Incidence and Risk Factors for Ocular Ischemic Syndrome in Patients with Complete Internal Carotid Artery Occlusion

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Research Article

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Abstract

Purpose Ocular ischemic syndrome could lead to irreversible blindness and death. To investigate the incidence of and risk factors for ocular ischemic syndrome in patients with complete internal carotid artery occlusion.

Methods This retrospective study included 55 patients with complete internal carotid artery occlusion from January 2016 to January 2021 in our hospital. Ophthalmic evaluations and blood test results were recorded.

Results Thirty-four (61.8%) eyes with homolateral complete internal carotid artery occlusion were diagnosed with ocular ischemic syndrome. Among the 34 first-visit cases in the Department of Ophthalmology, 32 were misdiagnosed with other ocular diseases. A lower D-dimer level (odds ratio = 0.007, 95% confidence interval: 0.000-0.182) was associated with the presence of ocular ischemic syndrome in patients with complete internal carotid artery occlusion.

Conclusions Ophthalmologists should pay close attention to patients with complete internal carotid artery occlusion and suspected or confirmed ocular ischemic syndrome, especially those with lower D-dimer levels.

Introduction

Ocular ischemic syndrome (OIS) is a disorder of ocular function that occurs subsequent to severe stenosis of the carotid artery.¹ It was reported in 1963 by Hedges.² The incidence of OIS is estimated at 7.5 cases per million annually.³ Since OIS may result in delayed diagnosis and misdiagnosis in many patients, this figure may be an underestimation. The 5-year mortality rate for patients with OIS is 40%, most commonly from cardiovascular disease, followed by cerebrovascular disease.¹

The incidence of OIS increases when the degree of internal carotid artery stenosis is greater than 50%.⁴ Moreover, few studies have attempted to identify the incidence of and risk factors for the presence of OIS in patients with complete internal carotid artery occlusion. To our knowledge, this is the first study to examine the risk factors for OIS in patients with complete internal carotid artery occlusion.

Methods

Ethics approval and consent to participate

This study complied with the tenets of the Declaration of Helsinki. This study was approved by the local Ethics Committee of the Eye Hospital China Academy of Chinese Medical Sciences, and the requirement for informed consent was waived owing to the retrospective nature of the study.

Patient data

This was a retrospective, observational case series. We reviewed medical records from January 2016 to January 2021. All the patients underwent carotid artery color Doppler flow imaging (HD15, Philips, America) to identify the complete occlusion of the internal carotid artery. Diagnostic criteria of OIS is as follows: (1) Symptom of loss of vision in the affected eyes; (2) clinical manifestations of anterior segment and posterior segment changes; (3) fundus fluorescence angiograph findings of prolonged retinal arteriovenous transit time, delayed and/or patchy choroidal filling; (4) carotid artery color Doppler flow imaging revealing ipsilateral complete internal carotid artery occlusion. Exclusion criteria included patients with a history of ocular trauma, a history of prior ocular surgery, or age-related macular degeneration.

Data collection

Ophthalmic evaluations included the following: best-corrected visual acuity; intraocular pressure measurement; slit-lamp examination of the anterior segment, lens, and vitreous; and color fundus photography. The results of the carotid ultrasound, fundus fluorescence angiograph, and blood tests were recorded. Patients with a detailed history of systemic diseases were included.

Statistical analyses

Statistical analyses were performed using the International Business Machines (IBM) Statistical Package for the Social Sciences Statistics for Windows, version 26.0 (IBM Corp., Armonk, NY, USA). Summary statistics included the mean and standard deviation, where appropriate. Categorical data are presented as percentages. Binary logistic regression models were used to assess the association between clinical parameters and the presence of OIS. Multiple logistic regression analysis was used to determine the risk factors for the presence of OIS. P-values < 0.05 were considered statistically significant.

Results

Based on the database of the Eye Hospital China Academy of Chinese Medical Sciences between 2016 and 2021, 55 patients with complete internal carotid artery occlusion were included in the study. The mean age was 67.5 ± 11.5 years, and 42 (76.4%) patients were male. The level of total homocysteine (tHcy) in the blood was high in patients with complete internal carotid artery occlusion.

Thirty-four (61.8%) eyes with homolateral complete internal carotid artery occlusion were diagnosed with OIS. Thirty-three patients had one or more systemic diseases. Twenty-seven patients had two or more systemic diseases. The level of tHcy in the blood was high in patients with OIS. Three patients had cerebral infarction at the time of OIS during hospitalization. Table 1 shows the demographic characteristics of the participants.

Patients with OIS had various clinical features, including neovascularization of the iris, hyphema, neovascular glaucoma (NVG), posterior synechia of the iris, new vessels on the disc, optic atrophy, retinal artery occlusion, retinal soft exudates, retinal hemorrhage, vitreous hemorrhage, and retinal detachment. The ocular characteristics of OIS are listed in Table 2.

Among the 34 first-visit cases in the Department of Ophthalmology, 32 were misdiagnosed with other ocular diseases before carotid ultrasound and fundus fluorescence angiograph. Two patients were initially diagnosed with diabetic retinopathy, two patients were initially diagnosed with central retinal vein occlusion, three patients were initially diagnosed with retinal artery occlusion, three patients were initially diagnosed with anterior ischemic optic neuropathy, five patients were initially diagnosed with vitreous hemorrhage, one patient was initially diagnosed with hyphema, 10 patients were initially diagnosed with glaucoma, four patients were initially diagnosed with cataract, one patient was initially diagnosed with cortical blindness, and one patient was initially diagnosed with amaurosis.

In the univariate analysis, age (odds ratio [OR] = 0.935, 95% confidence interval [CI]: 0.881–0.992) and D-dimer (OR = 0.007, 95% CI: 0.000–0.182) were found to be associated with the risk of development of OIS in patients with complete internal carotid artery occlusion. However, triglyceride, total homocysteine, and serum fasting glucose, were not significantly different between presence or absence of OIS.

Multivariate logistic regression analysis revealed that a lower D-dimer level (OR = 0.007, 95% CI: 0.000–0.182) was associated with the presence of OIS in patients with complete internal carotid artery occlusion (Table 3).

Discussion

The present study describes the ocular manifestations of OIS in patients with complete internal carotid artery occlusion. Thirty-four (61.8%) eyes with homolateral complete internal carotid artery occlusion were diagnosed with OIS. A lower D-dimer level was associated with the presence of OIS in patients with complete internal carotid artery occlusion.

In our study, the majority of OIS patients were older men with more than one systemic disease, which is consistent with the findings by Luo J et al.⁶ Thirty-four patients with OIS were recruited in our study, including 28 males and 6 females. The mean patient age was 65 years. Thirty-three patients had one or more systemic diseases. Furthermore, 27 patients had two or more systemic diseases.

Annually, 7.5 people per million are diagnosed with OIS.¹ However, the actual prevalence is considered to be higher because OIS was easily undiagnosed due to its asymptomatic onset and complicated ocular manifestations.⁶ In the present study, 34 (61.8%) eyes with homolateral complete internal carotid artery occlusion were diagnosed with OIS. Among the 34 first-visit cases in the Department of Ophthalmology, 32 were misdiagnosed with other ocular diseases before carotid ultrasound. Detailed ocular examinations and carotid artery color Doppler flow imaging are essential to exclude the possibility of OIS.⁶ Since complete internal carotid artery occlusion might result in decreased blood flow to the anterior

chamber angle and posterior segment, it predisposes the eye to NVG and retinal neovascularization⁷ and may lead to irreversible blindness.⁷ Therefore, close attention should be paid to patients with complete internal carotid artery occlusion and suspected or confirmed OIS. Early and accurate diagnosis is important to help prevent permanent ischemic and irreversible blindness.

Our study demonstrated that 53%, 56%, 50%, and 59% of patients had hypertension, diabetes, cardiovascular disease, and cerebrovascular accident, respectively. In a study by Sivalingam et al.⁸, hypertension, diabetes, cardiovascular disease, and a history of a cerebrovascular accident were observed in 73%, 56%, 48%, and 27% of patients, respectively. According to a study by Kim et al.⁷, hypertension, diabetes, cardiovascular disease, and a history of a cerebrovascular accident were observed in 52%, 52%, 20%, and 44% of patients, respectively. These results are consistent with the findings of the present study. This may be explained by the pathogenic similarity between the aforementioned systemic conditions and OIS.⁷ Previous studies have suggested that the tHcy levels is a marker of atherosclerosis.⁹ Our study demonstrated high tHcy levels in the blood in patients with OIS and complete internal carotid artery occlusion. A previous study demonstrated that tHcy levels were associated with the development of OIS in patients with preexisting stenosis of the internal carotid artery.⁹ The sensitivity and specificity of hyperhomocysteinemia for diagnosing OIS in patients with stenosis of the internal carotid artery were 70% and 79%, respectively.⁹ In patients with preexisting carotid artery diseases, elevated tHcy levels in the blood are considered a risk factor for the future development of stroke.⁹ We found that three patients with OIS suffered a stroke during hospitalization. The 5-year survival rate for patients with OIS is only 60%; thus, an astute clinical diagnosis, targeted workup for systemic examination, and prompt referral are important for patients with OIS.⁵ We recommend that ophthalmologists should pay close attention to patients with suspected or confirmed ISO and establish a cooperative relationship with neurologists and cardiologists in order to maximally improve the quality of life and decrease the mortality rate in patients with OIS.

Not all patients with internal carotid artery occlusion develop OIS.¹⁰ In a previous study, a complete occlusion of the carotid artery on the affected side was found in 50% of all patients with OIS.¹¹ In our study, OIS was found in 62% of all patients with a complete occlusion of the carotid artery. Why do some patients diagnosed with complete occlusion of the carotid artery have associated OIS, while others do not? In cases of total occlusion of the internal carotid artery, OIS may not occur if the circle of Willis is well developed.^{7,12} Moreover, anastomoses between the middle meningeal artery and ophthalmic artery may persist.¹³ When complete occlusion of the carotid artery occurs in patients with an obstruction of the circle of Willis, reversal of blood flow in the ophthalmic artery will occur after the establishment of plentiful collateral circulation between the internal and external carotid arteries, leading to OIS.¹⁰ Therefore, close attention should be paid to patients with complete carotid artery occlusion, especially those with an obstacle of the circle of Willis.

Multivariate logistic regression showed that a lower D-dimer level indicated a significantly higher risk of OIS. The clinical characteristics of OIS include chronic ischemia, which primarily occurs in patients with

an obstacle of the circle of Willis.¹⁴ We inferred that the D-dimer maybe low in the development of chronic ischemia. Therefore, D-dimer levels are considered to be associated with the development of OIS in patients with complete internal carotid artery occlusion. However, the exact reason for this finding should to be determined.

This study has some limitations. The sample size was small, which may have influenced the association between OIS and the risk factors. Future prospective and long-term studies are needed for a more accurate analysis.

Conclusion

In conclusion, we recommend that ophthalmologists should pay close attention to patients with complete internal carotid artery occlusion and suspected or confirmed OIS, especially those with lower D-dimer levels. In addition, we should establish a cooperative relationship between neurologists and cardiologists. In this way, we can maximally prevent irreversible blindness, improve the quality of life, and decrease the mortality rate in patients with OIS.

Declarations

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Conflict of interest

The authors declare that they have no competing interests.

Compliance with ethical standards

Consent to participate

Not applicable

Consent for publication

Not applicable

Authors' contributions

XYZ collected data, performed all statistical analysis, and wrote the manuscript. XFH and CW analyzed the data and assisted in manuscript writing. LKX designed the study and collected data. All authors read and approved the final manuscript.

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Table 1

General characteristics of the 34 patients with ocular ischemic syndrome

Characteristics	Ocular ischemic syndrome (N = 34)
Age (years)	64.618 ± 11.688 (30-85)
Sex	
Female	6
Male	28
Hypertension	18
Diabetes	19
Cardiovascular disease	17
Cerebrovascular accident	20
Hyperlipidemia	10
Triglyceride (mmol/L)	1.421 ± 0.913 (0.42-4.56)
Total homocysteine (umol/L)	15.968 ± 9.662 (2.7-44.7)
D-dimer (mg/L)	0.275 ± 0.175 (0.1-0.89)
Serum fasting glucose (mmol/L)	7.04 ± 2.733 (4.12-17.8)

Table 2

Clinical characteristics of 34 eyes with ocular ischemic syndrome

Characteristic	Number of eyes (N=34)
Hyphema	2
Neovascular glaucoma	12
Neovascularization of the iris	13
Posterior synechia of the iris	2
Vitreous hemorrhage	3
Retinal artery occlusion	4
New vessels on the disc	2
Optic atrophy	9
Retinal soft exudates	7
Retinal hemorrhage	11
Retinal detachment	3

Table 3

Risk factors for the presence of ocular ischemic syndrome in patients with complete internal carotid artery occlusion

Factors	OR	95%CI
D-dimer	0.007	0.000-0.182

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [Dataset.xlsx](#)