Research Article

Multimodality Image Analysis in a Cohort of Patients with Atypical Juvenile Ocular Toxocariasis

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Purpose. To analysis the multimodal imaging of a group of patients diagnosed clinically with atypical juvenile ocular toxocariasis (OT). Methods. In this case series study, we examined 9 young patients diagnosed with atypical OT. Routine ophthalmological examinations, fundus photography, optical-coherence tomography (OCT), fluorescein angiography (FFA), and B-mode ultrasound were performed. A questionnaire was used to record whether the patients were newly diagnosed and whether they had a history of exposure to a cat and dog. Aqueous humor and serum samples were taken for serological tests. Results. In all the patients, yellow-and-white dot-shaped lesions and perivascular white sheath were seen in the fundus. Heterogeneous changes including hyper-reflection in the disrupted neuroretina, hyper-reflection in the outer retinal layer, high-reflection mass on the surface of the neuroretina accompanied with reflective attenuation, and high-reflection mass involving the entire neuroretina or high-reflection mass in the vitreous body were noticed in OCT images. On FFA, seven of these patients (77.8%) showed leakage of fluorescein in the small- and medium-branch veins of the retina, and a “bristle-like” change indicated increased permeability of the vessels. B-mode ultrasound showed proliferative membranes and proliferative bands (33.3%), as well as spotted opacity in the vitreous (66.7%). The antibodies to Toxocara canis in the aqueous humor and serum were positive, and the Goldmann–Witmer coefficient was significantly increased in 6 out of 7 patients. Conclusions. Multimodality images are useful in the diagnosis of atypical juvenile OT, which could be easily overlooked and misdiagnosed.

1. Introduction

Toxocariasis is a parasitic disease caused by Toxocara canis or T. cati larvae worldwide. Eggs ingested by humans hatch into parasitic larvae in the small intestine. Through blood circulation, larvae may invade the eyes and cause ocular toxocariasis (OT). OT usually is unilateral and commonly affects adolescent patients in the European, American, and Chinese populations. Due to the involvement of many factors including the site of invasion and the course of the disease, the clinical manifestations of OT are heterogeneous, which makes a correct diagnosis difficult. Although biopsy is the most valuable method for the diagnosis of OT [1], aqueous humor and blood serological tests, together with a history of pet exposure, are also among diagnostic criteria. Unfortunately, some relevant data usually are not always available from all patients. Therefore, the importance of careful observation of the ocular manifestations for the diagnosis of OT is exaggerated.

According to its manifestations, OT can be divided into four types: peripheral granuloma, posterior polar granuloma, chronic endophthalmitis, and mixed type. Although typical OT can be diagnosed by signs of retinal granulomatosis or toxocariasis endophthalmitis [2], OT patients with atypical manifestations are likely to be misdiagnosed. These atypical OTs include involvement of the ciliary-body [3] or lens [4] invasion, intraocular tumors, and optic-nerve swelling [5]. Recently, improved multimodal ophthalmic-imaging technologies have unveiled the details of retinal lesions in OT. Analysis of multimodal ophthalmic images, combined with medical history and immunological examinations, has markedly improved the diagnosis for this
relatively unaware condition. In this study, we performed
multimodal-imaging analysis in a cohort of patients di-
agnosed clinically with atypical juvenile OT and explored the
characteristics of the imaging.

2. Patients and Methods

Nine OT patients diagnosed clinically with atypical granu-
lomas in our hospital from January 2016 to December 2019
were included. The aqueous humor was collected, and an
enzyme-linked immunosorbent assay (ELISA) was per-
formed to detect *Toxocara* antibodies. The Gold-
mann–Witmer coefficient (GWC), which was calculated as
((specific IgG in aqueous humor/specific IgG in serum)/
[total IgG in aqueous humor/total IgG in serum]), was
obtained [6]. The diagnosis of OT was made when the
specific *Toxocara* IgG in the aqueous humor was positive.
Patients with granuloma that could be caused by other
conditions including toxoplasmosis, sarcoidosis, uveitis, and
fungal infections were excluded. Patients with a history of
ocular trauma or surgery were also excluded. The research
procedure was approved by the Institutional Ethics Com-
mittee of the Henan Eye Hospital. Guardians of all patients
signed an informed consent form.

Best corrected visual acuity (BCVA), slit lamp, and direct
ophthalmoscopic results of all patients were obtained. A
questionnaire was used to record whether patients were
newly diagnosed and whether they had a history of exposure
to a cat and dog. An Optos Optomap Panoramic 200 laser
scanning ophthalmoscope (Optos PLC, Dunermine, UK)
was used to collect color photographs of the fundus with a
range of 200°. We used either spectral-domain or swept-
source optical-coherence tomography (Heidelberg SD-OCT,
Germany and VG200D SVision Imaging SS-OCT, China)
for scanning the retina. Fluorescein angiography (FFA) was
performed with a Heidelberg confocal laser scanning fluo-
rescein angiography apparatus (Heidelberg Engineering
GbH, Heidelberg, Germany). An ultrasound (MD-2400S
MEDA, China) was used to observe the vitreous bodies.

3. Results

Nine patients with OT were included in this study (6 males
and 3 females; aged from 6 to 16 years, average 10.11 years).
All the patients presented unilateral OT. The BCVA range
was 0.01–0.8, with an average visual acuity of 0.31. Slit-lamp
examination showed flare (+) and cells (+) in the anterior
chamber in 5 patients (55.6%), while the remaining 4
(44.4%) did not exhibit noticeable abnormalities in the
anterior segment. Fundus examination revealed no typical
peripheral or posterior-pole granulomas. Six patients
(66.7%) had histories of exposure to a cat or dog, while the
other 3 (33.3%) did not. Immunological examinations of
both serum and the aqueous humor were performed in 7
patients (77.8%), and only of those of the aqueous humor
were conducted in the other 2 patients (22.2%). Details of all
9 patients are shown in Table 1.

In 8 out of 9 patients (88.9%), yellow-and-white dot-
shaped lesions ranging from 80 to 300 μm in diameter were
observed in the fundus (Figure 1). In the remaining cases
(11.1%), no obvious yellow-and-white dot-shaped lesions
were seen. In panoramic fundus photos, a perivascular white
sheath was evident (Figure 1, B1 B2 B3 B4). A total of 20
yellow-and-white dot-shaped lesions were seen in eight
patients. Ten of these lesions (50%) were able to be scanned
by OCT. Among them, 2 (20%) showed heterogeneous
hyper-reflection in the disrupted neuroretina (Figure 2(a)
arrow and 2(d)) and 2 (20%) showed hyper-reflection in the
outer layer of the neuroretina (Figure 2(a) triangle). In 3
(30%) lesions, a high-reflection mass was seen on the surface
of the neuroretina (Figures 2(b) and 2(f)). In 2 (20%) lesions,
a high-reflection mass involving the entire neuroretina was
seen (Figure 2(e) and 2(g)). One lesion (10%) was a high-
reflection mass located in the vitreous body (Figure 2(c)).

FFA was not performed in one patient due to allergies
and in another 6-year-old patient who was uncooperative.
In the remaining 7 patients (77.8%), the yellow-and-white
fundus lesions observed in fundus pictures showed blocked
fluorescence or leakage on FFA. Six of these patients (85.7%)
showed “bristle-like” leakage of fluorescein in the small-
and medium-branch veins of the retina in the middle and late
stages of angiography, suggesting the permeability of the
blood vessels was increased. No retinal blood vessel leakage
was observed in the remaining patients (11.1%) (Figure 3).

In B-mode ultrasound, 3 cases (33.3%) exhibited vitreous
membranes and bands and 6 cases (66.7%) showed punctate
interfaces usually related to inflammatory responses of the
vitreous (Figure 4).

4. Discussion

Although toxocariasis is the most common helminth in-
fection of humans in industrialized countries [7], the public
is poorly aware of its complications [8]. In addition to the
typical granulomatous manifestations, there are also atypical
toxocariasis-related fundus manifestations. The variable
clinical manifestations make a correct diagnosis of OT
difficult, and patients tend to be misdiagnosed in clinical
practice.

According to previous reports, the demographic char-
acteristics of OT differ by region. In the European and US
populations, most OT patients were children, while in South
Korea and Japan, most affected patients were adults, pre-
sumably attributed to food habits [9, 10]. In this case series,
all 9 patients were young. As young patients may often have
ambiguous complaints and atypical manifestations, ocular
toxocariasis, especially at earlier stages, could be
misdiagnosed.

In this study, four of atypical OT patients (44.4%) were
misdiagnosed in other hospitals before visiting our clinic.
They had received diagnoses of perilimbalitis, uveitis, vas-
culitis, and/or retinal vasculitis in local hospitals. Conse-
quently, it might have caused delays in treatment or even
inappropriate management. Therefore, it is crucial to apply
multiple imaging techniques to improve the diagnosis of the
disease. Three patients (33.3%) in this study had no histories
of exposure to pets, and they might have been exposed to soil
contaminated with *Toxocara* eggs. A study found that 13%–
87.1% soil samples collected from parks were 13%–87.1% positive for Toxocara eggs, especially samples taken in certain rural and urban areas [11, 12]. In this study, 6 atypical OT patients (66.7%) had a BCVA of 0.2 or higher, which might also interfere diagnosis. Because the remaining visual acuity of these children was still useful, the disease itself was likely to be overlooked. Two patients (22.2%) underwent vitrectomy due to vitreous opacities in this study, while no obvious granulomas were seen during the operations. Nevertheless, a diagnosis of OT was made based on immunological detection combined with postoperative imaging findings. It is recommended that OT should be considered in patients with unknown causes of uveitis and endophthalmitis.

All patients in this study were clinically diagnosed based on intraocular inflammation, and immunological findings after other ocular infections were excluded. It has been confirmed that specific antibodies exist in the eyes of OT patients. In our study, serum and aqueous humor anti-Toxocara canis IgGs were positive in all 7 patients tested, and all patients but 1 (11.1%) displayed a Goldmann–Witmer coefficient greater than 4. Although the GWC of the remaining one patient was less than 4, both serum and aqueous humor Anti-Toxocara canis IgG levels were significantly increased in this case, indicating a status of infection.

We applied multimodal fundus imaging to illustrate changes in the fundus associated with OT. In particular, we used high-resolution OCT combined with panoramic fundus photography to describe the lesion. Ultra-wide-angle fundus photos showed scattered yellow-and-white lesions with diameters ranging 80–300 μm located at the posterior pole or near the equator. Unlike the common granuloma of typical OT, these yellow-and-white ocular lesions were small in size (microgranulomatous) [13]. Microgranulomas were located outside or inside the neuroretina [14]. At the same time, premacular membrane, intraocular proliferative membrane, and vitreous opacity were among the common concomitant symptoms of OT. We showed that the yellow-and-white lesions (microgranulomas) in the eye displayed not only at all layers of the neuroretina but also in the vitreous. Nevertheless, the specific components of the lesion deserve further investigation.

### Table 1: The clinical data and immunological detection results of 9 patients with OT.

| Case | Gender | Age (year) | Newly diagnosed patient: yes or no | Contacted with dogs or cats: yes or no | Affected eye | Slit-lamp examination | Aqueous humor anti-Toxocara canis IgG (U/L) | Serum anti-Toxocara canis IgG (U/L) | GWC |
|------|--------|------------|-----------------------------------|----------------------------------------|-------------|----------------------|------------------------------------------|--------------------------------------|-----|
| 1    | Male   | 7          | Yes                               | Yes                                    | OS          | 0.8                  | No Anterior chamber flare (+) cells (+) | 5.45                                 | 15.08 | 31.41 |
| 2    | Female | 14         | No (diagnosed as periphlebitis)   | Yes                                    | OD          | 0.3                  | No Anterior chamber flare (+) cells (+) | 6.68                                 | 5.96  | 194.19 |
| 3    | Male   | 8          | Yes                               | Yes                                    | OD          | 0.15                 | No Anterior chamber flare (+) cells (+) | 31.72                                | 39.89 | 21.7  |
| 4    | Male   | 10         | Yes                               | Yes                                    | OS          | 0.07                 | No Anterior chamber flare (+) cells (+) | 4.92                                 | 5.94  | 70.18 |
| 5    | Female | 12         | Yes                               | Yes                                    | OD          | 0.8                  | No Anterior chamber flare (+) cells (+) | 7.04                                 | 11.9  | 102.9 |
| 6    | Male   | 7          | No (diagnosed as fundus hemorrhage) | No                                    | OS          | 0.2                  | No Anterior chamber flare (+) cells (+) | 27.91                                | 7.64  | 97.84 |
| 7    | Male   | 6          | Yes                               | Yes                                    | OS          | 0.01                 | No Anterior chamber flare (+) cells (+) | 50.43                                | 41.61 | 2.39  |
| 8    | Male   | 11         | No (diagnosed as uveitis)         | No                                    | OS          | 0.25                 | No Anterior chamber flare (+) cells (+) | 31.18                                |       |       |
| 9    | Female | 16         | No (diagnosed as retinal vasculitis) | No                                    | OS          | 0.2                  | No Anterior chamber flare (+) cells (+) | 37.89                                |       |       |

Note: patient no. 6 and 7 underwent vitrectomy because of vitreous opacity, no obvious granuloma was found during the operation, and the imaging examinations (except B-mode ultrasound) were the results of postoperative examination. Patient no. 8 and 9 performed only an aqueous humor test for Ascaris lumbricoides IgG. GWC: Goldmann–Witmer coefficient. The GWC was calculated as ([specific IgG in aqueous humor/specific IgG in serum]/[total IgG in aqueous humor/total IgG in serum]).
related to the damage of the outer blood retinal barrier, presumably caused by migration of larvae from the choroid to the retina. It also might be related to retinal and choroidal inflammation associated with the lesion. In one patient, we saw no significant leakage or dilatation of small blood vessels. Possibly, this patient was at a late phases of OT. In younger children, vision loss might be overlooked and the patient might be misdiagnosed. When the symptom was finally noticed and a correct diagnosis was made, the inflammatory response might have been controlled and the permeability of the blood vessel recovered.

Ocular B-mode ultrasound can reflect various vitreoretinopathies in OT, especially the severity of intraocular proliferation and inflammation. Various proliferative membranes and bands in the affected eye made them supplement evidence for OT diagnosis.

Figure 1: Panoramic fundus photos: yellow-and-white dot-shaped lesions were visible. Enlarged fundus photos show the perivascular white sheath (oval dotted lines indicate the selected area corresponding to figure (B1), (B2), (B3), and (B4), and A, B, C, D, E, F, and G scan lines correspond to Figure 2).
Figure 2: OCT images of yellow-and-white punctate lesions marked in Figure 1. The lesions were heterogeneous hyper-reflective in the neuroretina (a (arrow) and d), hyper-reflective in the outer retina (a (triangle)), high-reflective mass on the surface of the neuroretina with a reflective attenuation beneath (b and f), high-reflective mass involving the entire layer of the disrupted retina (e and g), and high-reflective mass located in the vitreous body (c).

Figure 3: Continued.
5. Conclusions

In summary, imaging manifestations of atypical juvenile OT presented the following characteristics: intraocular proliferative membranes and bands, vascular white sheaths, yellow-and-white lesions of the fundus that could affect any layer of the retina, and “bristle-like” leakage of small and medium veins in FFA. For children with such manifestations, the possibility of OT should be considered. Multi-modality image analysis combined with immunological tests, as well as a history of pet exposure, should be used for diagnosis.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

The authors have no conflicts of interest.

Acknowledgments

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