Central Fusion Disruption Following Irradiation of Neoplasms in the Pineal Region

In 1935, Bielschowsky described a syndrome in which the ability to fuse 2 images was lost because of a longstanding sensory deprivation. The main symptom was intractable diplopia following the removal of the cause of sensory deprivation. Bielschowsky called this syndrome horor fusionis. This syndrome, now known as acquired central fusion disruption, has been reported following cataract extraction, aphakia, severe head trauma, and brain surgery. We report 2 cases of central fusion disruption that developed after irradiation to the pineal area.

Report of Cases. Case 1. A 12-year-old boy had a chief symptom of double vision. One month earlier, the patient had visited a neurologist for headaches and visual disturbances. A biopsy obtained during a third ventriculostomy demonstrated a pineal region tumor consistent with germinoma. He subsequently received radiation therapy of 2550 cGy (the conversion of centigray to rad is 1:1) with a 2160 cGy boost in the pineal region. During this treatment, he started to have diplopia and was referred to our service. On examination, corrected visual acuity was 20/20 OD and 20/20 OS with a manifest refraction of +1.25 − 2.00 × 180° OD and plano −0.50 × 180° OS. Prism and cover testing revealed an intermitent exotropia of 25 prism diopeters (PD) at distance and 16 PD at near. During the following months, the diplopia worsened and finally became constant. Ten months after the initial visit, the patient was treated with a right lateral rectus recession of 5.0 mm and a right medial rectus recession of 4.0 mm.

Three months after the procedure, he continued to have double vision. On examination, he had 8 PD of esotropia at distance and no deviation at near. Double Maddox rod testing showed 5° of exyclotorsion in each eye. There was no vertical deviation on head tilt to the right or to the left. The patient was felt to have bilateral fourth nerve palsies.

Owing to persistent double vision, he underwent a second eye muscle surgery consisting of bilateral Harada-Ito procedures as well as a right inferior rectus recession of 1.0 mm and a left medial rectus recession of 5.0 mm on adjustable sutures. Postoperatively, he continued to have double vision. Prisms were prescribed to superimpose the images as closely as possible. On examination 10 years later, corrected visual acuity was 20/30 OD and 20/20 OS with −1.75 + 0.50 × 113° OD and −2.25 + 2.00 × 85° OS. The glasses also contained prisms of 3 base-out and 3 base-up OD and 3 base-out and 3 base-down OS. On sensorimotor evaluation, the patient had a left eye fixation preference with −3 limitation of elevation on the right (scale, 0 to −4 limitation) and −2 limitation on the left. Prism and cover testing with correction revealed a left hypertropia of 4 PD at distance and near. Double Maddox rod testing showed 5° of exyclotorsion on the right. Stereopsis was not detectable with Titmus test and vertical diplopia was found on the Worth 4-dot test. Synoptophore measurements were obtained. The objective angle of the esotropia was 4.5° (10 PD) and the objective angle of the left hypertropia was 5° (10 PD). The subjective angle was similar but with an additional exyclotorsion of 2° to 4°. Even with the exyclotorsion eliminated and the horizontal and vertical strabismus neutralized, the patient noted only simultaneous perception of the 2 overlapping images.

Despite the lack of fusion, he stated that he was able to function normally including driving without difficulty. He was diagnosed with central fusion disruption secondary to pineal tumor irradiation.

Case 2. A 15-year-old previously healthy boy had a chief symptom of double vision. The patient had visited a neurologist 2 months before for headaches, vision changes, and vomiting. Magnetic resonance imaging of the brain revealed a pineal region tumor with hydrocephalus. He underwent an endoscopic third ventriculostomy and biopsy of the tumor in an outside hospital. The tumor biopsy and markers that were taken were inconclusive. Two weeks later, he underwent a right occipital craniotomy with transtentorial microscopical subtotal resection of the tumor. Pathological findings were consistent with germinoma. Three days after surgery, he was seen in the ophthalmology clinic with diplopia. On examination, uncorrected visual acuity was 20/30 OD and 20/60 OS. Ductions and versions showed −4 limitation of elevation in all of the horizontal gaze positions, −1/2 abduction deficit in both eyes, and −2 depression deficit in both eyes. In primary position, he had 10 PD of esotropia, which increased to 15 PD in both left and right gaze. The clinical impression was consistent with resolving increased intracranial pressure and herniation syndrome resulting in bilateral sixth cranial nerve palsies. The patient then was treated with radiation therapy to the pineal region with a maximum dose of 5040 cGy to the primary tumor site and an estimated total dose of 2520 cGy to the hypothalamus and pituitary.

Six months after his initial visit, he still had diplopia. On examination, visual acuity was 20/20 OU with a cycloplegic refraction of +2.50 + 0.75 × 90° OD and +3.00 + 0.50 × 90° OS. He had a right eye fixation preference for...
distance and near. Pupils were notable for light-near dissociation. Ductions and versions showed limitation of elevation in all of the horizontal gaze positions. Prism and cover testing revealed 4 PD of left hypertropia at distance and near. The patient was fitted with prisms in an attempt to reduce his diplopia.

One year later, he returned for evaluation and had persistent double vision despite prism use. Examination revealed an exotropia of 12 PD along with a right hypertropia of 6 PD at distance and near. Double Maddox rod testing showed 5° of excyclotorsion on the right and 3° of excyclotorsion on the left. Three months after the initial visit, he was treated with a right inferior oblique disinsertion and an adjustable right lateral rectus recession of 2.5 mm.

The patient was then lost to follow-up until 1 year and 5 months postoperatively, when he returned to have double vision. On examination, corrected visual acuity was 20/20 OD and 20/20 OS with a manifest refraction of plano + 0.50 × 90° OD and +0.25 + 0.50 × 19° OS. He had a right eye fixation preference for distance and near. Ductions and versions showed –2 limitation of elevation in all of the horizontal gaze positions. Prism and cover testing revealed 6 PD of exotropia and 6 PD of left hypertropia at distance and 12 PD of exotropia and 4 PD of left hypertropia at near. Double Maddox rod testing showed 2° of incyclotorsion on the right and 4° of excyclotorsion on the left. Stereopsis was not detectable, and diplopia was found on Worth 4-dot testing. Using prisms, the patient was able to superimpose both images but not fuse them. Prisms were prescribed as they improved his comfort, but he remains unable to fuse images into a single visual impression.

The patient was diagnosed with central fusion disruption secondary to pineal tumor irradiation and surgery.

**Comment.** Central fusion disruption refers to an acquired deficiency in fusion caused by intracranial insult or prolonged visual deprivation. Characteristically, patients with central fusion disruption experience diplopia in all positions of gaze associated with strabismus of any angle. If the eyes are aligned with prisms, patients can experience transient superimposition of images but not fusion. Suppression does not occur by subjective report or on objective testing. In both of our patients, eye muscle surgery reduced the strabismus and torsion sufficiently to have allowed fusion to take place with prisms if normal fusional mechanisms had been intact.

To our knowledge, our patients represent the first reported cases of central fusion disruption associated with irradiation to the pineal area. Gruzensky and Palmer reported 1 case of central fusion disruption following surgical resection of a pineal teratoma. While both of our patients had surgical biopsies and 1 of them had a therapeutic resection of his tumor, the patient whose tumor was not resected did not have persistent double vision until after radiation therapy had been completed. In the other patient, there was double vision immediately after surgery owing to transient abducens nerve palsies, but the diplopia never resolved despite resolution of the abduction limitation.

Once central fusion is disrupted, it is rarely regained. Although prisms did not restore fusion in either of our cases, the patients were most comfortable when the 2 images were maximally superimposed. In our clinical experience, this has been the case in patients with central fusion disruption of any cause, contrary to the clinical teaching that it is easier for patients to ignore double images when they are not nearly superimposed. We therefore recommend offering prism therapy to affected patients.

The possible complication of central fusion disruption is considered when planning interventions in patients who have had prolonged visual deprivation or who require surgery to areas surrounding the midbrain, cerebellum, or connecting pathways. Our cases extend this caution to interventions in the pineal region and raise the possibility that neurons in this area contribute to central fusion. Furthermore, the possibility that radiation alone can damage these areas, even in the absence of surgical transection, is important to note.

Sashank K. Reddy, PhD
David G. Hunter, MD, PhD
Cristian M. Salgado, MD

Correspondence: Dr Hunter, Department of Ophthalmology, Children's Hospital Boston, 300 Longwood Ave, Fegan 4, Boston, MA 02115 (david.hunter@childrens.harvard.edu).

Author Contributions: Drs Reddy and Salgado contributed equally to this work.

Financial Disclosure: None reported.

Funding/Support: This work was supported by the Research to Prevent Blindness Walt and Lily Disney Amblyopia Research Award (Dr Hunter), the Medical Scientist Training Program (Dr Reddy), and the Children's Hospital Ophthalmology Foundation (Dr Salgado).