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Syphiloma/Gumma of the Optic Nerve and Human Immunodeficiency Virus Seropositivity

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A 68-year-old man developed the sudden onset of transient obscurations of vision in the right eye in November 1988. Two weeks later he noted floaters, photophobia, and blurred vision in the left eye. He presented with unilateral optic disc edema in the right eye. The left eye showed anterior uveitis but a normal optic disc. He was found to be violently seroreactive for *Treponema pallidum* infection and was also human immunodeficiency virus (HIV) seropositive. Ultrasonography confirmed the presence of a solid thickening of the anterior optic nerve sheath in the right eye. An interesting and dramatic response to penicillin therapy occurred. This is the first instance of a gumma or solid syphiloma of the optic nerve documented by ophthalmic ultrasonography.

Key Words: Syphiloma—Gumma—Human immunodeficiency virus.

Syphiloma or gumma of the optic nerve is so rare that Walsh and Hoyt (1) stated they had not observed such a case, and to our knowledge, the last reported instance was by Koff (2) 50 years ago. We recently encountered a 68-year-old man who presented with a unilateral choked disc with solid thickening of the retrobulbar optic nerve sheath confirmed by quantitative orbital echography with negative 30° tests (3). Serologic and cerebrospinal fluid findings confirmed the diagnosis of active neuro-ocular syphilis, which led to the detection of previously unsuspected human immunodeficiency virus (HIV) seropositivity. The lesion responded in an interesting way to intravenous penicillin therapy. This case prompted this report with a review of the literature of optic nerve gummata.

CASE REPORT

A 68-year-old right-handed white man had no eye complaints until November 1988. As he got out of bed one morning his right eye vision suddenly became "totally black". This was painless and cleared totally within 10–12 seconds. These episodes of transient visual loss in the right eye began to recur, were not necessarily related to changes of posture, and shortly increased in frequency to many times a day. He had no problems with the left eye at all. These classic transient obscurations of vision prompted ophthalmological examination on November 19, 1988. At that time, visual acuity was 20/20 in the right eye and 20/50 in the left eye, but improved in the left eye with a pinhole to 20/30. Examination revealed some edema of the right optic nerve with dilated vessels on its surface and a bit of hemorrhage around the papilla. There was no other evidence of ocular inflammation.

The patient was referred to his internist and had an extensive medical workup, including SMAC-24,

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serum TORCH profile, ANA, pattern reversal visual evoked response, BAER, and duplex doppler carotid studies, which were all normal. A neurologic consultation was also negative and magnetic resonance imaging (MRI) of the brain with limited study of the orbits on November 29, 1988, was reported as normal. A sedimentation rate of 48 prompted a right temporal artery biopsy on December 16, 1988, which was negative. A 3-week course of oral prednisone (up to 40 mg/day) produced no change in symptoms.

Within less than a month after noting the onset of transient obscurations in the right eye, the patient began to notice floaters in the left eye, became photophobic, and developed persistent blurring of vision in the left eye. Repeat eye examination on January 3, 1989, revealed persistent right optic disc edema; fine keratitic precipitates and 1+ cells and flare were now evident in both eyes, with beginning posterior synechiae in the left eye. He was placed on topical steroids and referred to the Bascom Palmer Eye Institute.

The patient had had a right colectomy for colon carcinoma in April 1981. He required no chemotherapy or irradiation therapy thereafter, and regular follow-ups for this were negative. His last colon studies were 2 1/2 years ago. He had lost 15 pounds in the preceding 3 months. There were no other complaints.

Neuro-ophthalmologic examination on January 9, 1989, revealed a corrected vision of 20/20 in the right eye and 20/20+3 in the left eye. External examination revealed that the eyes were white and ocular rotations were full. The left pupil was equivocally larger than the right and was slightly peaked from posterior synechiae. The pupils reacted 2+ to light on the right and 2.5+ on the left, and a subtle afferent (Marcus Gunn) pupillary response was noted on the right.

Visual field examination showed normal peripheral fields in both eyes, but on the tangent screen the blind spot was grossly enlarged in the right eye to two to three times as large as the normal left blind spot. Exophthalmometry at base 100 was 23 right and 22 left. The patient identified 11 of 11 Ishihara color plates with each eye.

Slit lamp biomicroscopy was essentially normal in the right eye except for 1+ vitreous cells. The left eye had a few small lymphocyte-like deposits on corneal endothelia, but no iris nodules. After dilatation, extensive posterior synechiae of the entire nasal half of the iris (Fig. 1) and a 1–2+ vitritis was evident in the left eye.

Ophthalmoscopy of the right eye showed clear media, but the optic nerve was grossly abnormal

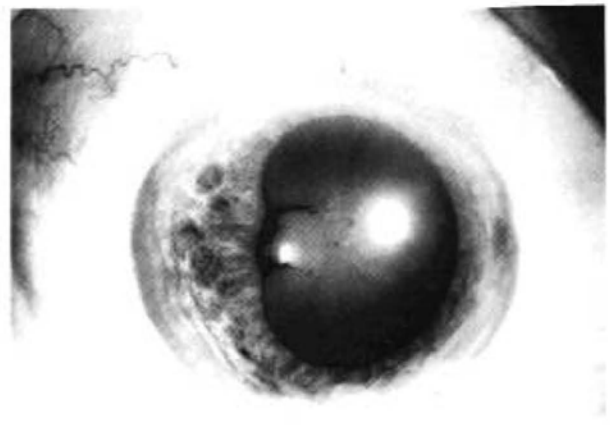

FIG. 1. Left eye, showing extensive posterior synechiae on nasal half of iris with anterior uveitis.

(Fig. 2). High-grade optic disc edema to at least two to three times normal size was evident. Some newly formed vessels were evident on the surface and a few refractile glial-like balls were seen on the temporal side. A few folds in the retina concentric with the papilla (Paton's lines) were noted. The central vein was full and one had to push on the lid with the finger up to the point of making the artery pulse in order to get the vein to collapse. The macula and peripheral fundus were normal. No inflammatory or metastatic lesions were seen in the choroid or elsewhere in the right fundus.

In the left eye, the optic disc was sharp in outline and appeared normal (Fig. 3). The vein was not distended but no good spontaneous venous pulse was seen. Intraocular pressures were 17 right and 14 left.

Ophthalmic ultrasonography showed marked disc elevation on the right without calcium and no evident orbital mass. The right optic nerve sheath measured 3.7 mm anteriorly and 3.9 mm posteri-

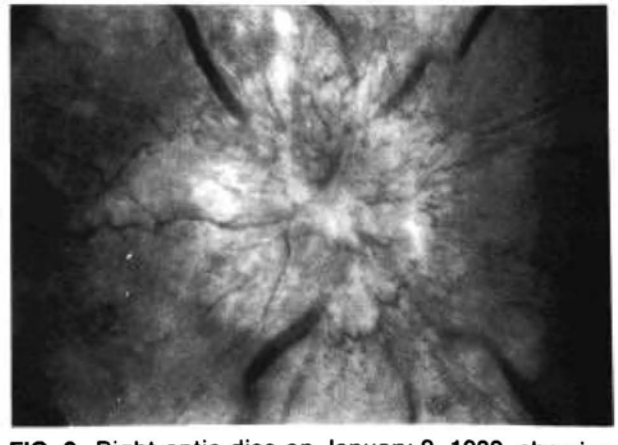

FIG. 2. Right optic disc on January 9, 1989, showing extensive disc edema with dilated and newly formed vessels on surface.

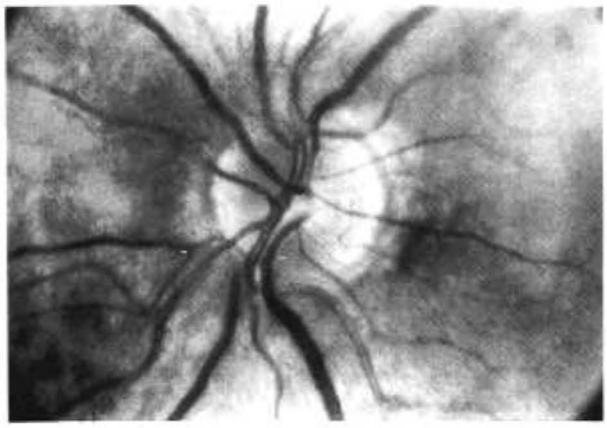

FIG. 3. Left optic disc on January 9, 1989; normal appearance.

orly in the primary position, and was 3.7 mm front and back on 30° eccentric gaze (Fig. 4). The left optic nerve was 2.9 mm anteriorly, 2.7 mm posteriorly, and was 2.7 mm front and back on 30° eccentric gaze (Fig. 5). Normal optic nerve size is <3.3 mm and averages about 2.7 mm by this technique. Testing in 30° eccentric gaze allows differentiation in acoustically enlarged retrobulbar optic nerve sheaths between compressible lesions (as increased subarachnoid fluid; a positive 30° test) and noncompressible processes (as infiltrating or optic nerve mass lesions; a negative 30° test) (4). Thus, the right optic disc was choked, the right retrobulbar optic nerve sheath was enlarged by a solid noncompressible thickening, and the left optic nerve was normal.

The impression was optic disc edema of the right eye, producing classic transient obscurations of vision, and an associated solid enlargement of right optic nerve sheath. In addition, there was an asymmetric anterior uveitis and vitritis, much more marked in the left eye. A complete medical investigation was begun. Because of the prior history of colon carcinoma, carcinoembryonic antigen was obtained and was 3.0 ng/ml (normal 0–5.0 ml). A routine Lyme/treponemal panel was drawn on January 9, 1989, and was reported by telephone as follows: serum rapid plasma reagin (RPR) test was reactive (1:1,024). Serum fluorescent treponemal antibody–absorbed (FTA-ABS) test enzyme-linked immunosorbent assay was reactive (4+). Lyme (ELISA) was 1.5 (normal <1.0), and Lyme IFA immunoglobulin (Ig)G was 1:256 and IgM was <1:16. The results were consistent with extremely active syphilitic disease and some serocross-reactivity to *B. burgdorferi* (5).

The patient was promptly hospitalized elsewhere. Lumbar puncture on January 20, 1989, revealed normal opening pressure, six erythrocytes, no lymphocytes, glucose 41, protein 83, culture negative, and the cerebrospinal fluid (CSF VDRL) test was reactive. Repeat serum VDRL was reactive (1:512). The patient was treated with 20 million U/day of i.v. aqueous penicillin G for 10 days. He promptly improved on this regimen so that the transient obscurations stopped completely while he was in the hospital.

The patient was seen at the Bascom Palmer Institute for a follow-up on March 21, 1989. Corrected vision was 20/15-1 in the right eye and 20/30+2 in the left eye (20/25+2 with pinhole). The right optic disc appeared notably improved on ophthalmoscopy (Fig. 6) and blind spot sizes were now within normal limits in both eyes. The iritis and vitritis in the left eye was much improved and

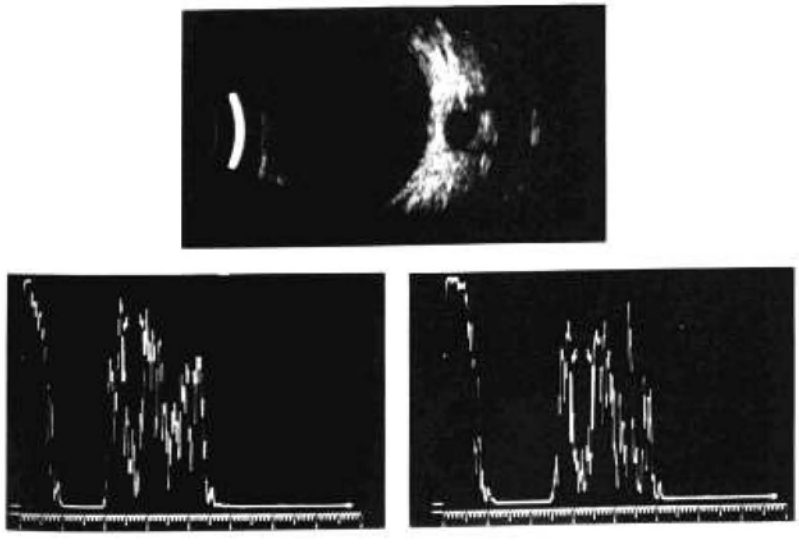

FIG. 4. Right optic nerve evaluated on January 9, 1989. **Top:** Transverse B-scan shows optic nerve (arrow) in cross-section. **Bottom left:** Standardized A-scan at tissue sensitivity shows maximal diameter of optic nerve measured in primary gaze. Arrows correspond to arachnoidal sheath diameter (3.9 mm). **Bottom right:** Remeasurement at 30° gaze toward the probe shows no change in diameter of nerve pattern.

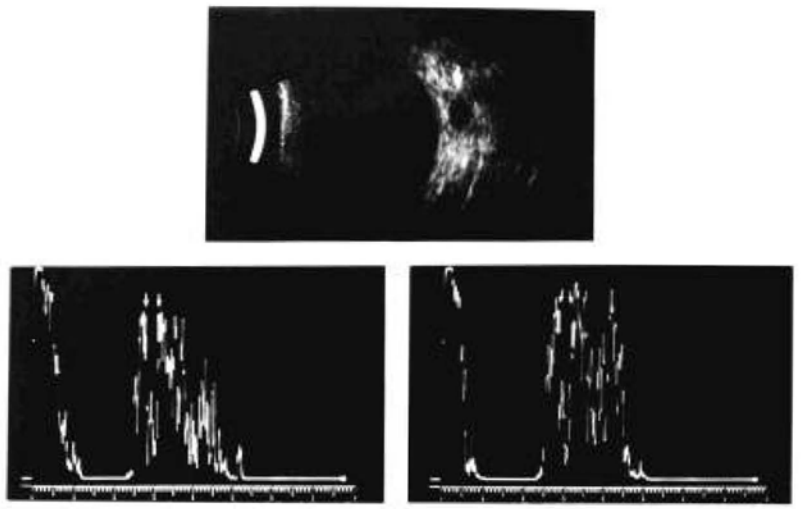

FIG. 5. Left optic nerve on January 9, 1989. This normal optic nerve remained the same size throughout all evaluations. Top: Transverse B-scan shows optic nerve (arrow) in cross-section. **Bottom left:** Standardized A-scan at tissue sensitivity shows maximal diameter of optic nerve measured in primary gaze. Arrows correspond to arachnoidal sheaths (2.9 mm). **Bottom right:** Remeasurement at 30° gaze toward the probe shows no change in diameter of nerve pattern (2.9 mm).

posterior synechiae had largely broken. A repeat blood test on March 21, 1989 showed RPR reactive 1:128, FTA-ABS reactive 4+, Lyme ELISA 1.8, Lyme IFA IgG 1:128, and Lyme IFA IgM <1:16. However, repeat ultrasonography revealed that the right optic nerve was 3.9 mm front and back, and the same in primary and eccentric gaze; the left optic nerve was 2.9 mm front and back (Fig. 7). In other words, although clinically much better, the ultrasound revealed no decrease in size of the enlarged right optic nerve sheath at all. At the suggestion of Dr. Culbertson, a serum HIV test was ordered. This showed the HIV screen to be repeatedly reactive and this was confirmed by an HIV-agen test. The patient was notified of this in confidence and advised to have this repeated by his general physician. This was done and he was again found to be HIV seropositive.

The patient was seen again at the Bascom Palmer Institute on July 6, 1989. He had no complaints at that time and reported no transient obscurations since the penicillin therapy. Slit lamp revealed normal findings in the right eye and only a slightly oval pupil on the left, but no evident vitritis was now seen. Ophthalmoscopy showed that the right disc was now essentially normal. Some slight periarteriolar sheathing was seen. The left disc was normal and a small-amplitide venous pulse was seen. Repeat serum VDRL test on July 6, 1989, was reactive (1:8). A total white blood cell count was 4,200/mm^3 with lymphocytes 38.1% or 1,600/mm^3 total lymphocyte count. Total T lymphocytes were 81.6% (1,306/mm^3), helper/inducer subset was 29.6% (473/mm^3), and suppressor/cytotoxic subset was 48.0% (767/mm^3). Thus T4/T8 ratio was 0.61. It was concluded that there was a decreased number of T helper cells (T4) a normal number of T suppressor cells (T8), and a decreased ratio of T cell subsets (T4/T8). Repeat ultrasonography on July 6, 1989, (Fig. 8) revealed right optic nerve 2.9 mm anteriorly and posteriorly in primary gaze and unchanged on 30° eccentric gaze, and left optic nerve also 2.9 mm (Fig. 8). Thus, the optic nerve was now normal by echography.

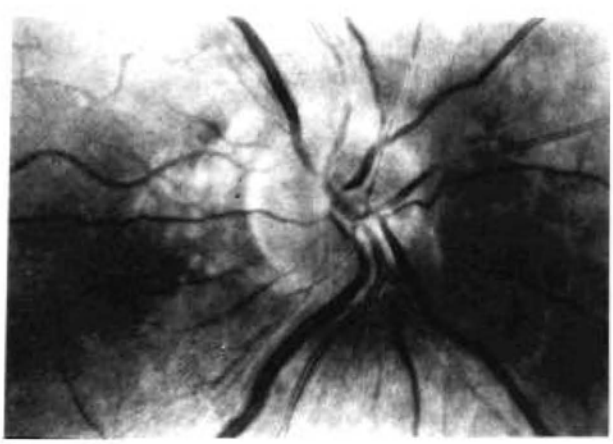

FIG. 6. Right optic nerve on March 31, 1989 (after penicillin therapy). The optic disc edema has cleared remarkably and disc is ophthalmoscopically nearly normal in appearance.

COMMENT

In summary, a 68-year-old man noted the sudden onset of transient obscurations of vision in the right eye in November 1988. He was found to have high-grade optic disc edema in that eye, which prompted an extensive medical and neurologic workup up through and including MRI of the brain. Within 2 weeks, however, he noticed the onset of floaters in the left eye and photophobia, and repeat eye examination showed iritis and vit-

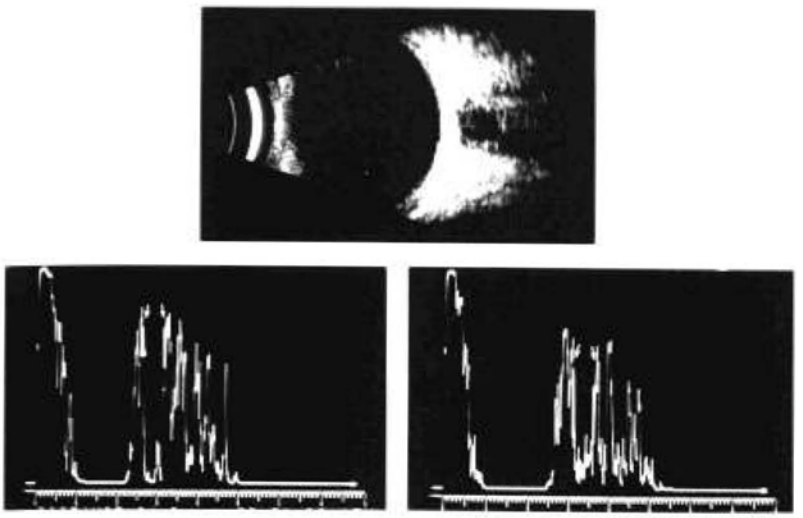

FIG. 7. Right optic nerve on March 21, 1989. Echograms indicate no significant change in width of optic nerve sheath. **Top:** Transverse B-scan shows optic nerve (arrow) in cross-section. **Bottom left:** Standardized A-scan at tissue sensitivity shows maximal diameter of optic nerve measured in primary gaze. Arrows correspond to arachnoidal sheath diameter (3.9 mm). **Bottom right:** Remeasurement at 30° toward the probe shows no change in diameter of nerve pattern (3.9 mm).

ritis, much more marked in left eye, which had a normal appearing optic disc.

Neuro-ophthalmologic examination showed good visual acuity, normal fields except for an enlarged right blind spot, and confirmed the highly choked disc in the right eye with a normal optic disc in the left eye. Ultrasonography showed an enlarged right optic nerve sheath due to a solid, noncompressible lesion. With a history of former colon carcinoma in 1981, the possibility of a metastatic lesion to the optic nerve was considered. However, general physical examination and carcinoembryonic antigen study were normal. Routine serologic testing showed a reactive serum reagin test to 1,024 dils with a 4+ serum FTA-ABS test. Lumbar puncture revealed a clear acellular fluid under normal pressure with an elevated spinal fluid protein and the CSF VDRL test was reactive. The diagnosis of active syphilis with an optic nerve syphiloma/gumma in the right eye and bilateral asymmetric syphilitic uveitis was made. Treatment with 200 million U of i.v. aqueous penicillin gave a dramatic clearing of optic disc swelling and of the iritis and vitritis.

A particularly interesting point in this patient was that the optic disc swelling had virtually totally cleared in the fundus when the patient was seen 6 weeks after penicillin treatment, yet quantitative ocular echography showed that the distended segment of the retrobulbar optic nerve sheath was unchanged. Thus, the optic nerve syphiloma appeared to have cleared from anterior to posterior, whereas one might have predicted the opposite. A follow-up ultrasound study at 6 months, however, confirmed the normal clinical findings in that the optic nerve lesion had now returned to normal size. A dramatic serologic response was noted with VDRL being reactive 1,024 dils on January 9, 1989 (before treatment), 128 dils on March 21, 1989, and 8 dilutions on July 6, 1989.

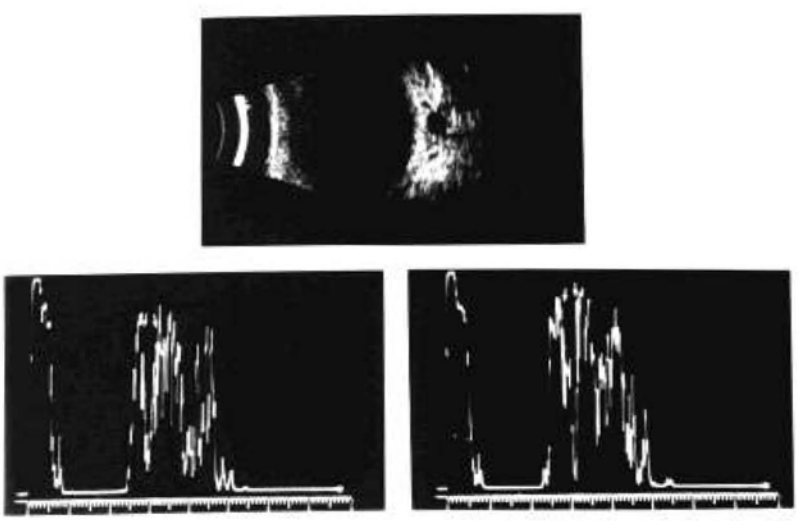

FIG. 8. Right optic nerve reevaluated on July 6, 1989. Optic nerve pattern has significantly decreased since last examination. **Top:** Transverse B-scan shows optic nerve (arrow) in cross-section. **Bottom left:** Standardized A-scan at tissue sensitivity shows maximal diameter of optic nerve measured in primary gaze. Arrows correspond to arachnoidal sheath diameter (2.9 mm). **Bottom right:** Remeasurement at 30° gaze toward the probe shows no change in diameter of nerve pattern (2.9 mm).

The patient was incidentally found to have a repeatedly reactive serum HIV test with a decreased T4/T8 ratio, and this was discovered only because of the recommendation of routine HIV testing of all patients with ocular or neurosyphilis.

DISCUSSION

Primary gummata or syphilomata of the optic disc are rare. The last such case in the literature to our knowledge was 50 years ago by Koff (1), who stated that fewer than 20 cases had been reported up to 1939. Koff commented that few ophthalmologists have seen a gumma of the papilla, and considered this rather surprising in view of the frequency with which the optic nerve is involved in syphilis. The general subject of syphilitic involvement of the optic nerve is too extensive to be considered here. In Uhthoff's classic studies (1893–1903) (5) he concluded that the intracranial part of the optic nerve and the chiasm were most commonly affected, either by direct involvement or by extension of a syphilitic basal meningitis, which is rather frequent in the chiasmal region. In such a case the optic nerve may be surrounded by granuloma, and the process frequently proceeds distally down the optic nerve sheath, most often resulting in the clinical appearance of a descending primary optic atrophy. This report, however, will be restricted specifically to reports of gummata or syphilomata involving the optic disc. It is of interest to note that Verhoeff in 1910 stated that in all of Uhthoff's extensive experience, he did not report one such case.

Koff stated that the possibility of a gumma should be considered in the differential diagnosis of any neoplasm of the optic papilla. Ronne stated that the ophthalmoscopic picture was variable, "occasionally reminding one of a tumor; generally, however, giving the impression of a choked disc, often enough obscured by a clouding of the vitreous" (6). Frequent associated signs are an anterior uveitis, yellowish dots in the fundus periphery, and flame-shaped hemorrhages around the disc. Koff's patient (1) was a known paretic with a 4+ blood and spinal fluid Wassermann reaction, who had been treated with tryparsamide and bismuth in a mental hospital. Vision had been failing for 1 1/2 years and when seen the patient had no light perception in the involved eye and 20/30 in the other eye, which also showed some general constriction of the visual field. Slit lamp examinations were otherwise negative. Ophthalmoscopy revealed a glistening yellowish-gray tumor about 1 1/2 disc diameters in diameter, with a raspberrylike surface. It covered the lower temporal third of the nerve head. Vessels coursed directly over it. The remaining portion of the nerve was pale white with fuzzy borders. The retina appeared gray and atrophic about the tumor and high-grade perivascular sheathing extended into the periphery of the fundus. The general physical examination otherwise showed only luetic involvement of the nasal septum. No histologic proof was available in Koff's case and he stated that the differential diagnosis rested on (a) serology of the blood and spinal fluid; (b) frequently associated inflammation of the anterior segment; and all above (c) a response to antiluetic therapy, with the lesions regressing markedly and rapidly. He added that under strenuous antisyphilitic therapy some eyes might regain normal vision, while others go on inexorably to total blindness. That report and our case prompted a literature review of optic nerve gummata, hopefully to be considered in detail in another paper.

It should be remembered that the *T pallidum* organism was first described by Schaudinn and Hoffman in 1905 and the first serologic test for syphilis was reported by Wassermann in 1906. Reports prior to that time need to be assessed with that in mind, and consideration will therefore be given here only to those cases with histologic verification of the diagnosis.

There have been only six histopathologically verified cases of optic nerve gummata reported to our knowledge. These were by Juler in 1897 (7), Wagner in 1903 (8), Stock in 1905 (9), Parsons in 1905 (10), Verhoeff in 1910 (11), and Matsukawa in 1913 (12). The first histologically verified case was by Juler in 1897 (7). A 32-year-old man contracted syphilis in April 1894. He was treated then with mercury and potassium iodide with disappearance of his symptoms. In July 1896 he noted the onset of blurred vision in the left eye. This initially involved the inner aspect of his visual field, but later the entire field so that he had a complete loss of vision in that eye. On July 26, 1896, after the loss of vision, the eye became inflamed and very painful. Pain was increased on motion of the eye, and the pain increased without relief by atropine or hot compresses.

The patient was seen for the first time on August 8, 1896. The right eye was normal and had good vision. The patient had no symptoms of intracranial disease otherwise. The left eye was totally blind. The tension was normal, and the eye showed iritis with complete posterior synechiae.

The fundus could not be visualized. Pain was also present around the orbit. All therapy (hot fomentations, leeches, atropine, opium) gave no relief and because of the suspicion of an intraocular tumor, the eye was enucleated on August 26, 1898. This was followed by complete relief of his pain.

The patient developed inflammation of the throat in October 1898, and in November large red plaques on the forehead, cheek, shoulders, and back, and later developed diarrhea and skin lesions. Later he completely recovered and regained excellent health over 2 months.

Examination of the enucleated eye, which was fixed in formalin and sectioned, revealed that the papilla was swollen and the adjacent retina was very thickened and detached. The optic nerve was twice normal thickness, and measured 6 mm immediately behind the globe. It presented longitudinal striae alternately opaque and white, and transparent and grey. The vitreous was diffusely cloudy with some membranous bands passing in front of the swollen papilla. The pupil was obliterated; the lens was normal.

Microscopically, the optic papilla was infiltrated by leukocytes. The nerve fiber layer of the retina was also densely infiltrated with such cells, and the external layers had a membrane as seen with a severe papillitis. The nerve near the globe was infiltrated with leukocytes, and these were grouped in a massive process. The choroid also showed a diffuse cellular proliferation. Hemorrhages were noted principally in the nerve fiber layers.

This case was thought to be interesting for the following reasons. (a) It showed a true inflammation of the optic nerve, both behind the globe and in the papilla. This was proven by the leukocytic cellular infiltration, and thus was not a simple edema of the papilla as seen with intracranial tumors. (b) The author stated that this was undoubtedly a case of acquired syphilis because a cutaneous eruption and peripheral neuritis were observed after excising the eye, proving, in his opinion, that this was a case of late secondary syphilis. The inflammatory exudation was pronounced behind the globe, and probably was of the same cause.

The author stated that the cause of retrobulbar neuritis with the presence of a central scotoma to colors as the principal symptom is often very obscure. Juler observed several cases that responded to mercurial treatment and was then persuaded that the principal cause was syphilitic inflammation in such instances. He saw a navy officer who contracted syphilis and developed a papillitis with a large central scotoma to red and green in the two eyes. The vision decreased to Jaeger 20, but he had a complete recovery of the two eyes after prolonged treatment with mercury inunctions.

In 1903 Wagner (8) reported a 35-year-old man who gave no history of former syphilitic infection, but presented with a history of episodes of inflammation in both eyes for 8 years. On July 1, 1902, the patient suddenly went blind in the left eye overnight. When seen at the university eye clinic a diagnosis of iritis in both eyes with secondary glaucoma in the left eye was made. General examination revealed an ulcer on the tongue and multiple drusenlike lesions on the body, and the clinical impression was lues. The eye later developed a hyphema, secondary glaucoma, and became painful, and on December 2, 1902, the left globe was enucleated.

The eye was fixed in formalin and then alcohol, embedded in celloidin, and cut in sections in an inclined fashion. Sections showed a cellular infiltration in the orbital fatty tissues, but the optic nerve was strongly infiltrated with inflammatory cells. Cellular infiltration showed spindle-formed cells, round cells, and cells with a definitely epithelioid character with dark-staining nuclei.

Serial sections showed that from the temporal side of the optic nerve (an obliterated intervaginal space and an enormously swollen optic nerve sheath), 2 mm behind the temporal side in the region of the lamina cribrosa, severe infiltration could be seen with diffuse necrosis. The infiltration consisted of spindle-shaped round cells and some dark-staining epithelioid cells. These involved the septae of the optic nerves.

Parsons wrote in 1905:

> Syphilitic affection of the optic nerve may simulate an intra-ocular tumor, as in Juler's case, and in one which I have examined. In the former the papilla was swollen and the surrounding retina much thickened and partially detached. The optic nerve was twice as thick as normal, being 6 mm in diameter close behind the globe. Microscopically there was intense leucocytic infiltration of the nerve, retina, and choroid, with some hemorrhage into the retina, principally in the nerve fiber layer. The case I examined showed similar microscopic appearances, the head of the nerve being quite necrotic. Though the anatomical examination of these cases showed nothing pathognomonic, the clinical features were such as to scarcely admit of doubt as to the syphilitic nature of the disease" (10).

Parson's comments about his case can be summarized as simply mentioning that he had seen a case histologically similar to Juler's report.

In 1905 Stock (9) reported on a gummatous mass

of the optic nerve behind the papilla and an associated gummatous choroiditis in an eye enucleated from a 58-year-old woman whose loss of vision began 8 weeks before presentation. Within 14 days, she was completely blind in her left eye. Examination showed the right eye to be completely normal. The left eye was amaurotic, with extremely high tension, and was enucleated because of pain. The optic nerve was found to be twice the normal size, and 5 mm behind the lamina cribrosa a nodular mass was found with necrosis extending to the papilla.

The most definitive case of optic nerve syphiloma or gumma reported to date was by Verhoeff in 1910 (11). He cited the previous observations of Juler, Wagner, and Stock, and mentioned Parsons' brief note. He also stated that in the extensive work of Uhthoff no similar case had been described.

Verhoeff's case merits consideration. A 55-year-old woman presented to the Massachusetts Eye and Ear Infirmary on October 27, 1909, complaining of haziness of vision. She had had a cutaneous eruption for 13 months that her doctor had designated as syphilitic, and had been on therapy for this. Her vision started to become blurry 7 months after the onset of the eruption. Examination revealed 20/50 vision in the right eye and finger counting in the left eye. Both visual fields were concentrically constricted down to 10–20° from fixation. The eyes appeared normal externally, but fine cloudy cells were seen in the vitreous of both eyes, the left papilla was intensely swollen, the surrounding retina was opaque, and some yellowish-white flecks were seen in the choroid. The right eye had a hemorrhage temporally near the disc.

More intensive therapy with mercury ointments and potassium iodide was given. The eye became worse, the vitritis progressed so that the fundus could no longer be visualized, an insidious iritis developed, and the eye became painful. Exophthalmos, with edema of lids and conjunctiva, appeared, and the eye was enucleated on March 24, 1910, because of the pain. At surgery a tumorlike thickening of the optic nerve was found, which appeared to be a syphiloma. Mercury and potassium iodide were again increased to 40 grains a day. The orbital wound healed nicely, and visual function of the left eye improved so that she could be discharged from the clinic by April 16, with 20/200 acuity.

Pathological study showed that the subvaginal space of the optic nerve was crowded with granulation tissue, and the papilla was 2 mm high, 3.5 mm broad, and notably necrotic. Levaditi-stained sections showed numerous spirochetes throughout the optic nerve.

Verhoeff (11) went into a careful consideration of whether his case belonged to the secondary or the tertiary stage of syphilis. He thought that the distinction might hinge on the immunity of the individual. He considered that the long interval between skin rash and eye disease (7 months), the absence of other syphilitic symptoms, and the presence of extensive necrosis favored a gummatous character. On the other hand, the predominantly infiltrative changes associated with numerous spirochetes and lack of systemic involvements with epithelioid and giant cells would make one favor the process as secondary. He concluded that the entire illness seemed to be a transition form for which the name *syphiloma* was suitable.

Verhoeff compared his case with the previously reported cases. in Juler's case there was only a modest infiltration without necrosis; in Wagner's case necrosis had already begun; and in Stock's case (as in Verhoeff's) a total necrosis was present. Juler's and Wagner's patients had secondary lesions elsewhere in the body, but Stock's patient had disease isolated to the eyes and, with necrosis, considered it a gumma. Wagner's patient was relatively young (35 years old), whereas the others were 52, 55, and 58 years of age. All of the patients had pain in common. Stock enucleated because of pain, and in the other cases enucleation was performed to rule out tumor. Verhoeff's patient was the only one seen early enough to permit an ophthalmoscopic examination. He pointed out that the presence of vitritis was important because otherwise the disc edema might be considered evidence of a brain tumor. Verhoeff's case was the only reported case in which spirochetes were identified.

Another excellent report was by Matsukawa in 1913 (12). A 32-year-old Japanese man had syphilis in April 1911 with a hard chancre and painless inguinal buboes. He had no other systemic symptoms for 8 months. However, in mid-January 1912 he developed iritis in the right eye, which persisted for 2 months. When seen March 25, 1912, he showed a strong pericorneal injection of the right eye, grayish-white exudation in the pupillary border, and a small pea-sized tumor on the right iris surface. The Wassermann reaction was strongly positive. The diagnosis was made of "syphilitic iritis papulosa" and i.v. salvarsan was given. The eye changes promptly reverted and he continued on mercury and iodine therapy for another month.

However, in August 1912 the patient developed recurrent inflammation in the right eye, and when seen again on October 30, he was totally blind in the right eye and had such severe pain that the eye was enucleated. The Wassermann reaction was again strongly positive.

The clinical impression was ciliary body gumma. The eye was enucleated on December 2 and at surgery the optic nerve was found to be quite thickened. Histologic study revealed that the nerve sheath was thickened all around and infiltrated with small cells in the arachnoid layer. These were also in the dural sheath and were chiefly mononuclear cells with occasional polynuclear leukocytes. A distinct perivasculitis was evident around the arteries. Some 12 mm behind the papilla a dark gumma was found. This lay in the long axis of the nerve as an irregularly bluish-staining mass of necrosis. No normal nerve fibers could be seen. Nearby, strong cellular infiltration was seen and elsewhere a gumma of the ciliary body was found. Matsukawa considered this case a neurorecidive reaction after salvarsan injection. He mentioned Stock's and Verhoeff's cases, and emphasized that spirochetes were not found in his case, citing Verhoeff's as a rare exception. Two nice drawings are presented in his paper—one of the nerve sheath and another of the necrotic zone in the gumma. A careful discussion of neurorecidive reactions in syphilis is then presented.

In conclusion, it is seen that histologically verified cases of primary involvement of the retrobulbar and intraocular portions of the optic nerves with a solid inflammatory thickening of tissue in syphilitic inflammations, although a distinct entity, is apparently a great rarity. It is important to emphasize that we are not considering optic atrophy secondary to gummatous meningitis at the base of the brain (13), optic atrophy secondary to localized syphilitic involvement of the chiasm, or histologically undocumented cases of retrobulbar gumma (14). Fuchs, in his important paper on neuritis papulosa in syphilis in 1926 (15), found only five cases of isolated syphiloma or gumma involving the disc and optic nerve stem in the literature (7–9,11,12).

In our clinic patients frequently present with swollen optic discs in the presence of some vitreous cells and an associated mild iritis, as well as the typical maculopapular skin rash of secondary syphilis. These patients have good acuity, and optic nerve ultrasonography confirms the presence of increased subarachnoid fluid in the optic nerve sheaths and the diagnosis of syphilitic optic perineuritis. The case here reported is unique in our experience, in showing a solid inflammatory mass lesion in the retrobulbar optic nerve sheath with a repeatedly negative 30° test. To our knowledge, this is the first reported case of optic nerve syphiloma documented by ultrasonography. The lesion responded promptly to massive-dose i.v. penicillin therapy and cleared up from the optic disc back to the retrobulbar nerve. The patient was found to be HIV seropositive because of this lesion and had no other symptoms of the acquired immunodeficiency syndrome at that time.

The increasing frequency of syphilis with both ocular and neurologic manifestations (16,17), the difficulty encountered with serodiagnosis in immunocompromised patients (18) (with the frequent presentation of active disease in patients with nonreactive serum VDRL tests but with reactive FTA-ABS tests), and the recent recognition of more aggressive forms of syphilis (19) (e.g., optic nerve gumma, and syphilitic orbital periostitis seen in this department) in HIV-seropositive patients warrants renewed emphasis on consideration of ocular and neurosyphilis in differential diagnosis.

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