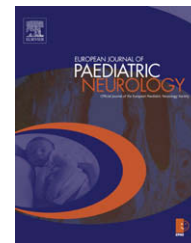




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Case study

Familial congenital oculomotor apraxia: Clinical and electro-oculographic features

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ABSTRACT

The electro-oculographic (EOG) features of both horizontal and vertical eye movements in congenital oculomotor apraxia (COMA) were not previously reported. A girl referred to the ophthalmologic department for abnormal eye movements was diagnosed as COMA. The same abnormal ocular movements were observed in her younger sister and her father who was unaware of his difficulties to initiate voluntary saccades. When performed, EOG recordings of all horizontal and vertical saccadic eye movements were severely altered whatever the age of the patient. Pursuit was normal for these patients. It confirms that the control of saccadic eye movements is still altered in adults in both directions horizontal and vertical that were never reported. EOG is necessary to rule out inherited form of this saccade initiation failure.

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1. Introduction

Congenital oculomotor apraxia (COMA), or congenital saccade initiation failure (c-SIF), is characterized by an inability to initiate voluntary saccades, mostly horizontal, and by a defective horizontal ocular attraction movement.^{1,2} To compensate for these oculomotor abnormalities, children break the fixation with a blink and perform a jerk and over-rotation of the head that goes beyond the target. Due to vestibulo-ocular reflex, the eyes deviate in the opposite direction and are aligned toward the target. Then, the head and eyes move slowly in order to centre again themselves.³ This condition improves during the first decade without completely disappearing.⁴ Inappropriate horizontal optokinetic nystagmus (OKN) and

apraxia of horizontal gaze are the only EOG abnormalities previously described. Although COMA is usually sporadic, familial cases are reported with different patterns of transmission.

We present the clinical and EOG findings obtained from a father and his two daughters, in whom a COMA was diagnosed. Recordings of the vertical eye movements of the father were performed and, to our knowledge, this had never been performed in COMA previously.

2. Case report

Complete clinical ophthalmologic and neuro-ophthalmologic examination was performed for all patients. Electro-oculographic

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(EOG) recordings were performed with Metrovision® Company Apparatus and software. Nine Beckmann® type electrodes were placed on the skin in the middle of the forehead, at the inner and the outer canthi of each eye and at the upper and lower orbital margins of each eye. Eye fixation was first recorded, then the horizontal pursuit (distance 40°; track speed: 30° per second), horizontal saccades (distance 40°), vertical pursuit (distance 30°; track speed: 30° per second), vertical saccades (distance 40°), horizontal OKN in both left–right or right–left directions and vertical upward and downward OKN.

2.1. Patient no. 1

A 2 year's old girl, first child of this non-consanguineous family, was referred for non-progressive abnormal eye movements observed nearly since birth. She has no past medical history. Her ophthalmologic examination was unremarkable. Oculomotor examination confirmed a typical aspect of COMA with horizontal saccade initiation failure. The horizontal pursuit and the vertical eye movements were clinically normal.

No horizontal saccades could be obtained during EOG recordings. The horizontal pursuit was almost normal, considering the age and condition of recording. Due to the age of the patient, we did not succeed to record any vertical ocular movement.

2.2. Patient no. 2

The father, a 34 years old man, was not aware of his difficulties to initiate voluntary saccades. However, minimal abnormal eye movements were observed in very rare occasions and were more evident when he was stressed. They consisted in a blink before performing horizontal saccades as well as a limited head jerk toward the target when voluntary saccades were speeded up. Vertical saccades were normal. The ophthalmologic examination was normal. His past medical history included a growth retardation and transient infertility. Biological measurements and neuroradiological exploration of the pituitary gland were normal. However, the cerebellum was not seen in this imagery.

Both horizontal and vertical saccadic eye movements were absent on EOG recordings (Fig. 1A and B). The horizontal pursuit was almost normal (Fig. 1C). The vertical one was atypical, with periods of good ocular control and periods of absence of any coordinate movement (Fig. 1D). The horizontal OKN was absent in both directions (Fig. 1E and F). The vertical one was present, but with some errors of synchronization, especially when beating downward.

2.3. Patient no. 3

The 1 year old younger sister of Patient no. 1 had defective horizontal saccades since birth and eyes and head jerks characteristic of a COMA. Her ophthalmologic examination was unremarkable as well as her pediatric examination. Due to her young age, EOG recording was not possible.

3. Discussion

The COMA is characterized by abnormal eye and head jerks due to a failure of initiation of horizontal saccades in children.

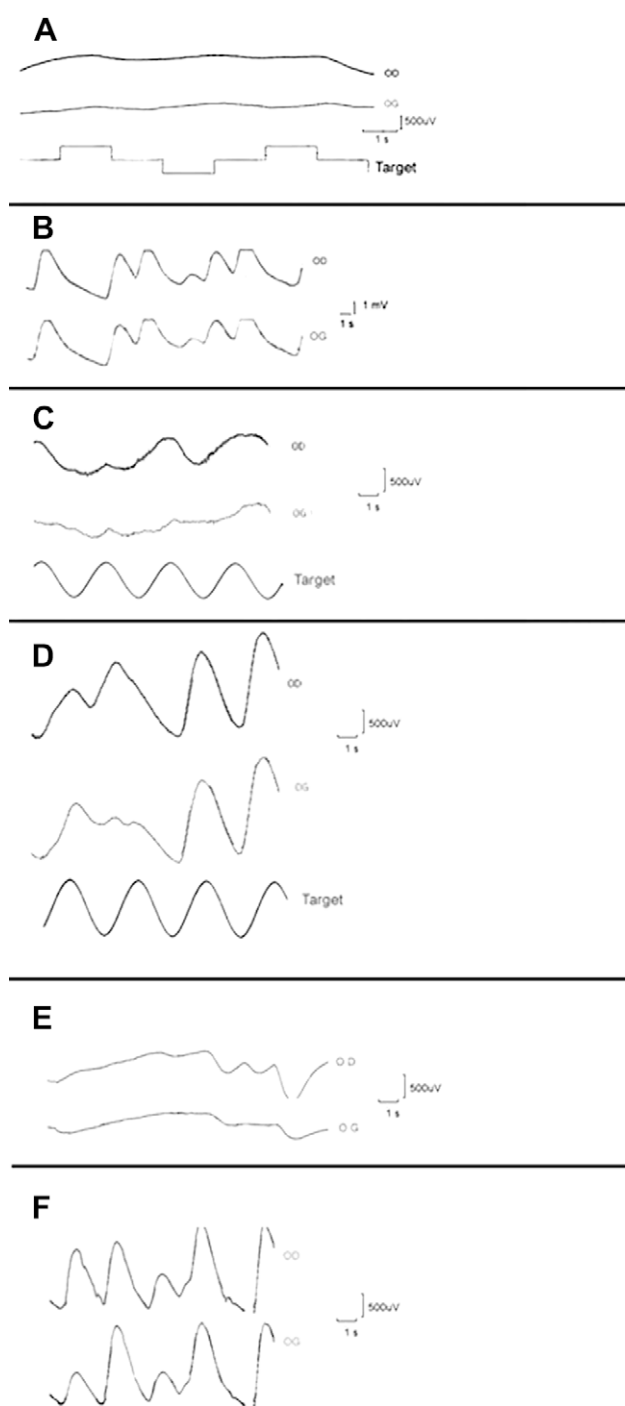


Fig. 1 – (A) Absence of horizontal saccadic eye movement. (B) Absence of vertical saccadic eye movement. (C) Normal horizontal pursuit. (D) Correct vertical pursuit. (E) Absence of horizontal OKN. (F) Vertical OKN. There is some errors of synchronization between both eyes.

Vertical saccades appear to be clinically normal and there is no other neurological, neurometabolic disease or dysmorphism.⁵ When both vertical and horizontal saccades are abnormal on the sole clinical examination, COMA is atypical. In these conditions, other diagnoses such as Joubert syndrome or Gaucher disease must be looked for.⁵

The clinical manifestations of COMA usually improve with age. Residual manifestations, easily compensated, can persist in adults and are more evident when they are stressed.^{4,6} They consist in typical head and eye jerk movements or blinks. Thus, adult patients are often unaware that they had a COMA during their childhood.⁷ Our observation is typical of such evolution.

To our knowledge, there was no previous report of vertical eye movement recordings in COMA patients. Our EOG recordings confirm that the control of saccadic eye movements is still abnormal in adults although these movements were quite normal clinically. In addition, this deficit does not only concern the horizontal saccades but also affects the vertical ones: vertical voluntary saccades and to a lesser degree the vertical OKN. On the other hand, pursuits are normal whatever their direction.

EOG recordings are essential to exclude a familial COMA. Our patient no. 1 could have been misdiagnosed as a sporadic form since abnormal eye and head movements of her father were inconstant and could have been missed. EOG recordings of this man confirm the inherited condition of COMA in the family. But we could not conclude concerning the pattern of inheritance. Different ones were reported in the literature.^{4,8–12} Thus it is difficult to rule out an inherited COMA as long as an EOG assessment had not been performed in the whole family.^{4,6}

The physio-pathogenic mechanisms of COMA are unclear. However, cerebellar vermis hypoplasia or abnormalities have been described in association with COMA.^{1,2,8,13,14} Some of these cerebellar abnormalities could be beyond MRI resolution since normal or pathologic vermis could be observed within the same family.² Abnormalities of cerebellar structures as well as lesions of the projections from the superior colliculus and the rostral interstitial nucleus to the brainstem could be also responsible for Joubert syndrome.¹⁵ In addition, atypical COMA with a deficit of vertical saccades has been described in association with periventricular hemorrhage.¹⁶ Thus, culprit lesion for deficit of vertical saccades, as well as horizontal ones, could be localized in the cerebellum or its projections although it is still impossible to exclude other territories.

The nephronophthisis-1 (NPHP-1) gene on 2q13, or a gene contiguous to it, is suspected to be responsible for COMA.^{13,17} Mutations of NPHP-1 gene have been reported in some cases of Joubert syndrome (JBTS4) in which vertical and horizontal oculomotor apraxia and cerebellar malformations have been also reported.¹⁸ Thus, it is of most interesting to propose a gene examination to patients with COMA to clarify the difference between this syndrome, Joubert syndrome and nephronophthisis-1.

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