Ocular Palsies in Children with Diabetes Mellitus

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SUMMARY

The findings in three children with ocular palsies are reported in this paper. Two had insulin-requiring diabetes and one demonstrated only an abnormal I.V. glucose tolerance test. In the first patient the condition resolved in four weeks; in the second it had not fully resolved after 21 months, and in the third patient surgery was required for correction after seven months. We suggest that any child who develops a sudden ocular palsy should be examined for diabetes mellitus. DIABETES 25:459-62, May, 1976.

The eye is an organ frequently affected in diabetes complications. These complications include refractive changes, changes in accomodation, ocular palsies, conjunctival capillary alterations, lens changes, and retinopathy.[1] In children eye changes are less common than in adults and even considered rare.

O'Brien and Allen[2] found 23 cases of diabetic retinopathy in 555 children, in whom six were transitory and resolved by two months with strict control after a six-month to one-year period of poor control. They also noted 36 cases of diabetic lens change in 260 patients,[2] all of whom were considered poorly controlled. Other changes noted by these authors in young diabetic patients were transient refractive changes consisting of a relative myopia during poor control and a relative hyperopia during reduction of blood sugar with insulin.[2]

In this paper we present three patients with ocular muscle involvement which we believe is related to their diabetes. We can find no previous cases described in children with this eye complication.

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CASE REPORTS

Case report 1. E. B., a 12-year-old boy, was referred to the Children's Mercy Hospital for determination of possible diabetes. He had been having polydipsia, polyuria, and lethargy for three days as well as an associated 8-pound weight loss over a three-week span.

Past medical history revealed that he was treated with phenobarbital and Dilantin from three to nine years of age for seizures but had had no recurrence since the medication was discontinued. Review of systems was unremarkable, and his admission physical examination was essentially normal. He had no signs of ketoacidosis.

His blood sugar on admission was 560 mg./dl. and he had both 4+ glycosuria and acetonuria. He was being treated and educated in relationship to his diabetes when he developed a left internal strabismus on the 10th hospital day. A skull series and brain scan were done because of this, and they revealed no abnormality. The ophthalmologist who was consulted felt that the child had hyperopia, with secondary accommodative esotropia, as well as a mild ptosis on the left. A Titmus visual screen had been normal eight months previously, and his mother had never known his eye to cross prior to his illness. His eyes were re-examined two months later. At that time he still had the hyperopic refractive changes, but his strabismus had essentially disappeared about three weeks after he left the hospital. Another eye examination one

month later was almost completely normal, with resolution of his refractive changes. It is of interest that his strabismus resolved clinically as he was having a rapid decrease in his insulin requirements. Six weeks after being hospitalized, he was in a complete "honeymoon" phase, with no exogenous insulin needed. This was two weeks after the eye findings had begun to normalize. This period lasted about a month, but his eye continued to improve while his insulin need again increased.

Case report 2. D. T., a 13-year-old boy, developed a swelling of his right eye that was first thought to be conjunctivitis. When this swelling did not resolve after three weeks he was seen by an ophthalmologist, who found that he had ptosis and a complete external ophthalmoplegia.

A Tensilon test was performed that yielded questionable results. Myasthenia gravis was suspected, and the patient was sent to a neurologist. That physician noted tiredness and lethargy but felt the eye findings might be due to orbital cellulitis. Therefore, he was admitted to the Children's Mercy Hospital for further study.

He was in special education because of mild retardation and because he was having behavior problems.

The physical examination was normal except for the eye findings. Laboratory data for myasthenia gravis included an LE cell preparation, antithyroid antibodies, CRP, ASO, ANA, immunoglobulins, spinal fluid examination, EEG, and skull x-ray series, all of which were normal. Another Tensilon test was equivocal. An EMG test demonstrated no evidence of myasthenia gravis, but an elevated seventh nerve threshold was noted. On admission, however, his urinalysis showed 3+ glycosuria and moderate acetonuria and he had a blood sugar of 410 mg./dl. Previous to this, diabetes was unsuspected; but later blood sugar levels were consistently much above normal, confirming the diagnosis. He was treated with insulin, his diabetes was regulated, and he was discharged and followed as an outpatient. His eye findings remained unchanged.

He continued to have ptosis; however, 10 months later the first signs of recovery were noted. He then improved slowly over the next 11 months and was well on the way to complete recovery at that time when he moved away and was lost to follow-up.

Case report 3. K. R., a 10-year-old white girl, was first seen by her ophthalmologist for poor right eye movement of six months' duration. She possibly had a mild flu-like illness just prior to the onset of the eye symptoms. Otherwise, she had been in good health.

One month later she was admitted for neurologic examination. Her past history was essentially negative. Review of systems revealed occasional bitemporal headaches of 20-minute duration, respiratory allergies, and occasional dizziness. The physical exam revealed mild obesity and lateral deviation of her right eye, with a larger and sluggish right pupil, but was otherwise negative. Skull and orbital x-rays, brain scan, and EEG were normal. Fasting blood sugar was 178 mg./dl. on one occasion and an oral glucose tolerance test curve was abnormally flat; therefore, she was referred to pediatric endocrinology, where an intravenous glucose tolerance test was done. The glucose utilization constant (K_t) was 0.89, which is compatible with diabetes mellitus.

Over the next several months her ocular palsy remained unchanged except that her pupils had returned to normal about one month after the initial exam. Her ophthalmologist gave eye-patch and vitamin therapy, but she remained essentially unchanged until corrective surgery was performed, 10 months after the initial ophthalmic examination (recession of the right lateral and right medial recti muscles) with good improvement noted postsurgery, with absence of double vision and resumption of normal head posture.

DISCUSSION

Table 1 summarizes the pertinent clinical and laboratory findings of our three patients. Our strong suspicion that we were seeing diabetic ocular palsies led to a review of the experiences of other authors. We found nothing in the literature concerning children and, therefore, based our comparisons on adult literature.

Ocular palsies are an uncommon complication of diabetes. Leopold felt that there was a 5 per cent incidence in diabetic patients whose disease was of more than 10 years' duration,[3] and Waite and Beetham found that 16 out of 4,001 patients with diabetes had ocular palsies.[4] Some cases described had juvenile-onset diabetes in the adult group. Weinstein[5] in 1948 described 14 patients with ocular palsies. Their youngest patient was a 32-year-old woman, though she had been a diabetic since age 10. A summary of their results demonstrated no correlation with the severity of the diabetes or with the patient's age. However, they felt that diabetes of long duration was associated with the palsy. Also, 13 of

TABLE 1

Pt.	Age when seen in hospital	Sex	Type of diabetes	Diagnostic test	Cranial nerves affected	Pupil involvment	Onset (related to diabetes)	Current status
E.B.	12	M	Insulin-requiring	FBS=560 mg./100 ml.	VI	No	3 wks. after dx of diabetes	Resolved after 4 weeks
D.T.	13	M	Insulin-requiring	FBS=410 mg./100 ml.	III (total)	No	3 wks. prior to dx of diabetes	Not fully resolved after 21 months
K.R.	11	F	Chemical	Abnormal I.V. Insulin tol. test (Kt=0.89)	III (partial)	Yes	Unknown	Surgery performed after 7 months

their 14 patients had retinal hemorrhage at the time the palsies developed, and all of their patients showed other signs of vascular degeneration, such as hypertension or albuminuria. They found the third and sixth nerves affected almost equally. The palsies developed rapidly and resolved by three months in all but one case. They also noted sparing of the pupil in six out of the seven patients with third-nerve palsies. Waite and Beetham felt the external rectus was most commonly affected and that there was no relation to the duration of diabetes.[4]

Walsh[6] noted the rarity of the fourth-nerve involvement and the characteristic sparing of the pupil with ocular palsies. He also stated that the severity of diabetes was not correlated with onset of the palsy.

King[7] also noted the sparing of the pupil. Most of his patients were between 50 and 70 years of age and had retinopathy as well as neuropathy. The cranial-nerve palsy cleared more rapidly than other peripheral neuropathies in his series. One of his patients had no manifestations of diabetes other than an abnormal glucose tolerance test at the time the neuropathy developed.

Goldstein[8] found 17 of 22 patients with third-nerve involvement to have sparing of the pupil. He concurred with the others in the early resolution (three to four months) and sudden onset. However, in 10 of his patients, the ocular palsy was the first manifestation of diabetes. Bell's palsy was also found in four patients and had previously been present in six.

These authors suggest several diseases in the differential diagnosis. These include aneurysm, neoplasm, hemorrhage, leukemia, sarcoidosis, metabolic disorders, myasthenia gravis, demyelinating disease, and ophthalmoplegic migraine.[9] Aneurysm is the most common cause in adults, but Ross notes that pupillary sparing is uncommon in aneurysm.[9]

The pathogenesis of the ocular palsy is still not settled. Weinstein[5] felt that a brain-stem lesion was involved with an intramedullary hemorrhage affecting the specific cranial nerve nuclei. Against this theory, however, is the finding that there are rarely other brain-stem signs and that on occasion, both the third and the sixth nerves are affected.

Other postulated mechanisms for the pathogenesis include inflammation, arterial disease with ischemic degeneration,[10] vitamin deficiency, toxins, polyneuritis,[11] and ophthalmoplegic migraine.[9] However, the recovery of the ocular palsy is not associated with other changes in diabetic patients.[6]

Several authors have suggested that the Schwann cell and the myelin sheath of nerves of diabetic patients are more prone to damage than those of nondiabetic subjects.[12,13]

Perhaps the best explanation is a peripheral vascular lesion. This theory is favored by the rapid onset, the slower recovery, the painful onset often noted in adults, and the known high incidence of vascular disease in diabetes.[6] Dreyfus et al.[10] performed an autopsy on a 62-year-old woman who had a third-nerve palsy when she died following an arteriogram to rule out an aneurysm. Their findings included destruction of about one-fourth of the central core of the nerve's intracavernous portion. They felt the paralysis was functional because the recovery occurred before regeneration could have taken place. Pupillary sparing was thought to be due to sparing of the peripheral fibers of the nerve that innervates the pupils. They could not ascertain the cause of the pain but suggested irritation of nearby trigeminal fibers. Occlusion of a nutrient artery was postulated to explain the focal ischemia, although they could find no occlusion at autopsy. There was no evidence of hemorrhage or inflammatory disease in the nerve.

Ross added his speculations to the theory of a peripheral vascular disorder.[9] He proposed that there is a specific diabetic angiopathy characterized by changes leading to edema and ischemia of the nerve,

with resultant conduction impairment and degenerative changes. He suggests that this sequence of events associated with diabetic metabolic changes could account for the rapid onset and short duration. When several nerves are affected the angiopathy is likely to be in the cavernous sinus or the carotid artery, with plasma transudation and nerve compression the result.

Our three patients have certain characteristics of ocular palsies seen in adults, while missing others. All three had rapid onset, but only E. B. had resolution within three months. None of our patients had acute pain associated with onset, though K. R. did have complaints of bitemporal headaches. Only E. B. developed his symptoms after the diabetic state was discovered. D. T.'s diabetes was discovered while hospitalized for examination and K. R.'s chemical-diabetic state was found during assay of her neurologic status. Goldstein[8] noted the occurrence of diabetic ocular palsies as a first manifestation of diabetes mellitus. He also noted several cases of Bell's palsy, as had some of the others. D. T.'s elevated seventh-nerve threshold is of interest in this regard.

Our patients' metabolic states could not be correlated with their ocular manifestations. K. R.'s chemical-diabetic state was apparently present and stable at the time she developed her palsy. D. T. probably was becoming more hyperglycemic and ketotic as he developed his disability, while E. B. was stabilizing his sugar from its initial high levels when he developed his esotropia.

Of interest is E. B.'s refractive changes associated with his blood sugar level. His hyperopia apparently developed while his blood glucose was elevated but started to resolve as he entered a "honeymoon" period, during which no exogenous insulin was needed. His hyperopia continued to resolve while he came out of this period, thus showing no correlation of hyperopic changes with blood sugar level. These correlations had previously been observed by others.[1,9] He was felt to have an accommodative esotropia by the ophthalmologist rather than a true ocular palsy, even though the esotropia resolved spontaneously before the hyperopic changes. It is our feeling that E. B. had an ocular palsy not recognized at the time, because of its rarity in children, but even if he had an accommodative esotropia this is also unique, as the literature on refractive changes in diabetes does not mention secondary accommodative esotropia.

Only K. R. showed evidence of pupillary involvement, which resolved after several months, although the eye muscle remained affected.

None of our patients had retinopathy or other neuropathy, as some authors have noted.[5,7]

We can offer no clues as to the pathogenesis of this condition, although we have no reason to believe that a different mechanism is operative in children. As to the rarity of ocular palsies in children, we can only speculate that perhaps the reason children are rarely affected is that diabetic vascular changes (and perhaps added metabolic changes), when combined with nonspecific aging changes needed as permissive factors, lead to the palsies. By this hypothesis a child's blood vessels and/or nerves are more resistant to the development of ocular palsies.

Most of the disorders noted in the discussion as being part of the differential diagnosis were able to be ruled out in these children, either by reason of age, lack of other findings, or specific laboratory tests. It is conceivable other diseases were present but missed. However, the diabetes in E. B. and D. T. was obvious, and no other abnormality could be found in K. R.

We conclude from this study that ocular palsies secondary to diabetes can be considered very rare in children but that sudden onset of an ocular palsy in a child with a previously normal eye should lead to a suspicion of diabetes, and we mention this unusual manifestation as a possible first sign of diabetes mellitus in children.

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