“Alice in Wonderland” Syndrome: a Manifestation of Infectious Mononucleosis in Children

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The association between “Alice in Wonderland” Syndrome (AWS) and infectious mononucleosis (IM) has been previously described in three patients.

We describe two additional cases in children, where in one case, the visual symptoms of AWS appeared during the course of active IM and in the second, 2 weeks following a clinically mild, but serologically proven attack.

Introduction

Visual illusions (metamorphopsia) characterized by distortion of form, size, reciprocal position of objects, movement or colour, was initially labelled as “Alice in Wonderland” syndrome (AWS) by Lippman (1952). At times visual images may fail to arouse visual memories and their associated effect, resulting in a sense of strangeness or inexplicable familiarity.

The syndrome has been described in various neurological and psychiatric conditions including epilepsy, following the ingestion of hallucinogenic drugs (lysergic acid, diethylamide or marijuana), acute febrile states, schizophrenia and migraine (Adams and Victor, 1985; Golden, 1979).

The association between AWS and infectious mononucleosis (IM) was originally described by Copperman (1977) reporting three children with visual illusions as the initial symptoms of IM.

We describe two additional cases with AWS associated with IM in whom the visual symptoms appeared during the active course of the illness and 2 weeks following IM respectively.

Case Descriptions

Case Report I

A 6½-year-old boy with an uneventful past history, with no history of migraine, was referred because of high fever for 9 days and a sore throat unresponsive to penicillin therapy. Seven days before referral, the child started complaining of distortions in the apparent sizes, shapes and spatial

relations of objects seen, causing a high degree of anxiety and fear. These symptoms recurred several times a day and lasted for a few minutes each time. Although the periodicity of the occurrence of the events was unchanged, the associated anxiety abated gradually. No headache, nausea, vomiting, dizziness or other symptoms were observed. According to his parents the child was slightly restless and a change in his behaviour was noted.

Physical examination revealed a child in good general condition with a body temperature of 37.5°C, redness of the throat and generalized lymphadenopathy. The liver was palpable at 5 cm and the spleen at 4 cm below the costal margins. Neurological examination showed an alert and comprehending child. Cerebellar functions, fundi and electrocephalogram were normal.

Laboratory findings included a white cell blood count of 18 000/mm³ with 20% large atypical lymphocytes (Downey's cells) and an erythrocyte sedimentation rate of 18 mm/h. Liver function tests revealed a total protein of 7.8 g/dl, albumin 5.5 g/dl, serum glutamic-oxaloacetic transaminase 80 u/l (normal range, 5 to 22), serum glutamicpyruvic transaminase 10 u/l (normal range, 3 to 23) and alkaline phosphatase 306 u/l (normal range, 82 to 248). Two weeks later the liver function tests had returned to the normal range. The initial viral capsid antibody titer for Epstein-Barr virus (EBV) was 1:10 and 4 weeks later it was 1:160. The Monospot test was negative. Epstein-Barr nuclear antigen titers were 1:10 and 1:20, 5 and 8 months respectively, after the initial episode.

During the next 3 weeks the subjective complaints gradually disappeared and the liver, spleen and lymph nodes reverted to normal size.

The child's father was hospitalized 11 days after the beginning of his son's symptoms because of high fever, blurred vision, hepatosplenomegaly and general lymphadenopathy. A possible diagnosis of infectious mononucleosis was suggested based on the clinical manifestations, multiple large atypical lymphocytes (30%) and viral capsid antibodies to EBV rising from less than 1:10 to 1:40 after 8 days.

Case Report II

A 6-year-old girl with an uneventful medical history and no history of migraine, epilepsy or behavioural abnormalities, was referred to us because of metamorphopsia associated with mild headache and anxiety. These episodes recurred several times a day lasting a few minutes each time. Detailed history revealed that 2 weeks before these symptoms the patient had a "throat infection" with high fever and enlarged cervical lymph nodes. Throat cultures were sterile and the symptoms disappeared gradually without treatment. Physical examination was unremarkable except for the spleen which was palpable 3 cm below the costal margin. Neurological examination showed an alert intelligent child who was able to describe her symptoms accurately.

Laboratory findings revealed a white cell blood count of 15 000/mm³ with 16% large atypical lymphocytes (Downey's cells). The initial viral

capsid antibody titer for Epstein-Barr virus (EBV) was 1:80 and 2 weeks later 1:20. Epstein-Barr nuclear antibody titers were 1:10 and 1:20 4 and 6 months respectively after the initial episode. Computerized tomography of the brain was normal. An EEG performed a week after the beginning of her complaints was abnormal showing normal background activity of alpha rhythm with a few generalized series of sharp high voltage waves mostly in the parietooccipital region. Repeat EEG 2 weeks later was normal. There was complete resolution of the visual symptoms after 4 weeks. During 12 months of follow up there were no visual complaints nor any other neurological symptoms.

Discussion

Various neurological and psychiatric symptoms and signs have been described in association with infectious mononucleosis (Copperman, 1977; Hendler *et al.*, 1978; Fisher *et al.*, 1980). Metamorphopsia or AWS, a rarely reported symptom, may appear before, during or after the resolution of all clinical symptoms as described in our second patient. In all the previously reported patients, including ours, no neurological deficits were observed. Electroencephalograms were either normal or showed parieto-temporal slow wave activity, suggesting an electrical dysfunction of this region. Computerized tomography of the brain performed in one patient did not reveal any pathological changes. The diagnosis of infectious mononucleosis was clearly established in all patients by the strongly positive hematological and serological findings (Copperman, 1977; Eshel *et al.*, 1987). The duration of the visual illusions ranged between 2 weeks and 7 months, and all patients recovered completely.

Visual illusions take the form of objects seeming too small (micropsia) and distant, or too large (macropsia) and moving towards the patient. In other cases, objects may appear elongated, swollen or run together, or the vertical and horizontal orientation of the image may shift. Inverted vision, irradiation of contour, disappearance of color (achromatopsia), illusional coloring (erythropsia), polyopia (one object appearing as two or more objects). Also, there may be a loss of stereoscopic vision, preservation of visual images (palinopsia), or a false orientation of objects in space (optic allesthesia) (Adams and Victor, 1985).

Illusions of these types have been reported with lesions of the occipital, occipitoparietal or occipitotemporal regions and the right hemisphere appears to be involved somewhat more often than the left.

The pathophysiology of AWS has not been fully determined, but in cases of migraine associated with visual illusions, the timing of the symptoms and their occasional occurrence without headaches suggest that the vasoconstrictive phase of the migraine phenomenon is involved. The variation in symptoms would be postulated to result from differences in the area of brain affected (Golden, 1979).

The picturesque term "Alice in Wonderland" syndrome was first applied to this symptom complex by Lippman (1952). One of his patients sponta-

neously stated that she felt short and wide as she walked along and she called this a "Tweedle Dum or Tweedle Dee" feeling.

It is clear that Lewis Carroll suffered from migraine and he did have some visual phenomena, whether or not he conceived some of the strange things that happened to Alice from his own experiences is currently only a matter of speculation (Golden, 1979).

Few patients with AWS secondary to IM have been reported, but this combination may not be that rare. The question of whether these visual illusions of AWS are specific to IM or might be seen in association with the other viral diseases, remains unsolved.

Awareness of the possible association between AWS and IM might prevent incorrect diagnosis and treatment of other conditions associated with AWS such as migraine and epilepsy.

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