Spontaneous Regression of Optic Gliomas

Thirteen Cases Documented by Serial Neuroimaging

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Objective: To demonstrate spontaneous regression of large, clinically symptomatic optic pathway gliomas in patients with and without neurofibromatosis type 1 (NF-1).

Methods: Patient cases were collected through surveys at 2 consecutive annual meetings of the North American Neuro-Ophthalmology Society (NANOS) and through requests on the NANOSNET Internet listserv. Serial documentation of tumor signal and size, using magnetic resonance imaging in 11 patients and computed tomography in 2 patients, was used to evaluate clinically symptomatic optic pathway gliomas. All tumors met radiologic criteria for the diagnosis of glioma and 4 patients had biopsy confirmation of their tumors. In 3 patients, some attempt at therapy had been made many years before regression occurred. In one of these, radiation treatment had been given 19 years before tumor regression, while in another, chemotherapy had been administered 5 years before signal changes in the tumor. In the third patient, minimal surgical debulking was performed 1 year before the tumor began to shrink.

Results: Spontaneous tumor shrinkage was noted in 12 patients. Eight patients did not have NF-1. In an additional patient without NF-1, a signal change within the tumor without associated shrinkage was detected. Tumor regression was associated with improvement in visual function in 10 of 13 patients, stability of function in 1, and deterioration in 2.

Conclusions: Large, clinically symptomatic optic gliomas may undergo spontaneous regression. Regression was seen in patients with and without NF-1. Regression may manifest either as an overall shrinkage in tumor size, or as a signal change on magnetic resonance imaging. A variable degree of improvement in visual function may accompany regression. The possibility of spontaneous regression of an optic glioma should be considered in the planning of treatment of patients with these tumors.


Computed tomographic neuroimaging studies are now standard for the diagnosis and management of optic gliomas. These studies are being applied widely in prospective serial evaluations of changes in these tumors over the course of months to years. Venes et al in 1984 reported the postoperative regression of a partially resected chiasmal glioma. Hoffman et al in 1993 reported the same postsurgical phenomenon, as did Takeuchi and colleagues in 1997. In 1992, Brzowski and associates presented the first evidence of spontaneous tumor regression recorded by magnetic resonance imaging (MRI), in a 2-year-old child with neurofibromatosis type 1 (NF-1). In 1995, Parazzini et al noted similar involution of small, asymptomatic optic gliomas in or around the chiasm in 4 children with NF-1. Perilongo et al and Gottschalk and colleagues reported similar findings in 4 other children in 1999. In 1998, Rubtsova et al reported, in Russian, the spontaneous regression of a large and clinically symptomatic optic nerve glioma, documented by serial MRI in a boy with probable NF-1. We report this case in English, along with 12 additional cases of spontaneously regressing optic gliomas documented by neuroimaging studies.

REPORT OF CASES

CASE 1

A healthy 5-year-old boy was believed to have severe amblyopia with hand motion vision in the right eye during a school examination. At age 7 years, right optic disc atrophy was recognized. His left eye was normal. He had 7 café-au-lait spots, but no Lisch nodules on his irides. There was no history of NF-1 or ocular problems in his family. Magnetic resonance
scans showed a large (3 × 3 × 3.2-cm) lobulated suprasellar tumor connected to an expanded right optic nerve within the optic canal and the orbital apex. In T1-weighted images, the mass seemed homogeneous (Figure 1A).

After neuro-ophthalmologic consultation at the University of California, San Francisco, the decision was made to follow his case without treatment.

Four years later, at age 11 years, MRI scans showed clear diminution in size of the suprasellar mass. There was prominent, but nonuniform paramagnetic enhancement of the central portion of the tumor and a surrounding rim of low-signal intensity (Figure 1B). Visual acuity in the right eye had not changed.

At age 15 years, visual function had improved to 20/200 OD. He could distinguish several pseudoisochromatic plates with the right eye. He had a generally depressed field most pronounced inferiorly, and atrophy of the right optic disc. He had been aware of a gradual visual improvement beginning 3 or 4 years earlier. Magnetic resonance imaging scans showed remarkable reduction in the size of the tumor; it appeared to involve the right optic nerve only. The area of paramagnetic enhancement within it was greatly reduced (Figure 1C). Four years later, his clinical examination remained unchanged and MRI scans revealed small areas of calcification within the tumor. During the 12-year period of follow-up, the patient grew normally. Molecular genetic analysis, with a sensitivity of 70% for detecting a mutation in the NF-1 gene, failed to verify or disprove its presence.

CASE 2

A healthy 4-year-old girl complained of intermittent right eye pain after having been struck in the right temple. She was brought to the Yale–New Haven emergency department and was found to have a swollen disc and decreased vision in the right eye. No family history or stigmata of NF-1 were present. Computed tomographic (CT) scans disclosed tubular enlargement of the right optic nerve in the orbit (Figure 2A). Right frontocranial craniotomy showed the optic nerve was thickened back up to the optic chiasm, and that the chiasm diameter thickened to approximately twice its normal size. The right optic tract was also enlarged. A biopsy specimen, measuring 2 mm in its greatest thickness, was taken anterior to the chiasm. This was read as pilocytic astrocytoma, type 1.

On her first neuro-ophthalmologic examination, visual acuity was 20/70 OD and 20/40 OS. A right afferent pupillary defect was present along with a 10–prism diopter (PD) esotropia. Visual fields by confrontation revealed a nasal depression in the right eye. The right optic disc was pale while the left, pink and flat. The patient was evaluated without treatment. Three months later, at age 5 years, her visual acuity had improved to 20/40 OD and 20/25 OS. After a course of patching of the left eye, the patient’s vision was 20/25 OU. Her examination remained stable subsequently, while MRI scans 5 years later, at age 10 years, revealed the right optic nerve to be essentially normal, with only trace enlargement when compared with the left (Figure 2B).

At age 12 years, visual acuity was 20/20 – 3 OD and 20/20 – 2 OS. The right disc was pale and cupped; the left, pink and flat. At age 17 years, visual acuity was unchanged, and no Lisch nodules were detected. Computerized static perimetry showed a depressed inferior field in the right eye. The left visual field was full. Magnetic resonance imaging was unchanged.

Figure 1. A, T1-weighted coronal magnetic resonance imaging (February 1988) shows a large (3 × 3 × 3.2-cm), predominantly hypointense, lobulated tumor in the suprasellar cistern. B, T1-weighted coronal magnetic resonance imaging after contrast (May 1992). The tumor had decreased in size, measuring approximately 2.1 cm in its greatest dimension (not shown). Central, nonenhancing foci are seen within the tumor mass. C, T1-weighted coronal magnetic resonance imaging after contrast (August 1996). There is marked reduction in size of the mass that now measured only 15 × 7 mm. The tumor involved only the right intracranial optic nerve. The chiasm was normal, and the enhancement is markedly reduced. Later images (January 2000, not shown) revealed small areas of calcification within the tumor.
for pain and disc edema. He had had an upper respiratory infection 6 weeks before evaluation, with the onset of “bad headaches” and pressure behind the left eye over the previous 4 weeks.

Corrected visual acuity was 20/20 OU. However, he had a mild relative afferent pupillary defect on the left. Computerized perimetry revealed minimal depression of the field with slight enlargement of the blind spot in the left eye. No Lisch nodules were present. The left disc was chronically swollen without hemorrhages. There were no stigmata of NF-1. Magnetic resonance imaging scans revealed a fusiform enlargement and kinking of the left optic nerve, extending from globe to the chiasm (Figure 4A-C).

Six months later headaches had resolved. Corrected visual acuity remained 20/20 OU, and there was only a trace afferent pupillary defect on the left. The left disc was hyperemic, but not swollen. Magnetic resonance imaging at age 14½ years revealed that the tumor no longer enhanced and that it had shrunk. At age 15 years, the relative afferent pupillary defect had disappeared and the fundi were normal. Magnetic resonance imaging 6 months afterward revealed that the tumor no longer enhanced and had also shrunk in size (Figure 4D). At 16½ years of age, another scan revealed further shrinkage of the tumor in its axial dimension.

CASE 5

A 13-year-old boy was evaluated at the University of Wisconsin, Madison, for bilateral decreased vision of 1 year’s duration. Visual acuity was 20/50 OD and 20/200 OS. He had bitemporal hemianopia and bilateral disc pallor. Magnetic resonance imaging revealed a large homogeneous (in T1-weighted images) chiasmal tumor consistent with glioma (Figure 5A). It enhanced with gadolinium and had a cystic area above the right optic nerve. Abnormal signal was present in both optic tracts in T2-weighted images. There was no family history of NF-1. The boy’s growth was subnormal. A craniotomy was performed. The optic nerve on the left side appeared grossly abnormal, with a large mass extruding laterally, inferiorly, and medially. Debulking of the tumor was performed by Cavitron ultrasonic aspiration. Debulking of the right side of the chiasm was not attempted. Tumor fragments submitted for pathological examination were in aggregate 3.0 × 2.0 × 1.0 mm and read as optic nerve glioma. Postoperatively, visual acuity was 20/80 OD and counting fingers at 1 ft OS with a total nasal field loss in the left eye. The postoperative MRI scans showed no perceptible change in the size of the tumor, no change in size of the cyst above the right optic nerve, persistent high signal intensity along both tracts, and continued enhancement. Seven months after surgery, visual acuity was 20/40 OD and 1/200 OS, with some improvement of the temporal field bilaterally, but with persistence of a quadrant inferior nasal field defect in the left eye.

At age 14 years, visual acuity was 20/20 OD and 2/200 OS. Magnetic resonance imaging scans now revealed shrinkage of both the solid and cystic components of the tumor as well as decreased enhancement of the tumor and decrease in the signal intensity along the optic tracts.

CASE 3

A 3-month-old girl presented with vomiting and signs of hydrocephalus. A CT scan revealed a large, well-circumscribed, midline globular tumor in the region of the chiasm. After several follow-up visits, a decision to defer surgery was made based on the stability of her head size. At age 3 years, the mother noticed that she was bumping into things. One year later, she was referred to the Neuroophthalmology Unit at Hospital Vargas in Caracas, Venezuela, for abnormal vision. By that time, the mother believed there had been consistent improvement in her child’s vision over the previous year. On examination, visual acuity was roughly 20/400 OU with sensory nystagmus. Both discs were chalk-white. There were no stigmata, nor any family history, of NF-1. Review of the CT scans previously obtained at ages 7 months, 1½ years, and 4 years revealed progressive shrinkage of her tumor (Figure 3A-C). Magnetic resonance imaging scans obtained at age 4 years showed small residual chiasmal tumor. The girl was visually handicapped, but otherwise healthy.

CASE 4

A 13½-year-old boy was referred to the Neuroophthalmology Unit at the Mayo Clinic, Rochester, Minn,
Figure 3. A, Axial computed tomographic imaging (May 1993) shows a large, midline, well-circumscribed mass at the chiasm. There is severe brain atrophy. B, Axial computed tomographic imaging (April 1994). There is marked reduction in the size of the mass. C, Axial computed tomographic imaging (September 1996) shows further reduction in the size of the mass.

Figure 4. A, Axial T1-weighted magnetic resonance imaging (December 1994) shows fusiform enlargement of the left optic nerve, extending from the anterior aspect of the chiasm up to the globe. The nerve had a prominent kink. B, After contrast, the nerve enhanced markedly, most notably at the chiasm. C, Coronal T1-weighted magnetic resonance imaging after contrast (December 1994) shows marked enlargement and enhancement of the left optic nerve. D, Coronal T1-weighted magnetic resonance imaging with paramagnetic contrast infusion 2 years later (December 1996) showed noteworthy shrinkage of the tumor with no enhancement.
At age 15 years, visual acuity was 20/20 OD and 20/40 OS. While the complete inferonasal defect persisted, the bitemporal field defects continued to resolve. Magnetic resonance imaging scans now revealed marked shrinkage in all dimensions of the tumor with minimal enhancement (Figure 5B). No abnormal signal was noted along the optic tracts on separate T2-weighted images. At age 16 years, visual acuity improved to 20/25 OS. No further changes were noted in his MRI scans. At 20 years of age, his tumor remained the same and he remained healthy.

CASE 6

A 14-year-old girl was referred to the Wilmer Ophthalmological Institute after incidentally discovering decreased vision in her left eye. Visual acuity was 20/15 OD and counting fingers at 4 ft OS. Automated threshold perimetry revealed a full field in the right eye and a small superotemporal island of vision in the left. The right disc was normal, while the left had mild temporal pallor. The left eye was slightly proptotic (3 mm). No Lisch nodules or other stigmata of NF-1 were present. Magnetic resonance imaging scans revealed an enhancing cranio-orbital glioma with a prominent distal kink (Figure 6A and B). The tumor abutted the chiasm. Three months later the patient reported improved vision. Her visual acuity was now 20/25−1 OS with pinhole. She had only a trace afferent pupillary defect. She could now distinguish 6 of 12 pseudoisochromatic plates. Computerized perim-

![Image](https://jamanetwork.com/)

Figure 5. A, Sagittal T1-weighted magnetic resonance imaging after paramagnetic contrast (October 1990) shows a large, homogeneous chiasmal tumor. Separate T2-weighted images showed abnormal signal along both optic tracts. B, Sagittal T1-weighted magnetic resonance imaging after paramagnetic contrast (September 1992). Marked shrinkage of the tumor occurred in all dimensions with minimal enhancement of the tumor. There was no abnormal signal along the optic tracts on separate T2-weighted images.

Figure 6. A, T2-weighted axial magnetic resonance imaging (August 1997) shows a fusiform enlargement of the optic nerve, hyperintense and homogeneous in signal intensity from the globe up to the chiasm, measuring 1.5 × 2.5 cm in its intraconal course. The left globe is proptotic. There is widening of the left neural foramen. B, T1-weighted coronal magnetic resonance imaging after contrast (August 1997). There is marked enlargement of the left intraorbital optic nerve, with prominent and homogeneous signal enhancement. C, T2-weighted magnetic resonance imaging (August 1998) shows shrinkage of the optic nerve tumor along its entire course, with decrease in signal intensity, now measuring 0.8 × 1.8 cm in its intraconal course. The left globe is no longer proptotic. D, T1-weighted coronal magnetic resonance imaging (March 1998) shows clear reduction in optic nerve diameter, with only trace signal enhancement centrally after paramagnetic contrast infusion.
etry showed the left field had broadened out and lightened remarkably. Magnetic resonance imaging scans showed the optic nerve to be smaller with less enhancement. Two months later, visual acuity had improved to 20/25 OS and the patient could distinguish 10 of 12 color plates. One month later, MRI scans revealed the nerve to be smaller still and only very mildly enhancing (Figure 6D). Five months later visual acuity was 20/20 + 3 OS. Stereopsis was normal. Perimetry revealed minimal reduction in sensitivity of the field of the left eye. Magnetic resonance imaging scans 1 month later showed continued shrinkage of the tumor along its entire course, with decrease in signal intensity (Figure 6C). Eight months later, visual acuity was 20/15 – 1 OS without an afferent pupil defect. Exophthalmometry now showed recession of the left eye compared with the right.

CASE 7

An 11-year-old girl with a family history of NF-1, diagnosed as having bilateral stable amblyopia since age 6 years, was referred to Foothills Hospital in Calgary, Alberta. Visual acuity was 20/70 OD and 20/60 OS. Tangent screen perimetry revealed a generalized depression, more so temporally, in the left eye, with an absolute temporal hemianopia in the right eye. Numerous Lisch nodules were present. Both optic discs were pale. Computed tomographic scans showed a slightly dense enhancing suprasellar lesion between 2 and 3 cm in diameter, with extension along both optic tracts. Three months later, the patient reported further loss of vision. Visual acuity was 20/80 – 1 OD and 20/70–1 OS. Tangent screen perimetry detected shrinkage of nasal field in the right eye. Three months later, visual acuity was somewhat improved and fields were unchanged. Magnetic resonance imaging scans revealed a globular enlargement of the chiasm that extended along the tracts bilaterally, corresponding to the previous CT scan findings. Signal intensity was inhomogeneous in T1-weighted images and lower on the right, possibly representing areas of tumor necrosis (Figure 7A). There was a large T2-weighted high-signal lesion in the region of the left internal capsule and lentiform nucleus without mass effect, probably representing a hamartoma or a very low-grade glioma (Figure 7E).

Eight months later, visual acuity dropped to 20/200 OD and 20/70 OS. Tangent screen examination showed further contraction of the nasal field in the right eye, but repeated MRI scans did not detect changes in the size of the tumor. Eighteen months later, visual acuity dropped to 20/400 OD, but remained 20/50 OS with further depression of the right nasal visual field. Six months later, visual acuity continued to drop in the right eye, down to counting fingers at 10 ft. Magnetic resonance imaging scans showed no change. Nine months later visual acuity continued to decline in the right eye, to counting fingers at 2 ft while remaining stable at 20/50 OS. Seven months later clinical and neuroimaging findings remained unchanged (Figure 7C). Sixteen months later, MRI scans showed uniform shrinkage of the tumor (Figure 7B and D). Areas of decreased signal intensity were again noted on the right side of the chiasm (Figure 7B). The T2-weighted hyperintensities in the basal ganglia were less bright (Figure 7F). Magnetic resonance imaging scans 1 year later, at age 18 years, showed a continued uniform shrinkage of the tumor. The patient’s vision remained unchanged.

CASE 8

A 4 1/2-month-old boy was referred to the Pediatric Ophthalmology Unit at the University of California, San Francisco, for progressive “shakiness” of the eyes, with extreme photophobia. Fixation was central in the right eye, and unmaintained in the left, with occasional head nodding. Both pupils reacted sluggishly to light, but no relative afferent pupillary defect was present. No family history of NF-1 was present. A CT scan detected an enhancing mass thickening the left optic nerve with widening of the left optic foramen along with mild thickening of the right optic nerve. Chiasmal involvement was not evident. Magnetic resonance imaging scans confirmed the presence of the tumor with extension into the chiasm and optic tracts (Figure 8A and B), with no other brain abnormalities. A 15-PD left esotropia developed over the following months and patching therapy was instituted while the nystagmus gradually dampened. By age 6 years, visual acuity was 20/20 OD and 20/400 OS with eccentric fixation, with full visual fields by confrontation. There no longer was any nystagmus and strabismus surgery was performed for a 30-PD left esotropia. Trace optic atrophy was present in the right eye, with marked atrophy in the left. Although MRI scans had clearly disclosed no tumor growth, it was later clear by age 5 years that substantial reduction of the chiasmal portion of the tumor had already occurred and that the left side of the chiasm was now smaller than the right (Figure 8C). By age 8 years, left eye visual acuity had declined to counting fingers at 2 ft, but was unchanged in the right eye with a full field on computerized perimetry. An MRI scan showed the entire chiasm to be essentially normal in size and signal intensity (Figure 8D). The optic nerves remained unchanged, with prominent tubular enlargement, kinking, and a “pseudo-CSF” sign. A genetics evaluation of the patient, his parents, his 2 siblings, and 2 grandmothers failed to diagnose NF-1 in any member. Computerized perimetry continued to show a full field in the right eye and he could identify all pseudoisochromatic plates with the right eye. Lisch nodules remained absent. At age 12 years, his MRI scan revealed that marked reduction of the diameters of both optic nerves had occurred. The right optic nerve was normal in size and signal intensity, while vision remained unchanged bilaterally. The boy grew normally and remained otherwise healthy.

CASE 9

A healthy 3-month-old boy with no family history of NF-1, but with multiple café-au-lait spots, underwent neurological and pediatric neuro-ophthalmological examinations at the University of California, San Francisco. All examinations were normal. High-quality MRI scans of the brain and spine, with and without paramagnetic contrast infusion, detected no abnormalities. Neither par-
ent had Lisch nodules or a history of NF-1. At 15 months of age, 2 small cutaneous neurofibromas developed in the boy. Six months later, MRI scans demonstrated an enhancing chiasmatic mass (2.0 × 1.2 × 1.2 cm) with some extension posteriorly into the optic tracts. Both intracranial portions of the nerves were enlarged and enhanced. No areas of high signal on T2-weighted images were present elsewhere in the brain. However, areas of mild T2-weighted increased signal intensity within the white matter tracts of the cerebellum and surrounding the occipital horns were present, thought to represent early glial rests. Observation was chosen. Magnetic resonance imaging scans were repeated 3 months later and demonstrated a slight increase in the size of the tumor (2.3 × 1.7 × 1.7 cm) (Figure 9A). His eye examination at that time revealed central, steady, and maintained vision in the right eye, with central, steady, but unmaintained vision in the left with a small angle esotropia. Four months later, visual acuity using picture optotypes was a brisk 20/20 OU. Visual fields were full to confrontation testing and there was no relative afferent pupillary defect. Trace left optic disc atrophy was noted. Repeat MRI revealed slightly less enhancement of the tumor, while a scan 3 months later detected no other changes in tumor characteristics. Another scan 3 months later, however, showed a significant decrease in contrast enhancement of the tumor with some possible shrinkage. Three months later, a scan detected clear-cut shrinkage with further reduction in enhancement. The mild T2-weighted abnormalities were not changed significantly in position or intensity, particularly in the area of the atria and occipital horns of the lateral ventricles. Four months later, continued decrease in tumor enhancement was noted, while 4 months thereafter, visual acuity (picture optotypes) remained a brisk 20/20 OU with full fields on confrontation testing. Magnetic resonance imaging at this time revealed further decrease in size and enhancement.

Figure 7. A, T1-weighted coronal magnetic resonance imaging (MRI) (February 1990) shows globular enlargement of the chiasm. Signal intensity is inhomogeneous to the right where it is lower. B, T1-weighted coronal MRI (December 1996). The tumor has shrunk in size, and in the midline, its signal intensity is less homogeneous. There are areas of decreased signal intensity mainly on the right side of the chiasm and midline. C, T1-weighted coronal MRI after contrast (April 1994). The tumor enhances irregularly, with very high intensity mostly to the right and midline. Little change was noted from previous MRI scans. D, T1-weighted coronal MRI after contrast (December 1996). The tumor has shrunk in size as has its enhancing portion. The enhancing portions correspond to the areas of low signal intensity on the images taken without contrast, shown top right. E, T2-weighted axial MRI image (February 1990). Reasonably large, high-signal lesion in the region of the left internal capsule, lentiform nucleus, and midline with no mass effect. These lesions probably represent hamartomas. F, T2-weighted axial MRI (December 1996). The hyperintensities are markedly reduced and are now barely perceptible.
time revealed a marked decrease in signal enhancement and a marked decrease in the size of the tumor; an MRI 6 months later revealed a continued spontaneous decrease in the size of the tumor, with an essentially normal chiasm (Figure 9B). The T2-weighted signal abnormalities in the brachium pontis bilaterally, dentate nucleus of the cerebellum, and optic tracts were similar to previous studies. At age 4 years, visual acuity remained 20/20 OU with no nystagmus or strabismus present. Lisch nodules were absent, while the boy remained healthy, well-developed, and quite bright.

**CASE 10**

A 6-month-old boy diagnosed as having spasmus nutans and right hemianopia was followed up at the Meir General Hospital in Kfar-Saba, Israel. No family history of NF-1 was present. Computed tomographic scans at 1 year of age showed an enhancing suprasellar mass and enlargement of the right optic nerve. Magnetic resonance imaging scans at 14 months of age disclosed tumor involving the optic chiasm, the left optic tract and some evidence of extension into the basal ganglia.

At 2½ years of age, the boy was nearly blind in the right eye. Both discs were pale temporally. At 3½ years of age, visual acuity had declined to finger counting at 6 ft OS. Repeat MRI scans revealed involvement of both optic tracts with the tumor extending to the left lateral geniculate body and the mesial portions of the temporal lobe. In view of the continued loss of vision, chemotherapy, consisting of vincristine and actinomycin D, was given over an 18-month period, from ages 3½ to 5 years. The patient’s vision continued to worsen, and on Goldmann perimetry, his remaining island of vision continued to shrink. From ages 7 to 9 years, no vision could be detected in his right eye. Magnetic resonance imaging scans at age 8 years showed tumor in the optic tracts bilaterally, a left thalamic component, and a left peduncular component. At age 9 years, he was seen at the University of California, San Francisco, where only light perception in the right eye was confirmed. Visual acuity was 20/200 OS with a constricted and depressed field. He remained otherwise healthy. Three months later, the patient reported the ability to see out of the right eye. Visual acuity was now counting fingers at 1.7 ft OD, and he had a large central scotoma within a small field. Visual acuity was 20/100 OS.
involved (ric, globular, relatively homogeneous suprasellar mass appeared atrophic. An MRI scan revealed a large, symmetrical mass. A biopsy confirmed the diagnosis of pilocytic astrocytoma, type 1. No stigmata of NF-1 were present. A ventriculoperitoneal shunt was placed and the patient underwent radiotherapy. Clinical signs of precocious puberty developed and she received hormonal treatment for gynecomastia. At that time, she was noted to have bilateral optic atrophy with impaired vision.

At age 10 years, she presented with left hemiplegia, left facial weakness, and moderate left-sided ataxia. A CT scan showed a large tumor deep in the right temporoparietal field defects with additional paracentral defects in the left eye. Magnetic resonance imaging scans at age 15 years revealed marked shrinkage of the tumor, with a now normal right optic tract. Fifteen months later, at age 16 years, visual acuity had improved to 20/20 OD and 20/40 OS, with a substantial reduction in the size of the tumor (Figure 11C and D). At 11 years of age, the boy remained healthy with moderate visual handicap.

CASE 12

A 3-year-old boy was referred for neuro-ophthalmologic consultation at the São Paulo University Hospital, São Paulo, Brazil, after reduced vision led to difficulties at school. Visual acuity was 20/80 OD and counting fingers at 10 ft OS. Goldmann perimetry revealed bitemporal field defects with additional paracentral defects in the left eye. The right optic disc was slightly pale and the left disc moderately so. Lisch nodules and café-au-lait spots were present in both the patient and his father. Magnetic resonance imaging revealed a large, lobulated suprasellar tumor, relatively homogeneous in T1-weighted images (Figure 12A). The boy had a slight delay in puberty, but no endocrine abnormalities were found. After consultation with the family, the decision was made to observe the boy. Nine months later, visual acuity had improved to 20/30 OD and to 20/200 OS. Corresponding improvements were also noted in the visual fields, obtained by the same experienced perimetrist. An MRI scan 5 months afterward, at age 15 years, revealed a substantial reduction in the size of the tumor (Figure 12B). Fifteen months later, at age 16 years, visual acuity continued to improve to 20/20 OD and 20/40 OS, with corresponding improvements in the visual fields. Magnetic resonance imaging revealed only minimal further reduction in the size of the tumor. Fifteen months later, visual acuity and fields were unchanged and the boy remained healthy.

CASE 13

In Glasgow, a 3-year-old girl with hydrocephalus was found to have a third ventricular tumor. The tumor was biopsied and found to be a juvenile pilocytic astrocytoma, type 1. No stigmata or family history of NF-1 were present. A ventriculoperitoneal shunt was placed and the patient underwent radiotherapy. Clinical signs of precocious puberty developed and she received hormonal treatment for gynecomastia. At that time, she was noted to have bilateral optic atrophy with impaired vision.

At age 10 years, she presented with left hemiplegia, left facial weakness, and moderate left-sided ataxia. A CT scan showed a large tumor deep in the right temporoparietal field. One year later, at age 6 years, visual acuity was 20/100 OU. At age 8 years, visual acuity was unchanged. Computerized perimetry at this point revealed a generalized depression of the field with bilateral, temporal defects, greater on the left. At age 10 years, magnetic resonance imaging revealed marked shrinkage of the tumor, with a now normal right optic tract. Only the right side of the chiasm enhanced with contrast (Figure 11C and D). At 11 years of age, the boy reported having improved vision. Visual acuity remained 20/100 OU, although brisker. Computerized static perimetry also revealed an improvement, with less dense defects. Magnetic resonance imaging scans showed complete regression of the tumor (Figure 11E and F). Trace, if any, contrast enhancement of the chiasm remained. At 12 years of age, the boy was healthy with moderate visual handicap.

CASE 11

A 2-year-old boy underwent CT imaging with contrast for spasms of spasmus nutans, which revealed the presence of a chiasmal mass. A biopsy confirmed the diagnosis of pilocytic astrocytoma, type 1. No stigmata of NF-1 were present. He was referred for follow-up to the Neuro-ophthalmology Unit at the British Hospital, Buenos Aires, Argentina. Visual acuity was difficult to assess at the time because of the lack of patient cooperation. At age 5 years, acuity was estimated to be 20/200 OU. His mother and his schoolteachers believed, however, that his vision had improved from previous years. Both optic discs appeared atrophic. An MRI scan revealed a large, symmetric, globular, relatively homogeneous suprasellar mass with preserved contours. Both optic tracts appeared involved (Figure 11A and B). One year later, at age 6 years, visual acuity had improved from previous years. Both optic nerves appeared atrophic. An MRI scan revealed a large, symmetrical mass. A biopsy confirmed the diagnosis of pilocytic astrocytoma, type 1. No stigmata or family history of NF-1 were present. A ventriculoperitoneal shunt was placed and the patient underwent radiotherapy. Clinical signs of precocious puberty developed and she received hormonal treatment for gynecomastia. At that time, she was noted to have bilateral optic atrophy with impaired vision.
rietal region with compression of the posterior end of the third ventricle. The lateral ventricles were enlarged. Her visual acuity was 20/80 OD and 20/40 OS, reportedly an improvement from her previous examination 4 years earlier. Visual acuity measurements from the previous examination, however, are no longer available. Pupillary reactions were noted to be sluggish. At age 11 years, best-corrected visual acuities were 20/200 OD and 20/60 OS.

Eight years later, at age 19 years, the patient’s visual function was unchanged. At age 20 years, she complained of intermittent dizziness with staggering, blurring, and deterioration of her vision, and frequency of urination. She was obese and had clinical panhypopituitarism. Visual acuity was counting fingers OD and 20/80 OS, with a bitemporal hemianopia. A CT scan showed a suprasellar tumor mass and dilatation of the ventricles (Figure 13A). Some calcification was noted on the right posterior aspect of the tumor.

Eight months later, the patient continued to gain weight and suffered from polyuria and polydipsia. A CT scan showed an increase in the size of the tumor, although vision remained unchanged. Ten months later, at age 21 years, the patient demonstrated continued stability of her visual function. She had her first MRI scan, which showed the tumor could not be differentiated from the optic chiasm, and that there was associated edema extending into the optic tracts. Eight months later, her appetite seemed to normalize along with her urinary frequency, while her vision remained unchanged. A year later, she showed signs of continued improvement with significant weight loss and return of her menstrual periods. A CT scan 1 year later showed spontaneous regression of the tumor by about 75% to 80% of its original size, with the calcified portions of the tumor now apparently pulled closer to midline (Figure 13B). Three years later, at 27 years of age, a CT scan showed more extensive bilateral basal calcification. Another CT scan 16 months later revealed further reduction in the size of the tumor, with calcified areas seen only in proximity to the midline (Figure 13C). Visual acuity was light perception OD and 20/200 OS. Visual field assessment revealed a small nasal field in the left eye. Repeat CT imaging 2 years later showed no change in the residual calcified suprasellar lesion. There was no significant change in her visual function. At 31 years of age, there were still no Lisch nodules or other stigmata of NF-1.

**COMMENT**

Spontaneous regression of juvenile pilocytic astrocytomas involving the optic nerves and chiasm is a fact as exemplified by the 13 serially imaged cases in this report. We do not know the frequency of this tumor behavior, but we suspect that it is relatively high. The occurrence of spontaneous regression of optic gliomas may be masked by several phenomena. Many gliomas occur and are not detected, as NF-1 neuroimaging surveys have shown. 1-3,13-17 These tumors can regress. Spontaneous regression can be overlooked in patients known to harbor an optic glioma whose clinical condition has remained stable for many
months or years and for whom repeat scans are not performed, or for whom the older scans are no longer available for comparison.

The cellular mechanisms in these low-grade gliomas that lead to their regression remain a mystery. Lindenberg et al. must have believed that an optic glioma could regress, for in 1973, he entitled such an event in a necropsy illustration of an incidentally discovered chiasmal thickening. Borit and Richardson in 1982 reported a case of biopsy-proven chiasmal glioma that spontaneously disappeared as proven at necropsy 13 years later. These neuropathologists also presented a second case of an incompletely resected orbital glioma that totally regressed. The report of Liesti et al. in 1996 exemplifies another histologically proven instance, wherein a juvenile pilocytic astrocytoma of the temporal-hypothalamic region regressed spontaneously. In 1999, Lazareff and colleagues referred to 4 cases of histologically proven hypothalamic chiasmatic gliomas that partially regressed. Schmandt and co-workers and Colosimo and associates in 2000 each reported a case of biopsy-proven chiasmal pilocytic astrocytoma that underwent spontaneous regression. Higher-

Figure 11. A, T1-weighted axial magnetic resonance imaging (MRI) (April 1992) shows a homogeneous, large, symmetric suprasellar mass. Both optic tracts appear involved. B, T1-weighted sagittal MRI (April 1992). A large, relatively homogeneous, globular tumor involving the chiasm completely occupies the suprasellar cistern. C, T1-weighted coronal MRI after contrast (December 1997) shows only mild enlargement of the chiasm. Contrast signal enhancement is limited to the right lateral aspect of the chiasm. D, T1-weighted sagittal MRI after contrast (December 1997) showed marked reduction in chiasmal size with normal right optic tract and right nerve. Contrast signal intensity was homogeneous in this off-midline sagittal section. E, T1-weighted coronal MRI after contrast (February 1999). The chiasm showed trace, if any, enhancement, and was normal in size. F, T1-weighted sagittal MRI after contrast (February 1999). There was no enlargement or enhancement of the chiasm. All structures appeared normal.
grade gliomas may also regress. Kernan and colleagues, and Lenard and coworkers in 1998 provided histological evidence for spontaneous regression of a fibrillary astrocytoma of the hypothalamus and pons respectively.

Various theories have been proposed in the past to account for cases in which spontaneous reduction in glial tumor size had been presumed or suspected. These include an endocrine-associated decrease in vascular engorgement of the glioma, resorption of glioma-secreted mucosubstance, or tumor cell necrosis secondary immunologic activity. We suggest that other mechanisms, such as programmed cell death (apoptosis) outpacing proliferation of cells may be involved. Given that the proliferation of juvenile pilocytic astrocytoma cells slows down with age, it is plausible to think that given enough time, and the patient ability to endure its presence, most such tumors would regress.

Several neuroimaging studies have shown that at least 20% of NF-1 patients have gliomas. These studies and others have also indicated or shown T2-weighted signal abnormalities at some point in as many as 80% of patients with NF-1. The fact that both T1- and T2-weighted MRI signal abnormalities in NF-1 patients disappear later in life is indicative that a process of spontaneous glial regression must be widespread. Neurofibromatosis type 1 is not a requirement for regression of an optic glioma. Only 4 of our 13 cases involved patients with NF-1 (Table).

It is crucially important that spontaneous regression of optic gliomas be taken into consideration whenever the results of therapy (surgical debulking, radiation, and chemotherapy) are being evaluated. We believe that examples of optic glioma regression following partial resection could represent examples of spontaneous tumor regression. In select cases, debulking could, however, create sufficient space for continued tumor growth while sparing adjacent structures. In some instances, this might permit the tumor to age sufficiently enough to enter a phase of regression. The role of radiation and chemotherapy in induction of tumor regression is more difficult to define.

Figure 12. A, T1-weighted coronal magnetic resonance imaging after contrast (May 1994) showed a large, lobulated tumor in the suprasellar cistern, homogeneous in signal intensity. Note that the tumor nearly filled much of the cistern both vertically and horizontally. B, T1-weighted coronal magnetic resonance imaging after contrast (July 1995). There was marked reduction in the size of the tumor. The pituitary stalk was visible in the midline inferiorly.

Figure 13. A, Axial computed tomographic scan (July 1988) reveals a suprasellar tumor. There was some calcification on the right posterior aspect of the mass. B, Axial computed tomographic scan (February 1992) showed marked regression of the tumor. Calcification within the tumor was located closer to midline. C, Axial computed tomographic scan (December 1996) showed continued regression of the tumor. Basal calcification was more extensive, in proximity to the midline.
### Summary of Clinical and Neuroimaging Findings*

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age at Tumor Detection</th>
<th>When Tumor Detection by Neuroimaging</th>
<th>Treatment</th>
<th>Approximate Age When Regression Began</th>
<th>Span of Regression in Years</th>
<th>NF-1 Status</th>
<th>Tumor Signal Change</th>
<th>Visual Acuity Changes in Worst Eye</th>
<th>Visual Field Changes in Worst Eye</th>
<th>Degree of Shrinkage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7 years</td>
<td>Observation</td>
<td></td>
<td>1 year</td>
<td>8</td>
<td>+</td>
<td>Yes</td>
<td>HM to 20/200</td>
<td>Improved</td>
<td>Marked</td>
</tr>
<tr>
<td>2</td>
<td>4 years</td>
<td>Biopsy, observation</td>
<td></td>
<td>4 years</td>
<td>5</td>
<td>-</td>
<td>Not seen (CT) and MRI</td>
<td>20/70 to 20/20</td>
<td>Improved</td>
<td>Moderate</td>
</tr>
<tr>
<td>3</td>
<td>7 months</td>
<td>Observation</td>
<td></td>
<td>7 months</td>
<td>3</td>
<td>-</td>
<td>Not seen (CT)</td>
<td>NA, improved visual behavior</td>
<td>NA</td>
<td>Marked</td>
</tr>
<tr>
<td>4</td>
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<td>Observation</td>
<td></td>
<td>13½ years</td>
<td>3</td>
<td>-</td>
<td>Yes</td>
<td>20/20, unchanged</td>
<td>Improved</td>
<td>Mild</td>
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<tr>
<td>5</td>
<td>13 years</td>
<td>Attempted surgical debulking (age 13 years)</td>
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<td>14 years</td>
<td>1</td>
<td>-</td>
<td>Yes</td>
<td>20/200 to 20/25</td>
<td>Improved</td>
<td>Marked</td>
</tr>
<tr>
<td>6</td>
<td>14 years</td>
<td>Observation</td>
<td></td>
<td>14.3 years</td>
<td>1.5</td>
<td>-</td>
<td>Yes</td>
<td>CF to 20/20</td>
<td>Improved</td>
<td>Moderate</td>
</tr>
<tr>
<td>7</td>
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<td>Observation</td>
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<td>15 years</td>
<td>2</td>
<td>+</td>
<td>Yes</td>
<td>CF, unchanged</td>
<td>Unchanged</td>
<td>Moderate</td>
</tr>
<tr>
<td>8</td>
<td>4 months</td>
<td>Observation</td>
<td></td>
<td>5 years</td>
<td>8</td>
<td>-</td>
<td>Yes</td>
<td>20/400 to CF</td>
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<td>Marked</td>
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<tr>
<td>9</td>
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<td>Observation</td>
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<td>2</td>
<td>+</td>
<td>Yes</td>
<td>CSUM to CSM</td>
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<tr>
<td>10</td>
<td>6 months</td>
<td>Chemotherapy (age 3 years)</td>
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<td>15 years</td>
<td>6</td>
<td>-</td>
<td>Yes</td>
<td>LP to 20/300</td>
<td>Improved</td>
<td>Unchanged</td>
</tr>
<tr>
<td>11</td>
<td>2 years</td>
<td>Biopsy, observation</td>
<td></td>
<td>10 years</td>
<td>6</td>
<td>-</td>
<td>Yes</td>
<td>20/200 to 20/100</td>
<td>Improved</td>
<td>Marked</td>
</tr>
<tr>
<td>12</td>
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<td>Observation</td>
<td></td>
<td>14 years</td>
<td>3</td>
<td>+</td>
<td>No</td>
<td>20/200 to 20/40</td>
<td>Improved</td>
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</tr>
<tr>
<td>13</td>
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<td>Biopsy, radiation therapy (age 3 years)</td>
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<td>21 years</td>
<td>8</td>
<td>-</td>
<td>Not seen (CT)</td>
<td>20/80 to 20/200</td>
<td>Worsened</td>
<td>Marked</td>
</tr>
</tbody>
</table>

* NF-1 indicates neurofibromatosis type 1; HM, hand motions; CT, computed tomography; MRI, magnetic resonance imaging; NA, not available; CF, counting fingers; CSUM, central, steady, and unmaintained vision; CSM, central, steady, and maintained vision; and LP, light perception.

However, delayed regression long after therapy should probably be regarded as spontaneous.

In this discussion, we wish to make several observations regarding visual function in patients with regressing gliomas. Ten of our 13 cases demonstrated improved vision with decrease in the size of the tumor or decrease in its signal intensity (Table). Improvement in vision was variable and did not correlate with the degree of tumor shrinkage.

Implications of these cases and others like them are obvious. The fact that clinically significant intracranial or intraorbital optic gliomas may spontaneously regress in patients with and without NF-1 must be entertained in planning their treatment. To assess the frequency of such regressions, a review of serial imaging collected to date, and additional time and observation, from ongoing prospective MRI studies of NF-1 gliomas and non-NF-1 gliomas is needed.

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