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Case report

Tumor-like enlargement of the optic chiasm in an infant with Alexander disease

Cyril Mignot [a,b,c], Isabelle Desguerre [d], Lydie Burglen [e], Lucie Hertz-Pannier [f,g], Florence Renaldo [a,b,c], Jean-François Gadisseux [h], Serge Gallet [i], Danielle Pham-Dinh [a,b,c], Odile Boespflug-Tanguy [j,k], Diana Rodriguez [a,b,c,*]

[a] *AP-HP, Service de Neuropédiatrie, Hôpital Armand Trousseau, F-750012 Paris, France*
[b] *Université Pierre et Marie Curie-Paris 6, F-75000 Paris, France*
[c] *INSERM UMR S546, F-75013 Paris, France*
[d] *AP-HP, Service de Neuropédiarie, Hôpital Necker-Enfants Malades, F-75015 Paris, France*
[e] *AP-HP, Service de Génétique, Hôpital Armand Trousseau, F-75012 Paris, France*
[f] *AP-HP, Service de Radiologie Pédiatrique, Hôpital Necker-Enfants Malades, F-75015 Paris, France*
[g] *INSERM U663, Université René Descartes, F-75005 Paris, France*
[h] *Hôpital Privé d'Antony, F-92166 Antony, France*
[i] *Serge Gallet, Service de Pédiatrie, Centre hospitalier de Montluçon, F-03100 Montluçon, France*
[j] *Service de Génétique Médicale, CHU de Clermont-Ferrand, Hôtel Dieu, F-63000 Clermont-Ferrand, France*
[k] *INSERM, UMR S384, Université Clermont 1, Faculté de Médecine, F-63001 Clermont-Ferrand, France*

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Abstract

We report a patient with infantile Alexander disease (AXD) due to the recurrent p.Arg79Cys GFAP mutation. In addition to typical AXD abnormalities, magnetic resonance imaging demonstrated a tumor-like lesion of the optic chiasm suggestive of a glioma. A transient papilloedema appeared during the follow-up and the lesion partially regressed despite a worsening of white matter involvement. Rare radiological and pathological tumor-like lesions have already been reported in AXD patients. This patient confirms that enlargement of the optic chiasm is a rare feature of AXD, possibly linked to abnormal astrocytic proliferation.

Keywords: Alexander disease; *GFAP* mutation; Optic pathway glioma

1. Introduction

Alexander disease (AXD) is a rare neurodegenerative disorder related to dominant mutations in the glial fibrillary acidic protein (*GFAP*) gene [1] producing astrocytic inclusions called Rosenthal fibers. The infantile form is the most frequent, characterized by mental and motor retardation, progressive megalencephaly and seizures, followed by neurological regression. The most prominent magnetic resonance imaging (MRI) features comprise a leukoencephalopathy displaying a rostrocaudal gradient associated with hypersignals of the basal ganglia and thalami on T2-weighted images, alongside contrast enhancement of specific regions including the ventricular edges, frontal white matter, basal ganglia and optic chiasm [2].

Here, we report on a patient with typical features of infantile AXD and exhibiting a tumor-like lesion of the optic chiasm on MRI transiently associated with a

* Corresponding author. Address: Service de Neuropédiatrie, Hôpital Armand Trousseau, 26 av du Dr Arnold Netter, F-75012 Paris, France. Tel.: +33 1 44 73 61 41; fax: +33 1 44 73 69 64.
E-mail address: diana.rodriguez@trs.aphp.fr (D. Rodriguez).

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papilloedema that spontaneously and partially regressed during follow-up. This case strengthens the link between *GFAP* mutation and transient enlargement of the optic chiasm.

2. Case report

The female patient is the only child of healthy unrelated parents, with normal birth history and head circumference. The girl was referred at 14 months of age because of developmental psychomotor delay. She was unable to sit without support. Examination revealed ataxia, hypotonia, and macrocephaly (50 cm, +3 SD). Brain MRI revealed extensive white matter hemispheric abnormalities with frontal predominance, associated with a T2 hypersignal in the basal ganglia predominating in the caudate nuclei (Fig. 1A), and gadolinium enhancement involving the head of the caudate nucleus, the ventricular edge, the fornix, and the mammillary bodies (Fig. 1B, C and E). In addition, the optic chiasm appeared heterogeneously enlarged, hyperintense on T2-weighted sequences and massively enhanced following gadolinium infusion (Fig. 1B–E). No calcifications were detected by computed tomographic (CT)-scan. Routine cerebrospinal fluid analyses were normal. The girl showed no signs of visual impairment and fundoscopy and visual evoked potentials (VEP) were normal. Neither clinical signs nor familial history of neurofibromatosis type 1 were present. At age 2, while the neurological condition progressively deteriorated, the optic lesion remained asymptomatic. A second MRI showed a worsening of the white matter abnormalities and ventricular dilatation, in contrast with a spontaneous partial regression of the enlarged chiasma that was no longer enhanced with gadolinium. At age 3, she had lost control of her head, had no language and could catch objects but did not manipulate them. Examination revealed pyramidal signs, axial hypotonia and dyskinetic movements of the upper limbs. At this time, while we identified no VEP responses, we noticed a transient papilloedema though visual pursuit was preserved and clinical signs of intracranial hyperpressure were absent. Head circumference remained stable 54.5 cm (+3 SD), as did the aspect of the MRI (Fig. 2A–C), although the optic nerves appeared to have thickened compared to previous images.

After informed consent, we extracted the genomic DNA from peripheral blood lymphocytes using standard protocols and directly sequenced the 9 exons of *GFAP* as described previously [3]. Sequencing of *GFAP* revealed a heterozygous c.235C>T mutation (exon 1), resulting in the recurrent p.Arg79Cys substitution.

3. Discussion

We have described a patient with typical clinical, radiological and genetic features of infantile AXD whose brain MRI reveals a chiasmatic tumor-like lesion which spontaneously regressed by the age of 2 years. Although showing normal visual pursuit, this patient presents an absence of VEP responses which could be related to the worsening of myelin involvement and hence not necessarily linked to the optic tumor-like lesion. This chiasmatic heterogeneous mass, displaying a hyperintense signal on T2-weighted images and strong contrast enhancement, fulfilled the criteria for chiasmatic glioma. Optic pathway tumors are frequently low-grade pilocytic astrocytomas often associated with Rosenthal fibers. Given that chiasmatic gliomas have an erratic natural history [4], the absence of symptoms and the spontaneous regression of the tumor do not preclude this diagnosis. Most optic pathway tumors are diagnosed on unequivocal MRI findings, avoiding the need for biopsy in the majority of cases. Therefore, chi-

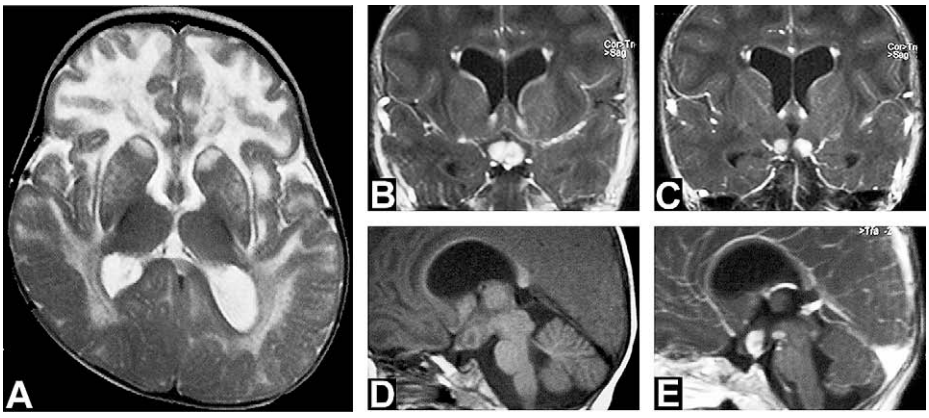

Fig. 1. The MRI at 14 months old showing typical features of infantile AXD: the T2-weighted image shows severe white matter abnormalities with frontal predominance and basal ganglia involvement (A), associated with enhancement of the ventricular lining following gadolinium infusion (B and C). In addition, an important enlargement of the optic chiasm with a heterogeneous signal on T1-weighted image (D) with massive enhancement (B, C, and E) is present.