Abstract

**Purpose:** To present a patient with radiation chiasma neuropathy, secondary to radiotherapy of paranasal sinus lymphoma who was referred for evaluation of gradual decrease of vision in both eyes

**Case report:** The patient was a 38-year-old male, with history of right maxillary sinus lymphoma, who underwent surgery, chemotherapy and radiation therapy. One year after radiotherapy, he noticed gradual decrease in his right eye vision. He referred to our center 6 months after onset of visual symptoms (1.5 years after radiotherapy). On his first examination, visual acuity (VA) of right eye was no light perception (NLP), and right optic disc was severely atrophic. Other examinations of right eye were unremarkable. The VA of left eye was \(10/10\) with correction, color vision was normal, slit lamp exam and tonometry was normal as well, but bow tie atrophy of left optic disc was detected. Visual field of left eye revealed temporal hemianopia. MRI showed thickening and enhancement of optic chiasm, especially in right side. In follow-up the enhanced lesion enlarged posteriorly and involved both optic tracts and optic radiations. In spite of treatment with high dose corticosteroid and hyperbaric oxygen, within two years following radiotherapy, vision of left eye gradually decreased to NLP too.

**Conclusion:** Radiation-induced optic neuropathy is an important differential diagnosis of decreased vision in a case with history of head and neck radiotherapy. Since this complication is very important with ominous consequence, ophthalmologists and radiotherapists should be aware of that; and decrease the chance of its occurrence by lowering the dosage, daily fractionation, stereotactic methods, and precise aiming of radiation beam.

**Keywords:** Paranasal Sinus, Radiotherapy, Radiation Optic Neuropathy

Introduction

Radiation-induced neuropathy occurs in nervous tissues adjacent to treated area with high doses of radiation. Nervous tissues develop some known changes secondary to radiation. Brain, because of low cellular proliferation, which happens only in glial tissue, is one of the most resistant tissues to radiation. Nevertheless, sometimes side effects of radiotherapy, are observed following treatment of brain neoplasms and also, cancers of nasopharynx, orbit, paranasal sinuses and visual pathways.

Mechanism of this event is considered to be direct damage to macromolecules and formation of free peroxide and superoxide radicals, especially in the presence of oxygen.

It is thought that radiation optic neuropathy (RON) is an ischemic disorder, which usually results in irreversible visual loss, within months to years after radiotherapy. In most cases this is a retrobulbar process and may occur following radiotherapy of head and neck.

Hereby we report a rare case of neuropathy in the visual pathway, secondary to radiation of optic chiasm, which we call "radiation chiasma neuropathy".

Case report

The patient was a 38-year-old male, who referred for evaluation of gradual visual loss in right eye since 6 months ago. He had history of right maxillary sinus lymphoma, which was recognized 1.5 years prior to referral. He underwent surgery, and subsequent chemotherapy and radiotherapy as adjuvant therapy. One year after radiotherapy, right eye vision started to decrease gradually. According to patient's explanation, pattern of visual loss has been similar to a hand-held lamp, whose battery dead gradually. In first exam, uncorrected visual acuity of right and left eye was no light perception (NLP) and 10/10 respectively. Ishihara color test showed normal color vision of left eye (10/10). Relative afferent pupillary defect (RAPD) was 4+ in right eye. Extraocular movement of both eyes were normal, with no limitation or any deviation. Slit lamp examination was unremarkable in both eyes. Intraocular pressure (IOP) was in normal range bilaterally. Severe optic disc pallor (4+) with loss of nerve fiber layer in right eye and bow tie atrophy of left optic disc were detected ophthalmoscopically. No any other pathology was seen in posterior segments of both eyes (Figure 1).

Standard automated perimetry showed left hemianopia of left eye (Figure 2). Thickening and enhancement of optic chiasm, especially in right side were observed in MRI (Figure 3). Visual evoked potential (VEP) was absent in right eye, and revealed low amplitude and high latency of P100 wave in left side.

Result of biopsies, before radiotherapy, was not available but after radiotherapy, biopsies of paranasal sinuses revealed no significant findings except for chronic radiation-induced polypoid inflammation of mucosa. Cerebrospinal fluid (CSF) analysis was normal, with no malignant cells. CSF culture was also negative.
Considering radiation-induced chiasma neuropathy as diagnosis, treatment with high dose steroid (250 mg four times a day for 3 days, followed by 1mg/kg/day for 2 weeks and then, gradual tapering in 3 days was administered. Furthermore, he treated with hyperbaric oxygen in several sessions.

In next visit, one month later, corrected visual acuity and color vision of left eye decreased to $5/10$ and $6/10$ respectively. Also diffused atrophy of left optic disc was present. Visual acuity and color vision of left eye gradually deteriorated, until four months later (about 2 years after radiotherapy) visual acuity of left eye was NLP.

Follow-up series of MRI showed progression of disorder posteriorly up to the level of both optic tracts and optic radiations which showed thickening and contrast enhancement (Figure 4).

Figure 4. Disease progression and involvement of entire optic chiasm and left optic radiation

Discussion

In most instances, RON occurs after radiotherapy of skull base and paranasal sinuses, although radiotherapy for pituitary adenomas, parasellar meningiomas, craniopharyngioma, temporal and frontal lobe gliomas and intraocular tumors may also results in this sequella.\textsuperscript{2,4} This injury can be acute, subacute or chronic.\textsuperscript{3} In one study between 1969-1985, among 219 patients, whom treated with radiotherapy for nasal and paranasal malignancies, 19 patients developed radionecrosis of chiasma and optic nerve.\textsuperscript{5}

Pathogenesis of delayed CNS radionecrosis is not clearly known. Formerly, this phenomenon was thought to be only a result of primary vascular injury and subsequent nervous tissue damage, however both vascular endothelial injury and direct damage to glial tissue are responsible for this disorder.\textsuperscript{2} Radiation to chiasma results in limited, but significant, decrease in oligodendroglial population.\textsuperscript{7} Histologic changes are similar to those changes, Which are observed in radiation to other parts of brain.\textsuperscript{3}
Pathologic specimens of involved optic nerve represent ischemic demyelination, axonal loss, reactive astrocytosis, endothelial hyperplasia, obliterative endarteritis and fibrinoid necrosis. Both total dose and daily fractionation of radiation are significant factors in delayed CNS radionecrosis. Hyperfractionation of total radiation to several smaller doses in multiple occasions can decrease risk of this phenomenon. Most authors believe that total dose less than 5000 cGy with divisions below 200 cGy decreases the risk of this neuropathy. In some exceptions as diabetic patients and those who are under chemotherapy, risk of radionecrosis is higher, and it may happen with lower doses of radiotherapy. More than 75% of reported radiation-induced optic neuropathies has occurred with total dose greater than 5000 cGy.

This disorder typically presents with acute painless visual loss in one or both eyes. Decreased vision in one eye may rapidly followed by visual loss in the other eye. Transient attacks of visual loss may occur several weeks before onset of optic neuropathy. Presentation time of visual symptoms varied from 3 months to 8 years after radiotherapy; however most cases happen during 3 years after radiotherapy, with a peak at 1.5 years.

Severity of visual loss has a wide range, and it’s progression during weeks to months is common. Spontaneous improvement in vision is unusual. Final vision is NLP in 45%, and in 85% of cases is equal or less than 20/200.

In clinical exam, optic disc is usually pale due to previous injury related to tumor itself and superimposed radiation damage. It may also be swelled with lower probability. In these occasions, which optic disc swelling is present initially, radiation retinopathy is also present. So cotton-wool patches, hard exudates, and retinal hemorrhages secondary to irradiation of intraocular or intraorbital components are observed.

Visual field may show altitudinal loss or a central scotoma. Junctional syndrome may also present with an optic neuropathy and contralateral temporal hemianopia, due to involvement of distal optic nerve. In chiasmal radionecrosis, bitemporal hemianopia is typically observed.

Several differential diagnoses should be considered for RON such as: recurrence of primary tumor, arachnoiditis, radiation-induced paraseellar tumors, secondary empty sella syndrome associated with optic nerve and chiasmal prolaps. In these conditions visual loss is gradual in pattern.

Diagnosis of RON is according to clinical findings, which may be established with neuroimaging. CT scanning is typically normal. Visual loss secondary to tumor recurrence can be distinguished from radiation damage with use of radiologic devices. MRI is the choice procedure for differentiation of tumor recurrence from RON. Development of fat-saturation techniques and use of paramagnetic contrast solutions permit fine imaging from optic chiasm and also intraorbital and intracranial parts of optic nerve. In majority of cases white matter hyperintensity is observed in T2-weighted MRI, but hypointensity in T1 images is not seen. In severe cases enhancement occurs after contrast injection. Occasionally enhancement may be present before visual loss.

CT scanning and MRI are not useful in coagulative necrosis. In this condition positron emission tomography (PET) scanning is necessary for diagnosis and therapeutic decision. Single photon emission computed tomography (SPECT) is another procedure for differentiation between tumor recurrence and radionecrosis.

Treatment of RON is controversial. Although delayed radionecrosis of CNS is treated with partial success with systemic corticosteroid, which is effective in reducing tissue edema and demyelination, but their use in RON, in oral or injectable form, has not had hopeful results. Only two cases from 16 treated cases with corticosteroid alone, had improvement.

Glantz and colleagues administered heparin and warfarin for 11 patients with CNS damage and no response to corticosteroid. Among 8 patients with radionecrosis, some improvement was observed in 5 cases. All patients with myelopathy and plexopathy (3 cases) showed evidences of improvement.

In general, the use of anticoagulants does not seem to have significant beneficial results for stabilization or reversal of CNS radionecrosis in patients with RON.
Since RON is an ischemic process, hyperbaric oxygen appears to be useful theoretically; however clinical results have not been identical. In one study, hyperbaric oxygen and corticosteroid was used for 13 patients with RON, 4 to 35 months after radiotherapy. No improvement was observed during 1 to 4 years follow-up.

Also hyperbaric oxygen was not effective in our patient, and he finally developed complete visual loss in both eyes.

**Conclusion**

In addition to RON, radiation chiasma neuropathy should also be considered as a differential diagnosis for a patient with history of radiation to the head and neck and subsequent visual loss. Although systemic corticosteroid and hyperbaric oxygen are used for treatment of this disorder, results are disappointing. Similarly these therapeutic modalities (systemic corticosteroid and hyperbaric oxygen) were not effective in our patient with poor final outcome of complete visual loss in both eyes.

Prevention of this disorder seems to be more effective than its treatment. Lower doses of radiation, daily fractionation of radiotherapy, exact focusing of radiation beam on target tissue and also, employment of stereotactic methods of radiotherapy, especially adjacent to vital and sensitive organs, all decrease the chance of this ominous sequella, and have been proposed.

**References**