Analysis of Multimodal Imaging Characteristics of Transient Central Retinal Artery Occlusion

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Research Article

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Abstract

Background To observe and analyze the multimodal imaging characteristics of transient central retinal artery occlusion (T-CRAO).

Methods Retrospective observational study. Eight patients (8 eyes) diagnosed as T-CRAO in Tianjin Medical University Eye Hospital were included in this study. There were 6 males (6 eyes) and 2 females (2 eyes) with an average age of 63.8 years (38-78years). The clinical manifestation was acute vision loss. All patients underwent best corrected visual acuity (BCVA), slit lamp microscope, color fundus photography (CFP), fundus fluorescein angiography (FFA), optical coherence tomography (OCT) and OCT angiography (OCTA). The clinical data and multimodal imaging characteristics of patients were analyzed.

Results There were 4 eyes with BCVA from 0.05 to 0.1 and 4 eyes from 0.1 to 0.3. CFP demonstrated multiple patchy “cotton-wool spot”-like lesions in posterior pole, without typical cherry-red spot. FFA manifested as sluggish filling of arteries, filling front, and delayed filling of vein. The filling was completed within 5 to 10 seconds. The “cotton-wool spot”-like lesions showed low fluorescence in early stage. Some lesions filled gradually; others still showed low fluorescence in late stage. OCT showed inner layer and local nerve fiber layer of retina was thickened. The reflexes of lesions were enhanced intermittently, especially the “hump-like” change of inner nuclear layer (INL). OCTA revealed the vascular density (VD) of superficial capillary plexus (SCP) and deep capillary plexus (DCP) of retina was decreased, the shape of the arcade was damaged, and the foveal avascular zone (FAZ) area was enlarged. En-face image showed isolated patchy hyperreflective lesions at SCP and fused patchy hyperreflective lesions at DCP.

Conclusions CFP demonstrated multiple patchy “cotton-wool spot”-like lesions in posterior pole; OCTA revealed decreased VD of SCP and DCP. After treatment, the “cotton-wool spot”-like lesions gradually vanished, and the VD partially recovered.

1. Background

Transient central retinal artery occlusion (T-CRAO) is a subtype of CRAO, accounting for about 15~17%, and the prognosis is relatively good.[1, 2] This disease mostly was monocular, manifested by varying degrees of acute vision loss. Fundus examination showed multiple patchy “cotton-wool spot”-like lesions in the posterior pole. Fundus fluorescein angiography (FFA) manifested as sluggish filling of retinal arteries, but no obvious nonperfusion area in the lesions, suggesting that the “cotton-wool spot”-like lesions were not caused by preretinal arteriole occlusion. There are few reports of this disease at present, and no reports about the multimodal imaging study, especially the optical coherence tomography angiography (OCTA). In order to better understand the clinical manifestations and multi-mode imaging features of T-CRAO, we retrospectively analyzed the clinical manifestations and multimodal imaging characteristics of a group cases of T-CRAO. The report is as follows.

2. Materials And Methods

This is a retrospective observational study. This study adhered to the tenets of the Declaration of Helsinki and was approved by the Ethics Committee of Tianjin Medical University Eye Hospital[2020KY-18]. Written informed consent was obtained from each participant prior to enrollment in the study.

Eight cases (8 eyes) of T-CRAO who were examined and diagnosed in the Tianjin Medical University Eye Hospital from January 2018 to November 2020 were included in the study. There were 6 males (6 eyes) and 2 females (2 eye), with an average age of 64 years (38-78 years old). The average time between onset of symptoms and consultation was 2.6 days (range 1-5d). All patients were diagnosed monocularly and complained of acute vision loss. The best corrected visual acuity (BCVA) was 0.05~0.1 in 4 eyes, 0.1~0.3 in another 4 eyes respectively. There were 6 patients with a history of hypertension, 1 patient with type 2 diabetes, and 1 patient with coronary heart disease. The demographics of patients with T-CRAO was shown in Table 1.

Table 1. Demographics of patients with T-CRAO

Case	Gender	Age(years)	Time of onset (days)	BCVA at first visit	Previous medical history
1	Male	73	3	0.08	Hypertension
2	Male	65	2	0.1	Hypertension
3	Male	78	1	0.05	Hypertension
4	Male	38	1	0.15	Hypertension
5	Female	63	5	0.3	type 2 diabetes
6	Male	69	2	0.06	Hypertension
7	Male	58	4	0.2	Hypertension
8	Female	66	3	0.05	Coronary heart disease

The diagnostic criteria[1, 2] of T-CRAO: 1) color fundus photography (CFP) demonstrated multiple patchy “cotton-wool spot”-like lesions in the posterior pole, 2) FFA manifested as sluggish filling of retinal arteries, and 3) optical coherence tomography (OCT) showed intermittent thickening of the inner layer of the retina and enhanced reflex in the lesions. The inclusion criteria: 1) acute vision loss within 1 week, 2) multiple patchy “cotton-wool spot”-like lesions was in the posterior pole without typical cherry-red spot, 3) FFA manifested as sluggish filling of retinal arteries and the filling front, and 4) OCT revealed intermittent thickening of the inner layer of the retina and enhanced reflex at the lesions. The exclusion criteria: 1) complications such as severe refractive interstitial opacity or vitreous hemorrhage that impaired observation of the fundus, 2) after repeated inspections, it was still unable to obtain clear multimodal imaging data that meets the analysis requirements.

All patients underwent BCVA, slit lamp microscope, CFP, FFA, OCT and OCTA. OCTA®RTVue XR Avanti with AngioVue; Optovue Inc., Fremont, CA, USA® was used in this study to acquire OCTA images. A 3×3mm scan, centered on the fovea, were performed in all eyes. The vascular area was automatically segmented into four layers: superficial capillary plexus (SCP), deep capillary plexus (DCP), outer retinal vascular plexus and choroidal capillary layer, while observing the changes of the shape of the capillary arcade and the foveal avascular zone (FAZ) area. SCP spanned from the inner limiting membrane (ILM) to the lower border of the inner plexiform layer (IPL), while DCP spanned from the inner nuclear layer (INL) to the outer plexiform layer (OPL).[3]

After diagnosis, patients strictly controlled systemic diseases. Additionally, they also actively controlled blood pressure, dilated blood vessels, nourished nerves, inhaled oxygen and reduced intraocular pressure in accordance with the treatment principles of acute CRAO in reference.[4]

3. Results

CFP demonstrated thinner arteries, no vein dilatation, multiple patchy "cotton-wool spot"-like lesions in the posterior pole without typical cherry-red spot in the macular area (figure 1A). FFA manifested as sluggish filling of retinal arteries, the filling front (figure 1B), and delayed filling of retinal vein (figure 1C). The filling was completed within 5 to 10 seconds. The "cotton-wool spot"-like lesions showed low fluorescence in the early stage. Some lesions filled gradually; others still showed low fluorescence in the late stage (figure 1D).

OCT showed that the inner layer of the retina was thickened, and the local nerve fiber layer was thickened obviously. The reflexes of the lesions were enhanced intermittently, especially the "hump-like" change of the INL (figure 2).

OCTA revealed that the vascular density (VD) of SCP and DCP was decreased, the shape of arcade was destroyed, and the FAZ area was enlarged in all affected eyes (figure 3A, 3C). En-face image showed that isolated patchy hyperreflective lesions of varying sizes in SCP, which were basically coincided with the missing area of the SCP. Fused patchy hyperreflective lesions could be seen in DCP, which were also basically coincided with the missing area of DCP (figure 3B, 3D).

After 2 weeks of active treatment, the visual acuity of all patients was improved in varying degrees, the BCVA was 0.1 to 0.3 in 5 eyes, 0.4 to 0.5 in 3 eyes. Compared with that before treatment (figure 4A), CFP demonstrated that most of the multiple patchy "cotton-wool spot"-like lesions in the posterior pole disappeared after treatment (figure 4B). OCTA revealed that the VD of SCP and DCP in the lesions was partially restored and the shape of arcade was improved (figure 4E, 4I) compared with that before treatment (figure 4C, 4G). En-face image showed that the patchy hyperreflective lesions partial reduced (figure 4F, 4J) compared with that before treatment (figure 4D, 4H).

4. Discussions

CRAO is a relatively common emergency in ophthalmology, and it is one of the main causes of acute vision loss in patients. The incidence is approximately 1 per 100,000 people, accounting for about 1 in 10,000 of ophthalmology outpatients.[5, 6] CRAO can be divided into 4 subtypes[1, 2]—permanent CRAO (P-CRAO), T-CRAO, CRAO with ciliary retinal artery, and arteritic CRAO. T-CRAO is one of these subtypes, with a relatively low incidence, accounting for only about 1/6 of all CRAO. Risk factors for CRAO include hypertension, obesity, previous stroke or transient ischemia, coronary heart disease, arrhythmia, valvular heart disease, smoking, hyperlipidemia, diabetes, etc., among which hypertension is considered the most common risk factor.[7, 8] Six patients in this study were accompanied by hypertension, indicating that hypertension was also the most common independent risk factor in patients with T-CRAO. The pathogenesis of T-CRAO is unclear currently, which is similar to the visual impairment caused by transient ischemic attack (TIA).[6] In a study on atherosclerotic monkeys, it found that serotonin, released by platelet aggregation on atherosclerotic plaques in the carotid artery, can cause transient, complete occlusion or impair blood flow in the central retinal artery by producing a transient spasm, resulting in transient ischemia and hypoxia of retinal tissue.[9]

FFA is the golden standard for diagnosing retinal ischemic diseases at present. All patients in this group manifested as sluggish filling of retinal arteries, with filling front, which was consistent with the diagnostic characteristics of CRAO. Although the FFA showed sluggish filling of retinal arteries, the retinal arteries filled completely in 5 to 10 seconds, which was significantly different from P-CRAO, indicating that the ischemia of T-CRAO was slighter than that of P-CRAO. Fundus examination showed multiple patchy "cotton-wool spot"-like lesions in the posterior pole observed in CFP, and no nonperfusion area in the lesions observed in FFA, indicating that the lesions were not caused by anterior retinal arteriole occlusion. Combined with OCT findings, it was considered that the patchy "cotton-wool spot"-like lesions were focal edema and thickening of the retinal nerve fiber layer caused by transient retinal ischemia.

FFA can only clearly show the large retinal vessels and some superficial capillaries, so it is difficult to detect the ischemia of middle and deep capillaries in the macular region for T-CRAO. The retinal capillaries in the macular area are divided into superficial, middle and deep layers. The superficial layer is located at the nerve fiber layer, the middle layer is located at the interface of INL and IPL, and the deep layer is located at the interface of INL, OPL and Henle fiber layers. OCTA can display the retinal capillaries in the macular area hierarchically, and provide B-scan image of SCP, DCP, outer retinal vascular plexus and choroid capillary layer. OCTA cannot distinguish the middle and deep retinal capillaries, so collectively called DCP. The essence of T-CRAO is the ischemic damage of the retina, the transient spasm of the central retinal artery leads to blood supply disorders in the superficial, middle and deep retinal capillaries. In this study, OCTA revealed that the VD of SCP and DCP were significantly decreased in lesions, and the decrease of VD of DCP was more severe than that of SCP, further confirming the pathological damage mechanism of the disease.

En-face image of OCTA showed patchy hyperreflective lesions in the SCP and DCP, which was the characteristic imaging manifestation of T-CRAO. It showed as isolated patchy hyperreflective lesions in SCP, which was completely consistent with the "cotton-wool spot"-like lesions observed in CFP and fused

patchy hyperreflective lesions in DCP. The above characteristic manifestations suggested that the DCP was more sensitive to ischemia and more prone to ischemic damage.

In the eyes with T-CRAO, OCT showed intermittent thickening and enhanced reflexes in the inner layer of the retina, while the outer retina was not involved. In the eyes with paracentral acute middle maculopathy (PAMM), OCT showed the hyperreflective band at INL.[10] In the eyes with acute macular neuroretinopathy (AMN), OCT showed patchy hyperreflective lesions in the outer nuclear layer (ONL), involving the ellipsoid zone and the myoid zone.[11] Characteristic manifestations in OCT are helpful in distinguishing T-CRAO, PAMM and AMN.

Studies found that in T-CRAO with initial visual acuity of counting finger or worse, visual acuity improved, remained stable, or deteriorated in 82%, 18%, and none, respectively.[2] In this study, after active treatments in accordance with the treatment principles of acute CRAO, the visual acuity of the affected eyes was improved in varying degrees, and OCTA revealed that the VD of SCP and DCP were significantly improved compared with the initial diagnosis. It indicated that the ischemic degree of T-CRAO was relatively mild compared with P-CRAO, the ischemia could be improved after active treatment, and the prognosis was relatively good. Unfortunately, the compliance of patients in this group was poor, and we didn't obtain long-term follow-up data, especially OCTA, so we couldn't determine whether the VD of SCP and DCP can be fully recovered.

5. Conclusions

This study analyzed the multimodal imaging characteristics of T-CRAO, CFP demonstrated multiple patchy "cotton-wool spot"-like lesions in posterior pole; OCTA revealed decreased VD of SCP and DCP. After treatment, the "cotton-wool spot"-like lesions gradually vanished, and the VD partially recovered. This study focused on the morphological observation of T-CRAO, lacked multifocal ERG, micro-visual field and other functional examinations, so there was a lack of analysis of the functional effects of T-CRAO. In addition, limited to the low incidence of this disease, the number of cases in this study was small. Further prospective studies with larger cohorts and standardized follow-up intervals could be important to analyze the clinical characteristics and disease outcome.

Abbreviations

T-CRAO	Transient central retinal artery occlusion
BCVA	Best corrected visual acuity
CFP	Color fundus photography
FFA	Fundus fluorescein angiography
OCT	Optical coherence tomography
OCTA	OCT angiography
VD	Vascular density
SCP	Superficial capillary plexus
DCP	Deep capillary plexus
FAZ	Foveal avascular zone
ILM	Inner limiting membrane
IPL	Inner plexiform layer
INL	Inner nuclear layer
OPL	Outer plexiform layer
TIA	Transient ischemic attack
P-CRAO	Permanent CRAO
PAMM	Paracentral acute middle maculopathy
AMN	Acute macular neuroretinopathy

Declarations

Ethics approval and consent to participate

This is a retrospective observational study. This study adhered to the tenets of the Declaration of Helsinki and was approved by the Ethics Committee of Tianjin Medical University Eye Hospital[2020KY-18]. Written informed consent was obtained from each participant prior to enrollment in the study.

Consent for publication

Consent for publication has been obtained.

Availability of data and materials

All data generated or analyzed during this study are included in this article.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

AWT and ZQ participated in data collection and drafted the manuscript. HJD conceived the idea of the study, designed the study and revised the manuscript critically. All authors read and approved the final manuscript.

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Figures

Figure 1

CFP and FFA examination of eyes with T-CRAO. CFP demonstrated multiple patchy "cotton-wool spot"-like lesions in the posterior pole without typical cherry-red spot in the macular area (1A). FFA manifested that the filling front of retinal arteries appeared at 16 seconds (1B), laminar flow appeared at 23 seconds in retinal veins (1C), and low fluorescence was still in some of the late "cotton-wool spot"-like lesions (1D).

Figure 2

OCT examination of eyes with T-CRAO. OCT showed thickening of the inner layer of the retina, intermittent enhancement of reflex, "hump-like" changes of INL, and thickening of the local retinal nerve fiber layer in the "cotton spot"-like lesions.

Figure 3

OCTA examination of eyes with T-CRAO. OCTA revealed that the VD of SCP and DCP was decreased, the shape of arcade was destroyed, and the FAZ area was enlarged (figure 3A, 3C). En-face image showed that patchy hyperreflective lesions of varying sizes in SCP and fused patchy hyperreflective lesions in DCP (figure 3B, 3D).

Figure 4

CFP and OCTA examination of eyes with T-CRAO before and after treatment. Before treatment, CFP demonstrated multiple patchy “cotton-wool spot”-like lesions in the posterior pole (figure 4A), OCTA revealed that the VD of SCP and DCP was decreased, the shape of arcade was destroyed, and the FAZ area was enlarged (figure 4C, 4G), En-face image showed patchy hyperreflective lesions in SCP and DCP (figure 4D, 4H). After treatment, CFP demonstrated most of the patchy “cotton-wool spot”-like lesions

disappeared (figure 4B), OCTA revealed that the VD of SCP and DCP was partially restored, and the shape of arcade was improved (figure 4E, 4I), En-face image showed that the patchy hyperreflective lesions partial reduced (figure 4F, 4J).