DELAYED VISUAL MATURATION

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Abstract

Some normal children in early infancy demonstrate a total lack of visual behaviors in the apparent absence of ocular pathology. This condition is termed Delayed Visual Maturation (DVM). There are four identified types. Their general development is impacted and electrophysiological findings, such as electroretinograms (ERG) and visually evoked potentials (VER) may be normal or abnormal. Normal visual function in some types eventually emerges and development catches up. This paper discusses the different types of DVM and their possible etiologies. Two cases are presented to demonstrate the very dramatic changes which take place over this short period of time and the extreme frustration experienced by the parents of these children. Knowledge of the signs and course of the various types of DVM is particularly important for the optometrists who are participating in the InfantSee program.

Key Words

delayed visual maturation, developmental lags, electroretinograms, patterned visually evoked potentials, visual inattentiveness

INTRODUCTION

There is a group of normal infants who fail to show normal maturation of visual function in early infancy, but who go on to develop normal visual capabilities. They have been characterized as having Delayed Visual Maturation (DVM). These children present as a diagnostic dilemma since in early life they appear to be severely visually impaired with no apparent ocular abnormality. These children present with the following signs:[1]

A. no fixation and/or tracking behaviors exhibited by 2-4 months
B. no eye contact
C. no explorative visual behaviors
D. apparent absence of pathology of visual pathways or brain

These children behave as if they are blind and functionally they are. There are different categories of DVM and the classifications are as follows[1]:

A. DVM I – Isolated DVM – includes all of the following:
    1. Neurological development and findings are normal
    2. No systemic abnormalities
    3. Electroretinogram (ERG) is often normal
    4. Flash visually evoked potentials (VEPs) may be normal or abnormal, but present
    5. Electroencephalogram (EEG) is normal
    6.. Normal ocular exam
    7. Most patients present by three months of age
    8. Resolution is rarely prolonged past 6-7 months

    DVM IA = DVM I with no perinatal complications

    DVM 1B = DVM I with perinatal complications
B. DVM II – DVM with systemic disease and/or neuro-developmental abnormalities
C. DVM III – DVM with associated nystagmus and oculo-cutaneous albinism, but where loss of visual function is significantly greater than would be predicted on the basis of the nystagmus or albinism alone.
D. DVM IV – DVM with congenital bilateral ocular anomalies, but where the loss of visual function is significantly greater than would be predicted on the basis of the ocular anomaly.

DVM I resolves faster than DVM III and IV resolves faster than DVM II.

DVM I – Although visual behaviors are absent, flash VEPs are present and sometimes normal. This would indicate that afferent pathways are intact. The etiology of DVM is still unclear, but there is general agreement that the central visual pathway is involved. Possible etiologies will be examined later.

In all forms of DVM infants initially behave as if they are blind. As blind individuals they are visually impaired. Visual impairment can significantly impact normal development. Aspects of development which are affected during this time period (birth to 6-7 months) include: parent/child bonding, motor development, visual awareness, hand regard, head lifting, exploration, spatial concepts, auditory orientation and balance. These children may also be delayed in speech development. Hoyt et al[2] noted general delays in motor development in seven of eight children they identified with DVM. Lambert et al[3] reported on nine children with DVM and found that four of the children were delayed by three to five months in achiev-

ing other developmental milestones such as sitting and walking, as compared to siblings without DVM. Cole et al[4] found that a number of children with DVM were slow in learning to speak. Any delays that occur seem to play "catch up" once visual function emerges.

Literature Overview

There is a significant amount of interesting research on children with DVM that may give some insights into its etiology. Mellor and Fielder[5] reported that flash VEPs were abnormal during the "blind" phase of DVM I and subsequently became normal as visual function emerged. Cole et al[4] found normal ERGs in four of their 16 DVM babies. However, they found VEPs were not normal. Latencies were normal, but configurations of waveform were not. Between four and six months all 16 babies who demonstrated no visual behaviors on presentation (6-12 weeks of age) became visually responsive. By 9-12 months all 16 had normal visual acuity. Harris et al[6] studied six infants with DVM, who at two to four months, were completely visually unresponsive. Saccades and tracking could not be elicited. However, a normal full field optokinetic nystagmus (OKN) response could be elicited from these children when viewing binocularly or monocularly and when the movement was in the temporo-nasal direction. No monocular OKN could be elicited in the naso-temporal direction. These researchers also found that VEPs were normal in both latency and amplitude.[6] They concluded from these observations that normal brain stem function was present and there was normal retino-geniculate-striate pathway function. In normal development, it is usual to find an asymmetric response on OKN. It is much easier to elicit the temporal-nasal OKN early in the infant's life. This asymmetry, in normal development, persists until 3-6 months. Persistence of the asymmetry beyond this time period is often seen in strabismic children. Good and Hou[7] employed sweep VEPs to determine if vernier and grating acuity were normal in patients with DVM. They found that in spite of the fact that visual behaviors were absent, their infants demonstrated normal thresholds for both vernier and grating acuity. This clearly indicated that afferent pathways were functional.

Cocker et al[8] observed that during the first two to three months of life, vision is probably subserved by subcortical pathways. The improvement in vision in DVM starts to occur around this time, suggesting that DVM has a subcortical basis that resolves as the cortex becomes functional. These researchers examined a set of identical twins, one of whom had DVM. They performed Teller Acuity Card (TAC) forced-choice preferential looking (FPL) and luminance and grating pupillometry. They posited that TAC reflects both cortical and subcortical function, while the pupillometry reflects only cortical activity. They found that development of both behavioral and pupillary responses was delayed in DVM; this indicated that although the underlying defect is primarily subcortical, secondarily it delays the emergence of cortically mediated responses. Mercuri et al[1] studied a group of 26 infants, all of whom had perinatal complications. They were all examined in the first months of life and followed longitudinally until at least one year of age. None showed ocular abnormalities. Reduced visual acuity for their age and/or inability to measure acuity was found in 10 of the 26 infants on the visual assessment performed between three and four months. In five of the 10, acuity was found to be normal on the assessment performed between 9 and 12 months. According to Fielder,[9] one of the five showed DVM IB and four showed DVM II. They performed magnetic resonance imaging (MRI) on the five infants with classical DVM and found that none of them had a normal MRI. One showed lesions of the optic radiations and all five showed lesions in the lentiform nuclei.

Proposed Etiologies of DVM

There are many different speculations about the cause of DVM. There is no one primary etiology of this dramatic absence of visual behaviors during early infancy. It is easier to rule out what probably is not causative than to identify the primary etiological factor(s). Mellor and Fielder[5] suggested that DVM could be due to "delayed maturation of the macular photoreceptors, delayed myelination of the visual pathways, and delayed dendritic formation and synaptic development in the occipital cortex."

Retinal immaturity can be ruled out as a cause of DVM because flash ERGs are generally normal for age.[10] In addition, visual function is much poorer than would be predicted on the basis of a foveal abnormality.

Incomplete myelination is unlikely to be the primary causative factor of the blind behaviors associated with DVM. Myelination is incomplete at the time of birth. Additionally, myelination is a gradual process which increases over the first two years of life.[10] As demonstrated by Sokol and Jones[11] the latency of the VEP matures rapidly between three and five months. Therefore, although a delay in myelination could be contributory to DVM, the gradual process of myelination can not explain the rapid behavioral improvements seen clinically. Doing MRI scans on DVM I patients, Hoyt and Good[12] found a delay in myelination in only three of 14 infants.

An abnormality in the striate cortex is unlikely to be responsible for the absence of visual behaviors in DVM. According to Lambert et al[3] patterned VEPs are believed to arise in the striate cortex. Patterned VEPs have been reported to be normal for age[6] in DVM I. Fielder and Evans[13] have suggested that normal infant vision is predominantly extra-geniculate (colliculus-pulvinar-parietal). Assuming this is true for a normal infant, the striate cortex can be ruled out as the primary cause of the visual inattentiveness associated with DVM.

Dubowitz et al[14] suggested that it is likely that lesions of the thalamus may have a bigger impact on the visual behavior of infants than lesions of the visual cortex. They speculated that the thalamus and dorsal brain stem may be especially vulnerable to perinatal hypoxia manifesting with subsequent damage. It is probable, however, that the lateral geniculate body is functional, as indicated by age-normal VEPs in DVM.

Fielder et al[10] proposed that DVM patients (including patients with DVM I), even in the absence of overt perinatal complications, may have mild brain damage which could be contributory to DVM.

Harris et al[6] have a unique approach to DVM, suggesting that it may represent a delayed development of the ability to distinguish visual objects from their visual backgrounds. They studied six infants with DVM (2-4 months) when they were at the stage of complete visual unresponsiveness. No saccades or visual tracking could be elicited, yet a normal full field OKN response occurred when viewing biocular or monocular stimulation in the tempero-nasal direction. VEPs were normal for age in amplitude and latency. They concluded that these infants with DVM "are delayed in orienting to local regions of the visual field, but can respond to full field motion."

The presence of normal OKN suggests normal brainstem function, and the presence of normal pattern VEPs suggests a normal retino-geniculo-striate pathway. The authors[6] state that**:**

> *These oculomotor and electrophysiological findings suggest delayed development of extrastriate cortical structures, possibly involving either an abnormality in figure-ground segregation or in attentional pathways.*

In another paper,[15] it was proposed that the abnormalities seen in DVM appear to be:

> *neither purely sensory nor purely motor as supported by ERG/VEP and eye movement studies.*
>
> *There may be a higher cortical, attentional deficit closely associated with parietal lobe function. DVM is not a single diagnostic condition, but rather a sign common to neurological abnormalities affecting several areas of the brain.*

Occasionally there can be a delay in cortical myelination. A structural defect which impinges on parietal cortical function may be a cause DVM in some cases.[13]

McGready et al[16] studied 38 babies born to Karen mothers (an ethnic group inhabiting Northern Thailand and Burma) living in refugee camps in northwestern Thailand. These infants had DVM I, and recovered all normal function by six months of age. They found that vitamin A concentrations were low in 16% of breast milk samples from lactating mothers and vitamin B concentrations were deficient in 60% of plasma samples. The levels of fatty acids in plasma and milk in Karen women were excellent at birth and in the postpartum period. The authors found that the degree of deficiencies in these vitamins and the concentration of essential fatty acids in spinal cord blood and maternal breast milk did not correlate significantly with visual impairment in the infants. They suggest that DVM might be caused by nutritional deficiency or toxic effects during critical periods of gestation that lead to delayed cortical myelination or structural defects which impinge on parietal cortex function.

Harel et al[17] studied three infants recognized as "blind" during the first four months of life. Their neurological and ophthalmological examinations were normal. Visual electro-diagnostic studies showed normal ERGs, but delayed conduction velocities and impaired visually-evoked responses over the occipital cortex. After age 6 months, normal vision developed gradually and all abnormalities resolved.

Kraemer and Sjostrom[18] studied three children, of various DVM classification who had ophthalmological and electrophysiological examinations. They found all the children had normal ERGs, but exhibited initial abnormal VEPs with marked delay of latency or grossly altered VEPs. When visual interest developed, normal VEPs followed. They concluded that children with DVM:

a) have a period of visual inattentiveness at a time when normal children are visually engaged
b) the VEP is abnormal during the period of visual inattentiveness
c) the improvement of vision in DVM can be measured with VEP recordings
d) the extra-geniculate system provides for the visual function early neonatally in the normal child and for a prolonged period in the DVM child as long as the VEPs are abnormal.

Interesting cases were reported by Goodman and Ashby[19] who followed three boys with a mixed developmental disorder who presented in early infancy with visual unresponsiveness (DVM II). This delayed visual maturation was accompanied or followed by severe autistic impairment, general developmental delay, hypotonia and clumsiness. As the visual function improved there was striking improvements in language, play, social interest and social competence. The authors posit that patchy delay in brain maturation could possibly account for this combination of delayed visual maturation and autism, with a good prognosis.

Two Cases of DVM

Case I

Visit #1

The patient first presented at three months of age. The parents were very concerned that the child was not making any eye contact. He responded to auditory stimuli, but nothing visual. The pregnancy was full-term with uncomplicated pre-, peri-, and postnatal periods. Birth weight was 7 lbs. 14 oz. At the time of presentation the child was in excellent health. The pediatrician suggested a visual exam because of parental concern.

The child showed no response to any visual stimulus. He had no awareness of a transilluminator light in a darkened room. There was no "fix and follow" response. The external and internal ocular examinations were normal. There was no significant refractive error present. The parents were asked to provide significant visual stimulation at home. A major reason for the visual stimulation was to get the parents actively involved in trying to help their child.

Visit #2

This evaluation was one month later at 4 months of age. The parents reported that there was no change from the previous visit. There was no fix and follow response present nor awareness of a transilluminator. A flash ERG and flash VEP were performed and both were normal for the patient's age. No significant refractive error was present. The parents were asked to continue with the visual stimulation at home and to return in one month.

Visit #3

This appointment occurred one month later at 5 months of age. Parents were noticing some improvements, but were very vague on the specifics. They did, however, feel that their child was occasionally looking at things. There were no changes in clinical findings. The parents were asked to continue with the visual stimulation at home and to return in one month.

Visit #4

This visit was one month later at 6 months of age. The parents reported very significant changes. The child was looking at things, following the parents around the room, exploring the environment and making eye to eye contact. Clinical findings showed the child was able to fix and follow. He responded to TACs to the 20/800 level binocularly. The child was able to fixate well enough for me to determine there was orthophoria on the near cover test. The parents were asked to continue with the visual stimulation at home and to return in one month.

Visit #5

This next examination was one and a half months later at 7.5 months of age. The parents reported that their child was visually alert and looking at things constantly. He was watching videos on television and catching up on motor development. Clinical findings were all normal – TAC VA was 20/100 OD and OS, cover testing at near was orthophoric, motilities were full and concomitant and ocular health was unremarkable. At this point, and only at this point, the diagnosis of DVM I was made by *retrospective confirmation*. It is only after the emergence of visual func-

tion in the absence of any abnormalities that a diagnosis of DVM can be made.

Case 2

Visit #1

The initial intake was at 4 months of age. The child was an oculocutaneous (universal) albino with large amplitude nystagmus. The parents reported that their child never looked at objects or people, including them. The pregnancy was full term and pre-, peri- and postnatal periods were uncomplicated. The child's birth weight was 6 lbs. 15 oz. The child was in good health, and not on medication.

The child showed no response to any visual stimulus, even at close range. There was no "fix and follow" response. The fundus was consistent with albinism - pale with no foveal reflex, but otherwise ocular health appeared normal. There was positive iris transillumination, and a high amplitude/moderate frequency, pendular nystagmus was present. There was no significant refractive error. The parents were instructed to provide significant visual stimulation at home and to return in one month.

Visit #2

The child presented two months later at the age of 6 months. Her parents reported that there was no change in the child's status. VEPs and VERs were performed and, while responses were depressed, they were present. The parents reported that the child was beginning to show lags in motor development. The parents were asked to continue the visual stimulation work and to return in one month.

Visit #3

This evaluation was two months later at the age of 8 months. Everything was exactly as it had been at the previous visit. The parents expressed concern and frustration in the lack of progress. They were asked to continue the visual stimulation work and to return in one month.

Visit #4

Child presented three months later at the age of 11 months. The parents reported that the child definitely looks at them and visually examines toys at near. However, she was not exploring anything outside of arm's reach. Clinical findings indicated that the child was able to localize a transilluminator. Fixation was sufficient so that a cover test could be performed; this indicated ocular alignment at distance and near. There was no significant refractive error. The parents were asked to continue the visual stimulation and to return in one month

Visit #5

This encounter occurred three months later at the age of 14 months. The parents reported very significant changes. The child was exploring all spaces. She started crawling and standing, but was not walking yet. TAC acuity was 20/260 binocularly. Tracking had improved and was accurate and relatively smooth. There was ocular alignment at distance and near. There was no significant refractive error and visual behaviors were appropriate.

At this point the diagnosis of DVM III was made by retrospective confirmation.

DISCUSSION

DVM is a condition which presents in infancy where the child presents as if "totally blind." However, over the first six-seven months (for DVM I and later for other types), the child develops normal visual responses and behaviors. The mechanism is not known, but the most current data indicates anomalies of the visual parietal cortex may be responsible. The change in visual behavior from presentation to resolution is quite dramatic and diagnosis can only be made by retrospective confirmation.

The InfantSee® program is a joint undertaking by the American Optometric Association and the Vision Care Institute of Johnson and Johnson Vision Care.[20] A knowledge of the signs, types and course of DVM is important for all eye and vision care providers. This knowledge is even more compelling for those optometrists in the InfantSee® program.

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