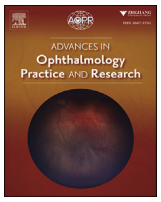
Advances in Ophthalmology Practice and Research 3 (2023) 141–146

Contents lists available at ScienceDirect

Advances in Ophthalmology Practice and Research

journal homepage: www.journals.elsevier.com/advances-in-ophthalmology-practice-and-research



Full Length Article

Clinical characteristics of radiation-induced optic neuropathy: A single-center retrospective study

Yongping Wang, Junxia Fu, Huanfen Zhou, Hongen Li, Quangang Xu, Shihui Wei *

Department of Ophthalmology, Chinese PLA General Hospital, Beijing, China

ARTICLE INFO

Keywords:
Radiation-induced optic neuropathy (RION)
Magnetic resonance imaging (MRI)
Optical coherence tomography (OCT)
Hyperbaric oxygen therapy (HBOT)
High-dose intravenous methyl prednisolone (IVMP)

ABSTRACT

Purpose: To observe the clinical and imaging characteristics of radiation-induced optic neuropathy (RION).
Methods: We retrospectively reviewed the clinical data of 43 patients (69 eyes) who were diagnosed with RION at the Chinese PLA General Hospital from 2010 to 2021.
Results: The latency from radiotherapy to onset of visual loss ranged from 1 to 132 (36.33 ± 30.48) months. Optic disc pallor and optic disc edema were found in 27.0% (10/37) and 8.1% (3/37) of the eyes, respectively, within 2 months. After treatment, the best corrected visual acuity (BCVA) was restored in 24.6% (17/69) of the eyes and the final BCVA improved in 13.0% (9/69) of the eyes. An 82.5% (33/40) of the eyes with magnetic resonance imaging (MRI) showed enhancement of the affected optic nerve, mostly (69.7%) in the intracranial segment, and 36.4% (12/33) of the eyes with expansion and T2-high signals also showed enhancement of the affected optic nerve. The superior retinal nerve fiber layer (RNFL) and the outer circle superior quadrant (OS) of the inner limiting membrane to retinal pigment epithelium (ILM-RPE) layer thinned significantly during the first month. The center of the ILM-RPE layer thickened significantly during the first two months and the inner circle temporal quadrant (IT) of the ILM-RPE layer thickened significantly from the third to sixth month. The RNFL thinned significantly after 6 months except for the temporal quadrant, and the average inner circle superior quadrant (IS) and outer circle of the ILM-RPE layer thinned significantly after 6 months. There was no significant difference between hyperbaric oxygen therapy (HBOT) and high-dose intravenous methylprednisolone (IVMP) therapy in improving BCVA recovery or final BCVA ($P > 0.05$).
Conclusions: The structural damage of the RNFL and ILM-RPE layer occurred during the first month, the RNFL showed progressive thinning during the follow-up period, while the ILM-RPE layer showed thinning during the first month, thickening from the third to sixth month, and thinning after 6 months. There was a discrete region of enhancement of the optic nerve, often with expansion and high-T2 signals on MRI. HBOT and high-dose IVMP therapy were hardly effective for treating RION in the non-acute stage.

1. Introduction

Radiation-induced optic neuropathy (RION) is a pathological change due to delayed radionecrosis in the CNS that can cause severe and acute monocular or binocular vision loss several months to years after radiotherapy. The latency interval from radiotherapy to onset of visual loss ranged from 3 months to 9 years, with an average of 18 months.[1–3] Optic discs are usually normal or pale at the time of initial visual loss.[3,4] Magnetic resonance imaging (MRI) of RION is essential to exclude compressive, inflammatory, and infiltrative neuropathy, and optical coherence tomography (OCT) is instructive in differentiating RION from inflammation and ischemic optic neuropathy. Therefore, it is clinically important to characterize the imaging features of MRI and OCT for the diagnosis of RION. Currently, it is believed that high-dose intravenous methylprednisolone (IVMP) and anticoagulant therapy have an uncertain effect on the outcome of patients with RION[5] while hyperbaric oxygen therapy (HBOT) has a good effect within 72 h of vision loss, but the improvement was not significant after 2 weeks.[2] Also, early bevacizumab therapy in steroid-refractory RION shows satisfactory results.[6] However, it is unclear whether HBOT should be used aggressively after 2 weeks of visual loss. The purpose of this study is to characterize the MRI and OCT imaging features of patients with RION, finding more clinical

* Corresponding author.
E-mail addresses: wangyongping@firsthosp-dmu.com (Y. Wang), fujunxiaeye@outlook.com (J. Fu), zhouzhoueye@163.com (H. Zhou), empyreal614@163.com (H. Li), xuquangang@126.com (Q. Xu), weishihui706@hotmail.com (S. Wei).

https://doi.org/10.1016/j.aopr.2023.05.003
Received 26 October 2022; Received in revised form 27 May 2023; Accepted 28 May 2023
Available online 29 May 2023

characteristics of RION which are of great significance in the diagnosis and treatment of RION.

2. Methods

Subjects: There were 53 patients (22 female) and 89 affected eyes in this study. After excluding 10 cases (20 eyes) of vision loss due to direct tumor invasion or other reasons, a total of 43 cases (69 eyes) were included. We collected details of the radiation protocol, chemotherapy, abnormal cerebrospinal fluid (CSF) constituents and optic disc appearance.

Spectral-domain Optical Coherence Tomography (SD-OCT) Examination: All the patients underwent Spectral-domain Optical Coherence Tomography (SD-OCT) examinations performed on a Cirrus SD-OCT system (Carl Zeiss Meditec AG, Jena, Germany) without pupil dilation. The RNFL was measured by SD-OCT using a 3.46-mm diameter circular scan centered around the optic disc, and the following parameters for the RNFL were calculated: average RNFL thickness, RNFL thickness in the 4 respective quadrants (superior, temporal, nasal and inferior). Total macular, excluding the fovea (1 mm central circle), is divided into 9 sectors according to the Early Treatment Diabetic Retinopathy Study (ETDRS).

Visual Function Testing: The visual field was measured using a Humphrey Field Analyzer II (Carl Zeiss Meditec AG) using a Goldmann size III stimulus. We collected information on vision loss, including the temporal relationship of vision loss to radiotherapy, the evolution of vision loss, pre- and post-treatment best corrected visual acuity (BCVA), final BCVA (6 months after onset). The BCVA was assessed using a Snellen Eye Chart (decimal acuity) and converted into logarithmic minimum angle of resolution (logMAR) units. Concerning the Macula Translocation in Age-related Neovascular disease (MARAN) protocol,[7] the visual acuity of no light perception (NLP), light perception (LP), hand motion (HM), finger count (FC)/10 cm, and FC/30 cm were assigned the logMAR values of 5.0, 4.0, 3.0, 2.7, and 2.2 logMAR units, respectively.

MRI: Two neuro-ophthalmologists evaluated all MRI scans, noting the enhancement, expansion and thinning of the optic nerves, high-T2 signals, and excluding demyelination or compressive lesions.

Treatment: All patients were treated with the same basic neurotrophic vasodilator drugs, including the control group (12 patients). In addition, 10 patients were treated with HBOT, 9 patients with high-dose IVMP, and 12 patients with HBOT combined with high-dose IVMP. The specific treatment scheme and course of HBOT: 2.5 atmospheric pressure, 40–60 min Qd, 10 times. The specific treatment scheme and course of high-dose IVMP: 1000 mg methylprednisolone intravenously Qd was given for 3 days, and changed to 500 mg for another 3 days, followed by 12 tablets of methylprednisolone taken orally and reduced in sequence.

Statistical Analysis: Statistical analysis was performed using the SPSS software version 26.0 (IBM Corporation, Armonk, NY, USA). An independent sample *t*-test was used to compare the OCT groups with different course of disease and different treatment schemes, $P < 0.05$ was considered statistically significant.

3. Results

3.1. Clinical features, ophthalmoscopy and visual function

Demographic Features: The age of patients at the time of radiation therapy ranged from 19 to 85 years (49.54 ± 13.14 years). Vision loss was monocular in 17 patients and binocular in 26 patients (Table 1). The main dose of radiotherapy for lesions was from 36–72.6 (58.83 ± 10.64) Gy. The tumor types and radiation doses and number of treatments (25 patients with a definite dose, of which 22 patients received a total dose ≥50 Gy and a single dose >2 Gy) are listed in Table 2. The latency interval from completion of radiation to onset of vision loss ranged from 1–132 (36.33 ± 30.48) months. Sixteen patients treated with chemoradiotherapy and they showed no statistically significant differences in short-term recovery of BCVA ($P = 0.466$) and final BCVA ($P = 0.699$) compared to those treated with radiotherapy only. The short-term recovery of BCVA was found in 24.6% (17/69), and the final BCVA (6 months after onset) improved in 13.0% (9/69) of the eyes (Table 1).

CSF constituents were collected from 27.9% (12/43) of the patients before the treatment. The CSF leukocyte count was $4.00 \pm 6.21 \times 10^6$/L in 66.7% (8/12) of the patients. The concentration of protein was clearly higher (616.85 ± 325.78 mg/L) in 33.3% (4/12) of the patients (Table 1).

Ophthalmoscopy showed that 40 eyes had optic disc pallor, and 26 eyes had normal-appearing optic discs (1 week–10 years after onset). Within 2 months of onset, 64.9% (24/37) of the eyes had normal-appearing optic discs, 27.0% (10/37) of the eyes had optic disc pallor and 8.1% (3/37) of the eyes showed edema (Table 1).

Vision Loss: When binocular vision loss occurred, it occurred consecutively in both eyes in 60.5% (26/43) of the patients, in an interval of 2 weeks–23 months. In one eye, vision loss was sudden and non-progressive, but in 27 eyes, sudden vision loss was followed by chronic progression. In 41 eyes, the decline of vision was subacute over 3 days –4 months. The BCVA values at different stage are shown in Table 3.

Visual Fields: Visual fields were available in 3.5% (30/69) of the eyes at the initial visit. There were 3 eyes with temporal and superior hemianopia, 2 eyes with inferior hemianopia, 4 eyes with normal visual fields and 18 eyes with diffuse defects.

Table 1
Demographic Features, CSF and ophthalmoscopy.

				Cases	Results
The age of patients at the time of radiation therapy				43	49.54 ± 13.14
The main dose of radiotherapy for lesions				43	58.83 ± 10.64
Vision loss	Monocular			17	39.5% (17/43)
	Binocular			26	60.1% (26/43)
	The latency interval from completion of radiation to onset (months)			43	36.33 ± 30.48
	Recovery of BCVA	short-term improved		17	24.6% (17/69)
		final BCVA (6 months after onset) improved		9	13.0% (9/69)
		chemoradiotherapy compared to those treated with	short-term improved	6	$P = 0.466$
		radiotherapy only (16 patients)	final BCVA improved	2	$P = 0.699$
CSF	Leukocyte count ($\times 10^6$ /L)			8	4.00 ± 6.21
	The concentration of protein (mg/L)			4	616.85 ± 325.78
Optic disc	1 week~10 years after onset	pallor		40	60.0% (40/69)
		normal-appearing		26	37.7% (26/69)
	Within 2 months of onset	normal-appearing		24	64.9% (24/37)
		pallor		10	27.0% (10/37)
		edema		3	8.1% (3/37)

Table 2
Tumor type, radiation doses and times.

	Nasopharyngeal carcinoma	Pituitary adenoma	Lymphoma	Intraorbital tumor	Skull base tumors	Olfactory neuroblastoma	Paranasal sinus tumor	Clivus tumor	Bone metastases	Cerebellar astrocytoma
Cases	14/43	8/43	6/43	3/43	2/43	3/43	3/43	2/43	1/43	1/43
Percentage	32.6%	18.6%	14.0%	7.0%	4.7%	7.0%	7.0%	4.7%	2.3%	2.3%
Definite dose	7/14	5/8	3/6	0	1/2	3/3	3/3	1/2	1/1	1/1
Dose (Gy)	64.9 ± 5.2	48.8 ± 11.5	45.5 ± 4.3	–	54.0	66.7 ± 5.8	69.2 ± 1.4	66.0	54.0	54.0
Number of radiotherapy sessions (F)	31.0 ± 3.5	28.0 ± 11.3	22.0 ± 5.7	–	–	32.7 ± 2.5	30.0 ± 4.4	22.0	30.0	27.0

3.2. SD-OCT

A 74.4% (32/43) of the patients were evaluated for their RNFL (46 eyes) and the thickness of the inner limiting membrane to retinal pigment epithelium (ILM-RPE) (36 eyes) using SD-OCT (Table 4). A total of 42 eyes were included after excluding 4 of the 46 eyes with optic disc edema (at 0.25, 1, 1.5 and 4.4 months). Except for the central part of the ILM-RPE layer, thinning occurred both in the RNFL and ILM-RPE layer in patients after 1 month, in which the thinning was significant in the superior quadrant of the RNFL (95% CI 2.08 to 66.56; $P = 0.038$) and the Outer circle Superior quadrant (OS) of the ILM-RPE layer (95% CI 4.37 to 45.39; $P = 0.021$). Moreover, except for the inferior quadrant of the RNFL, the RNFL showed further thinning in the first 2 months. However, thickening occurred in the central part and inner circle of the ILM-RPE layer in the first 2 months, in which significant thickening occurred in central part of the ILM-RPE layer (95% CI –32.95 to –4.20; $P = 0.015$). The ILM-RPE layer thickened both in the inner and outer circles in 3–6 months, in which the Inner circle Temporal quadrant (IT) was significantly thicker (95% CI –42.22 to –3.83; $P = 0.022$). The RNFL was significantly thinner ($P < 0.05$) after 6 months except for the temporal quadrant, and the ILM-RPE layer was thinner after 6 months, in which the average ILM-RPE layer thickness, Inner circle Superior quadrant (IS) and outer circles were significantly thinner ($P < 0.05$). (Table 4).

MRI: An 82.5% (33/40) of affected eyes showed ipsilateral enhancement of the optic nerve (1 week–2 years , 13.5 ± 19.97 weeks) on MRI (T1 Gado sequences and T2 sequences) (Table 5, Fig. 1).

Treatment: For the patients whose BCVA values were NLP, there was no improvement after treatment except for an early 50s patient (poorly differentiated squamous cell carcinoma of the right sphenoid sinus, 70 Gy/28 F, NLP in the left eye 32 months after radiotherapy, high-dose IVMP combined with HBOT 3 weeks after onset, BCVA improved to 0.7 LogMAR 6 months later). For the patients whose BCVA values were better than the NLP, the improvement rate was the highest in the HBOT treatment group (57.1%). Compared with the control group, there was no significant difference with the HBOT, high-dose IVMP and HBOT combined with high-dose IVMP groups in improving the BCVA and final BCVA ($P > 0.05$), (Supplemental Table 1).

4. Discussion

RION results from delayed radiation necrosis of the anterior visual pathway, leading to severe and irreversible vision loss due to radiation-induced deterioration of the optic nerves caused by radiation radiotherapy of intracranial and external cranial or paranasal sinus tumors. With the popularization of radiation therapy and the emergence of new radiotherapy devices, the complications due to radiation therapy have increased. Ophthalmologists are required to pay attention to the diagnosis and treatment of RION. In this study, the imaging characteristics and treatment of 43 RION patients were analyzed based on clinical data.

Table 3
BCVA at different stage.

	Under 1.0 logMAR (eyes, blindness)			1–0.3 logMAR (eyes)	above 0.3 logMAR (eyes)
	Total (eyes)	Monocular (cases)	Binocular (cases)		
Recovered BCVA	45/69 (65.2%)	23/43 (53.5%)	11/43 (25.6%)	14/69 (20.3%)	10/69 (14.5%)
Final BCVA	26/36 (72.2%)	14/36 (38.9%)	6/36 (16.7%)	8/36 (22.2%)	2/36 (5.6%)

Consistent with previous reports,[2,8–16] the vision loss in our patients was usually acute and severe (65.2% onset BCVA at 1.0 logMAR and 72.2% final BCVA irreversible). Also, more than half of the patients (59.4%, 41/69 eyes) showed progressive vision loss for several months (Table 3). Although the short-term recovery of the BCVA improved (BCVA above 0.3 logMAR increased from 8.7 to 14.5%), the final BCVA eventually worsened (the ratio of blindness increased from 65.2 to 72.2% and the BCVA above 0.3 logMAR dropped from 14.5 to 5.6%). Moreover, 27.8% of the final BCVA above 1.0 logMAR is consistent with the long-term results of Kim et al.,[17] who reported on the natural course of RION with BCVA retention rates of 20/200 or better in 29% of patients at 3 years and 23% of patients at 5 years.

The latency period from completion of radiation to onset of vision loss, which ranged from 1 month to 11 years (36.33 ± 30.48 months), was similar to that reported in previous studies.[2,3,18] Most reported RION cases were exposed to a total dose of at least 50 Gy.[2,9,10,13,14] However, 3 of our patients developed RION after receiving only 16 and 40 Gy (pituitary adenoma) and 41.4 Gy (NK-T lymphoma). Although these 3 patients received radiation distributed throughout the whole brain, the two pituitary adenoma patients showed enhancement of the optic nerve in the intracranial segment, suggesting that this region may be relatively susceptible to radiation-induced delayed necrosis.[2,13,19,20]

Within 2 months of symptom onset, 64.9% (24/37) of the eyes had normal-appearing optic discs, which was consistent with an earlier study,[4] 8.1% (3/37) of the eyes showed edema, which is also consistent with previously published cases[9,10,15] and 27.0% (10/37) of the eyes had optic disc pallor, indicating that axonal damage occurred in the preclinical period.[2]

In the early stage of RION (first month), thinning occurred both in the RNFL and ILM-RPE layer, in which significant thinning occurred in the superior quadrant of the RNFL ($P = 0.038$) and the OS of the ILM-RPE ($P = 0.021$). This result indicated that structural injury of the RNFL and total macular ganglion cell layer (mGCL) and retinal ganglion cell layer (RGCL) occurred simultaneously within the first month. This pathological change supported the theory that demyelination is secondary to glial cell mutations caused by radiotherapy.[18] Thickening occurred in the central part and inner circle of the ILM-RPE layer 2 months after onset and the central part of the ILM-RPE significantly thickened ($P = 0.015$). The ILM-RPE layer thickened both in the inner and outer circles 3–6 months after onset and the IT of the ILM-RPE layered thickened significantly ($P = 0.022$), which may be related to the development of ischemic hypoxia in ganglion cells secondary to inflammatory changes in the vascular endothelium.[2] It also suggested the presence of radiation maculopathy.[19] The RNFL and the ILM-RPE layer were significantly thinner ($P < 0.05$) after 6 months of onset, which illustrated that the mutated glial cells gradually increased after the onset of RION and demyelination

Table 4
The comparison of the RNFL & ILM-RPE thickness at each duration mean ± SD, μm.

Parameters	<1 month	1 month	P^a	2 months	P^b	3 months	P^c	3–6 months	P^d	>6 months	P^e
Average RNFL	91.50 ± 6.36	76.65 ± 15.08	0.194	74.60 ± 22.03	0.812	69.00 ± 10.47	0.236	76.00 ± 12.65	0.926	56.00 ± 7.91	0.009
Superior	133.50 ± 7.78	99.18 ± 20.98	0.038	98.20 ± 38.96	0.959	80.00 ± 23.16	0.061	97.67 ± 18.81	0.878	58.60 ± 7.02	0.000
Nasal	73.50 ± 2.12	62.47 ± 9.64	0.134	61.80 ± 12.93	0.900	65.57 ± 11.90	0.510	64.33 ± 10.09	0.692	52.20 ± 4.44	0.034
Inferior	107.00 ± 22.63	95.82 ± 27.04	0.584	87.80 ± 31.05	0.578	80.00 ± 17.64	0.170	90.50 ± 29.24	0.689	51.80 ± 6.06	0.000
Temporal	52.00 ± 1.41	49.12 ± 14.92	0.793	50.60 ± 14.89	0.847	50.29 ± 12.47	0.857	51.50 ± 11.69	0.728	45.40 ± 3.97	0.367
Average ILM-RPE	74.00 ± 5.29	257.50 ± 16.93	0.134	251.50 ± 7.78	0.644	253.25 ± 12.97	0.662	272.33 ± 8.50	0.180	212.00 ± 34.27	**0.005**
Center	229.33 ± 4.16	231.43 ± 10.84	0.751	250.00 ± 8.89	**0.015**	215.71 ± 35.42	0.291	218.33 ± 15.50	0.096	203.25 ± 31.57	0.172
IS	304.33 ± 1.53	286.50 ± 18.08	0.117	293.00 ± 9.85	0.562	279.14 ± 16.10	0.375	305.00 ± 18.52	0.130	235.75 ± 34.87	0.001
II	292.67 ± 8.02	283.14 ± 16.94	0.366	286.67 ± 6.81	0.734	281.57 ± 17.24	0.844	303.33 ± 21.03	0.091	238.50 ± 40.05	0.109
IN	297.33 ± 2.08	285.64 ± 17.95	0.289	297.67 ± 13.20	0.294	277.00 ± 20.58	0.334	302.00 ± 22.65	0.188	241.50 ± 40.55	0.115
IT	292.33 ± 11.02	276.64 ± 14.08	0.092	283.33 ± 2.89	0.436	274.29 ± 16.20	0.734	299.67 ± 14.64	0.022	230.50 ± 40.27	0.104
OS	281.67 ± 7.77	256.79 ± 15.96	0.021	255.33 ± 5.51	0.881	250.14 ± 14.45	0.366	274.67 ± 14.84	0.096	218.75 ± 21.39	0.001
OI	258.00 ± 8.66	245.14 ± 15.46	0.190	240.33 ± 10.26	0.619	241.43 ± 15.50	0.610	256.00 ± 10.82	0.271	217.25 ± 14.68	0.005
ON	286.00 ± 8.19	265.07 ± 19.65	0.096	267.00 ± 21.28	0.881	254.50 ± 20.10	0.288	281.00 ± 23.39	0.234	224.75 ± 25.91	0.004
OT	259.67 ± 8.39	244.43 ± 12.42	0.064	241.67 ± 8.39	0.722	241.67 ± 14.00	0.665	258.33 ± 6.81	0.084	213.75 ± 25.46	0.003

Significance of bold fonts: *P* values < 0.05.pRNFL: thickness of peripapillary retinal nerve fiber layer; ILM-RPE: thickness of total macular ganglion cell layer (mGCL) and retinal ganglion cell layer (RGCL) spanning from the inner limiting membrane-retinal pigment epithelium (ILM-RPE).
IS: Inner circle Superior quadrant; II: Inner circle Inferior quadrant; IN: Inner circle Nasal quadrant; IT: Inner circle Temporal quadrant.
OS: Outer circle Superior quadrant; OI: Outer circle Inferior quadrant; ON: Outer circle Nasal quadrant; OT: Outer circle Temporal quadrant.
P^a: <1 month *vs.* 1 month; P^b: 1 month *vs.* 2 months; P^c: 1 month *vs.* 3months; P^d: 1 month *vs.* 3–6 months; P^e: 1 month *vs.* >6 months.

Table 5
Lesions of RION on MRI examination.

	Optic nerve T1 enhancement (lesions)						T2
	Intraorbital	Canalicular	Intracranial	Chiasma	Expansion	Enhancing with expansion & T2-high signal	T2-high signal
Cases	11/33	9/33	23/33	4/33	13/33	12/33	27/33
Rates	33.3%	27.3%	69.7%	12.1%	39.4%	36.4%	81.8%

continued to aggravate, eventually leading to neuronal degeneration.[2] The RNFL continued thinning for half a year after onset, whereas the macular region showed radiation maculopathy with varying degrees of thickening of the ILM-RPE layer. This phenomenon is useful in clinical practice, as it can be used for differential diagnosis, since the RNFL thickness is reduced several months later after that of the ILM-RPE layer in many optic neuropathies, such as optic neuritis, ischemic optic neuropathy and Leber hereditary optic neuropathy (LHON).

An 82.5% (33/40) of the eyes showed ipsilateral enhancement of the optic nerve on MRI, in which 36.4% (12/33) of the eyes increased with the expansion and T2-high signals on the affected segment (Table 5, Fig. 1). The enhancement time was at least 5 days (3 weeks–24 months, 14.08 ± 20.64 weeks), but extended by one patient to at least 2 years, which exceeded the enhancement time of 3–13 months previously reported.[2,10] These imaging abnormalities are of great significance in the differential diagnosis of RION, as enhanced lesions with expansion or T2-high signal can be rarely seen in tumor-infiltrating optic neuropathy.[21] Inflammatory optic neuropathies may show RION-like MRI abnormalities that can be differentiated by the history of radiation and irreversible persistent vision loss. Among the patients who received radiotherapy for nasopharyngeal and maxillary sinus lesions, 12 eyes showed T1 enhancement in the orbital segment of the optic nerve which has been rarely reported, despite the available pathological evidence.[16,22] This indicated that the intraorbital segment of the optic nerve can be affected by radiation and be seen as T1 enhancement even with the presence of abundant connective tissue wrapping.

Previous studies have reported that HBOT can significantly improve the BCVA within 72 h from the onset of RION, but the improvement was not significant after 2 weeks.[2] In this study, HBOT treatment was performed 2 weeks after the onset of RION (2 weeks–19 months), and no significant difference was found in the improvement of BCVA and final BCVA ($P > 0.05$), which is consistent with the findings of a previous study by Lessell.[5] We also found that there was no significant difference between the high-dose IVMP group and the HBOT combined with high-dose IVMP group compared with the control group in the improvement of the BCVA and final BCVA. The observed therapeutic effect once again supports the finding that radiation induced somatic cell mutations in glial cells ultimately lead to demyelination and neuronal degeneration, a process that is irreversible after 2 weeks.[5]

We acknowledge some major limitations of this study, including the following. First, the main limitations are that this study includes the retrospective collection of subjects and the fact that our institution is a tertiary care center, likely resulting in referral bias for more critical cases. Second, a time delay from symptom onset to initial visit in our tertiary care institution may also have obscured the time of onset of visual

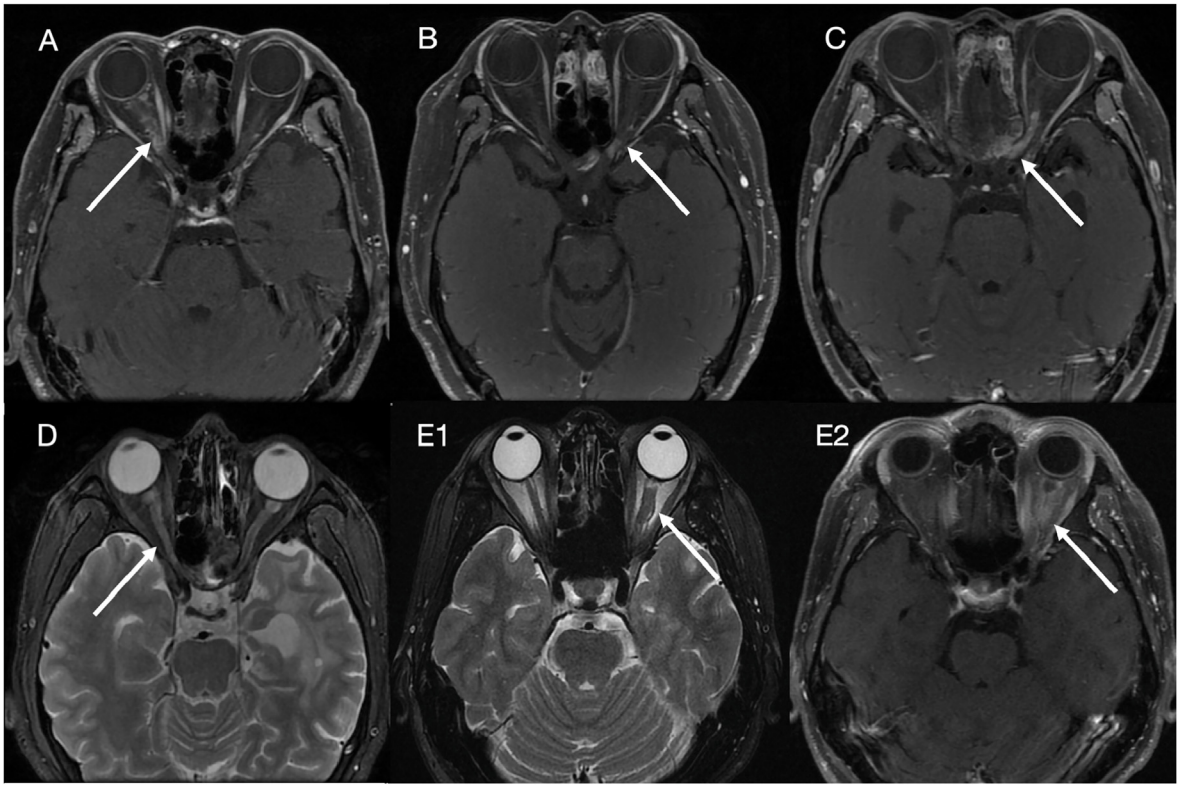


Fig. 1. Lesions of RION on MRI examination. (A) Intraorbital segment (T1 Gado sequences); (B) Canalicular segment (T1 Gado sequences); (C) Intracranial segment (T1 Gado sequences); (D) T2-high signal; (E1&E2) Nerve enhancement with expansion (D = 75 mm) (T1 Gado sequences) & T2-high signal.

symptoms in some cases. Third, only part of the final BCVA of the patients can be collected due to death and other reasons. Despite these limitations, we believe our data will contribute to a more comprehensive understanding of RION.

Study approval

The authors confirm that any aspect of the work covered in this manuscript that involved human patients or animals was conducted with the ethical approval of all relevant bodies and the study was performed in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee for Human Research of the hospital (approval number S2017-093-01).

Author contributions

Planning: YW, HZ; Conduct: YW, JF; Conception and design: YW, HZ; Acquisition of data or analysis and interpretation of data: YW, HL, QX; Writing original draft preparation: YW, JF; Funding acquisition: SW; Supervision: SW. All authors reviewed the results and approved the final version of the manuscript.

Funding

This work was supported by the National Key Research and Development Program. (Project code: 2018YFE0113900 to S·W.) and the National Natural Science Foundation of China (Project code: 81870662 to S·W.) on the study.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

Thanks to all the peer reviewers and editors for their opinions and suggestions.

Abbreviations

RION	Radiation-induced optic neuropathy
LHON	Leber hereditary optic neuropathy
BCVA	Best corrected visual acuity
MRI	Magnetic resonance imaging
RNFL	Retinal nerve fiber layer
ILM-RPE	Inner limiting membrane to retinal pigment epithelium
HBOT	Hyperbaric oxygen therapy
IVMP	Intravenous methylprednisolone
OCT	Optical coherence tomography

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.aopr.2023.05.003.

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