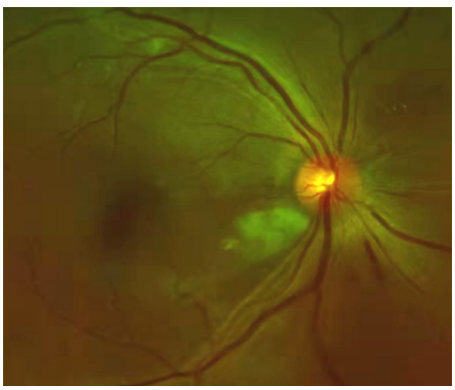

图13 右眼眼底彩照：动脉反光增强，静脉迂曲，后极部颞下、颞上视网膜棉绒斑，鼻下和鼻侧视网膜浅层出血，鼻上视网膜少许硬性渗出(发病10年)

Figure 13 Color fundus of the right eye showed enhanced arterial reflectance, tortuous veins, scattered cotton-wool spots of the Inferior temporal and superior temporal retina. There was superficial hemorrhage in the subnasal and lateral retinas and some rigid exudation in the supranasal retinas (oneset of 10 years)

2 讨论

RVO是常见的视网膜血管性疾病，常为多因素共同致病。引起视网膜分支静脉阻塞的主要因素为动静脉交叉处增厚硬化的动脉壁对静脉的压迫，其次要因素为局部或全身炎症诱发。研究[3]报道其常见的危险因素有高血压、糖尿病、血脂异常；而较少见的有凝血功能异常的疾病或情况

(如口服避孕药、骨髓增生性疾病、Waldenstrom巨球蛋白血症、V因子血栓栓塞症、蛋白S/C异常等)、阻塞性睡眠呼吸暂停综合征、系统性血管炎(如系统性红斑狼疮、白塞综合征、结节性多动脉炎、肉芽肿性多血管炎等)、阻塞性睡眠呼吸暂停综合征、以及累及眼部的系统性疾病(如甲状腺相关眼病、结节病等)和眼眶疾病(眼眶肿瘤等),均可引起RVO[4]。相关研究[5]指出：低于40岁的年轻型RVO无明确的危险因素，与社会压力、吸烟、系统性炎症(例如血管炎、白塞病等)、种族[3]、高血脂症、高同型半胱氨酸血症以及高强度的运动引起脱水等相关。本病例患者RVO考虑与患者高血压性视网膜动脉硬化相关，患者发病时有高血压病史，并口服药物控制治疗，否认糖尿病、冠心病、高血脂症病史。眼部检查双眼视网膜动脉反光增强，静脉略迂曲，患者10年后再次于济宁医学院附属医院门诊就诊，发现右眼高血压视网膜病变，门诊血压检查为230/197 mmHg (1 mmHg=0.133 kPa)。考虑患者左眼视网膜分支静脉阻塞与高血压病相关。因此我们还应关注RVO年轻患者相关的全身性疾病。研究[6]建议RVO患者应常规行血细胞计数、凝血功能、动态红细胞沉降率和C反应蛋白检查，尤其是年轻RVO患者。中青年RVO患者不能过于乐观，要做详细的全身检查寻找原发病，多年后仍有再次发生RVO的可能[7]。

视网膜分支静脉阻塞的治疗包括激光治疗、抗VEGF治疗、激素治疗及手术治疗[8]。有研究[9]指出：视网膜激光光凝的机制归因于激光破坏了缺血性视网膜组织，从而使剩余视网膜的血液供应改善和血管内皮生长因子(vascular endothelial growth factor，VEGF)的产生减少。对视网膜毛细血管无灌注区进行激光光凝仍是改善视网膜缺血和缺氧状态的针对性治疗手段。相关研究[10]报道：部分患眼在激光光凝治疗后可以停止抗VEGF治疗，并且可以保持较长时间无黄斑水肿状态和较好的视力。但在RVO发病初期有大片的网膜出血，激光无法穿透出血的视网膜，且大部分视网膜处于水肿状态，激光也无法达到治疗效果。本病例患者发病36 d就诊时行眼底荧光血管造影检查发现视网膜无灌注区，给予病变区激光治疗，因网膜出血及网膜水肿，部分病变区域无法完成视网膜激光治疗；在发病75 d就诊时发现视盘新生血管，及时给予补充病变区激光治疗；发病103 d复查时新生血管仍然活跃，再次补充病变区视网膜激光治疗。正如Hayreh[11-12]的研究表明：在所有RVO中，80%为非缺血型，因此不需要作全视网膜光凝(panretinal photocoagulation，PRP)，即使20%的缺血型RVO中，也只有45%的患者可能会发生新生血管性青光眼。所以Hayreh建议，对缺血型RVO应密切观察，必要时才做PRP。本病例患者10年前就诊，密切随访，根据病情需要多次给予病灶区域视网膜激光治疗，10年后患者视力较发病初期明显好转，且视盘新生血管膜机化萎缩，激光治疗起到了良好的作用。建议对于视网膜分支静脉阻塞的患者，完善眼底血管造影检查后及时给予病变部位无灌注区进行激光治疗，并密切随访，必要时补充激光治疗，可以改善静脉阻塞后视网膜的缺血缺氧状态。

该患者视网膜分支静脉阻塞后发生视盘新生血管膜增生，其发生机制考虑为RVO后发生视网膜缺氧，无灌注区的形成，进而引起眼内一些因子的表达变化，诱导视盘新生血管膜和RNV的形成。近年对这些因子的研究报道较多，如Alizadeh等[13]研究发现RVO后低氧诱导因子-1α(hypoxia-inducible factor-1α，HIF-1α)表达升高，进而转录并上调其下游靶分子表达，包括VEGF、胎盘生长因子(placental growth factor，PLGF)及VEGF受体1/2(VEGF receptor 1/2，VEGFR1/2)、单核细胞趋化因子-1(monocyte chemoattractant protein-1，MCP-1)、肿瘤坏死因子-α(tumor necrosis factor-α，TNF-α)、白细胞介素-1β(interleukin-1β，IL-1β)、IL-6及IL-8等，血管生成素-2(angiopoietin-2，Ang-2)、成纤维细胞生长因子等多种促血管生成分子表达上调，促使静止的血管内皮细胞向血管生成表型转化[14]。巨噬细胞也参与了眼内新生血管的清除或干预，王雅芬等[15]研究发现：减少循环中巨噬细胞总数或阻止巨噬细胞进入眼内可抑制视网膜或视网膜下新生血管形成。秦海峰等[16]研究表明长期的缺血缺氧会促进视网膜血管内皮细胞增生、迁移、成管，从而诱导新生血管形成。RVO后应积极改善视网膜缺血缺氧状态，尽早完善眼底荧光血管造影检查，及早发现无灌注区，积极给予治疗干预，预防新生血管的形成。

患者10年后就诊发现RNV的消退，考虑与给予病灶区域有效的视网膜激光治疗有关。视

网膜激光治疗可以破坏视网膜的光感受器复合体，降低视网膜氧耗量，从而促进RNV消退。王惠英等[17]通过对大鼠视网膜激光治疗的研究认为：视网膜光凝可促使眼新生血管性疾病中眼内VEGF表达降低，减少对新生血管形成的刺激，而且可以使视网膜色素上皮衍生因子蛋白表达升高，这都可能是引起眼内新生血管消退的重要因素。视网膜激光光凝可有效促使视网膜色素上皮产生尿激酶抑制剂，对RNV起到抑制作用，还可通过对视网膜血管的无灌注区进行封闭，促进机体的血液循环，减少视网膜细胞的受损程度，提高其营养摄取量，从而加速视网膜区域新生血管的消退进度[18-20]。

综上所述，对于年轻患者的视网膜分支静脉阻塞治疗，应积极寻找疾病的诱因，若合并全身疾病应同时给予治疗；在视网膜分支静脉阻塞的治疗过程中视网膜激光光凝具有重要价值；活跃的视盘新生血管增殖膜经视网膜激光治疗后可获得机化萎缩，患者长期预后良好。

开放获取声明

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