

# Arthrogryposis Multiplex Congenita Related to Third-Trimester Basal Ganglia Ischemia: A Case Report

Perrine Venot, MD<sup>1</sup>, Philippe Vo Van, MD<sup>1</sup>, Gratiella Mac Caby, MD<sup>2</sup>, Gauthier Loron, MD, PhD<sup>1</sup>, Jean Paul Bory, MD<sup>3</sup>, Ahmad Akhavi, MD<sup>1</sup>, and Nathalie Bednarek, MD, PhD<sup>1</sup>

## Abstract

Arthrogryposis multiplex congenita is a syndromic condition defined by contracture of 2 or more joints. A large range of etiologies has been reported such as neuromuscular disorders (peripheral dysfunction), chromosomal abnormalities, or cerebral malformations (central dysfunction) leading to fetal immobility. Severity of arthrogryposis depends on the etiology and duration of fetal immobility. The authors report a 34 gestational weeks infant presenting with severe diffuse arthrogryposis symptoms and respiratory failure at birth. Her mother experienced cardiac arrest at 29 gestational weeks due to carbon monoxide intoxication. Fetal magnetic resonance imaging revealed extensive corticospinal tract lesions. Antenatal ischemia of the deep gray matter needs to be considered as a possible arthrogryposis cause.

## Keywords

arthrogryposis, hypoxic–ischemic lesions, magnetic resonance imaging, fetus

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Arthrogryposis multiplex congenita is a syndromic condition, apparent at birth, defined by fixation of at least 2 different joints due to fetal immobility.<sup>1</sup> The incidence is estimated at 1 for 3000 live births. Most common manifestations are talipes equinovarus and flexion deformities of the wrists. Multiple etiologies are described and classified as central, peripheral causes (neuromuscular junction disorders, anterior horn cell disease, and connective tissues abnormalities), placental vascular compromise, intrauterine space limitation, maternal systemic pathologies (diabetes mellitus, multiple sclerosis, myotonic dystrophy, myasthenia gravis, and viral infection), and teratogenic intoxication.<sup>1,2</sup> However, 10% of cases with arthrogryposis multiplex congenita remained unexplained. As the exact pathophysiology remains unclear, the minimal investigations required at birth should include attentive clinical examination, cerebral magnetic resonance imaging, and karyotype.

The authors report the case of a 34 gestational weeks premature infant with severe arthrogryposis at birth, associated with respiratory failure requiring mechanical ventilation. Antenatal magnetic resonance imaging, 3 weeks earlier, showed diffuse bilateral basal ganglia, thalami, and cortical tract injuries mimicking

hypoxic–ischemic encephalopathy seen in term infants. These lesions were secondary to maternal hemodynamic compromise (circulatory arrest due to carbon monoxide poisoning at 29 gestational weeks). Acquired deep gray matter injuries need to be considered in the panel of arthrogryposis causes. The timing of the insult is also discussed in the genesis of the arthrogryposis.

## Case Report

A 22-year-old woman was exposed to severe acute carbon monoxide poisoning at 29 gestational weeks after an

<sup>1</sup> Neonatal Intensive Care Unit, Institut Alix de Champagne, Reims, France

<sup>2</sup> Department of Pediatric Radiology, Hôpital Robert Debré, Reims, France

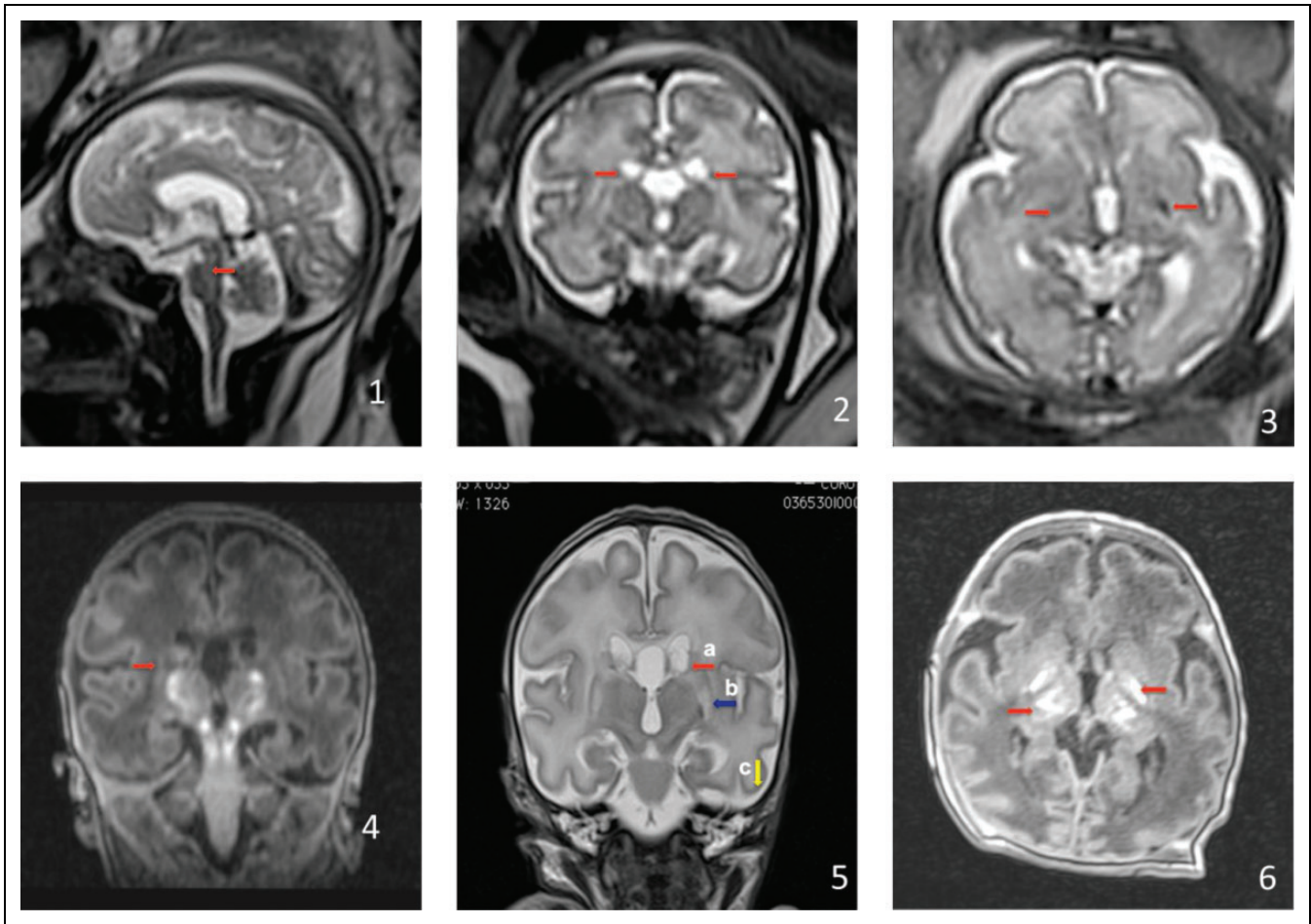
<sup>3</sup> Department of Obstetrics and Gynecology, Institut Alix de Champagne, Reims, France

## Corresponding Author:

Nathalie Bednarek, MD, PhD, Department of Pediatrics, Pediatric B Unit, Neonatal Intensive Care Unit, Institut Alix de Champagne, C.H.U, 47 Rue Cognacq Jay, REIMS 51092, France.

Email: nbednarek@chu-reims.fr





**Figure 1.** Antenatal brain imaging (1-3) T2-weighted sequences (1) sagittal view, hyposignal of the posterior brainstem (arrow); (2) coronal view: bilateral periventricular cysts (arrow); (3) axial view: bilateral hyposignal of the posterior limb of the internal capsule (arrows). Postnatal brain imaging (4-6). 4, Coronal T1-weighted sequence, bilateral hypersignal of the corticospinal tracts and putamen (arrow); (5) coronal T2-weighted sequence, bilateral periventricular cysts (arrow a), hypersignal of the putamen (arrow b), hyposignal of the cortical ribbon (arrow c); (6) axial T1-weighted sequence, bilateral hypersignal of the lentiform nuclei and thalami (arrows).

accidental home fire. She experienced a circulatory arrest successfully resuscitated. At the admission in intensive care, her carboxyl hemoglobin was 52% requiring hyperbaric therapy. She was extubated 24 hours after the cardiac arrest. She felt diminished fetal movements, and the cardiotocographic monitoring showed a micro oscillating and unresponsive fetal heart rate. Fetal cerebral magnetic resonance imaging at 31 gestational weeks exhibited bilateral basal ganglia, thalami, posterior brain stem, and corticospinal tract injuries (Figure 1, images 1-3). Frontal periventricular cysts revealed white matter injuries and a hyposignal of the posterior limb of the internal capsule was also observed (Figure 1, images 2 and 3). Transcerebellar diameter measured at 38 mm, below the fifth percentile for equivalent gestational week reflected cerebellar atrophy.<sup>3</sup> The couple declined any medical interruption of pregnancy. A premature delivery occurred at 34 gestational weeks secondary to a severe hydramnios. A female infant was born (birth weight: 2.340 kg [75th percentile], head circumference: 31 cm [50th percentile], height:

46 cm [75th percentile]). She was intubated at birth due to the absence of spontaneous respiratory movements. The chest was hypoplastic, and the face was amimic with a severe swallowing impairment. Neurologic examination displayed a diffuse arthrogryposis affecting all joints of the superior and inferior limbs leading to severe wrist and elbow contractures and hips dislocation. Bilateral epileptoid tremor on inferior limbs confirmed corticospinal tract injury. Neither weaning off mechanical ventilation nor enteral tube feeding were successful. Postnatal brain magnetic resonance imaging confirmed the antenatal lesions (Figure 1). She died 10 weeks after birth.

## Discussion

This observation shows that arthrogryposis multiplex congenita can be acquired after ischemic brain injury. Basal ganglia, thalami, posterior limb of the internal capsule, and corticospinal tracts should also be closely analyzed for all patients with

arthrogryposis multiplex congenita, even in less severe cases, requiring some expertise on fetal radiology.<sup>3</sup>

Severity of arthrogryposis multiplex congenita is related to its etiology and its time of occurrence; the second trimester causes are the severest. However, in this observation, the fetus developed extensive arthrogryposis multiplex congenita over 5 weeks only, suggesting that the severity of brain damage plays a key role. Charollais et al<sup>4</sup> described a fetus with normal vitality and brain morphology on ultrasound investigations up to 32 gestational weeks. At 36 gestational weeks, active movements diminished and finally the infant was born at 37 gestational weeks with a severe arthrogryposis multiplex congenita related to multicystic encephalopathy due to an acute ischemic event.

Multiple etiologies of arthrogryposis multiplex congenita have been reported. Neurological diseases (central or peripheral) are the most frequent (70%-80%) and have the poorest outcome.<sup>1,2,5</sup> Central disorders account for one-third of arthrogryposis multiplex congenita causes, including migration disorders, olivopontocerebellar-corticospinal tracts degeneration, and encephaloclastic process.<sup>1</sup> Peripheral disorders include peripheral neuropathy due to hypomyelination process, anterior horn diseases, neuromuscular junction disorders, and disease of the muscle. They remain the commonest etiologies.<sup>1,2</sup> Deep gray matter and corticospinal lesions are rare. In a cohort of 83 patients, a patient presented pyramidal tract degeneration and 2 other patients evidenced acquired brain ischemic injuries with no further details.<sup>6</sup> In another report of a cohort of 68 cases, 2 patients with arthrogryposis multiplex congenita had a history of intrauterine ischemia, with a gestation marked by a severe maternal hemorrhagic shock occurring the second trimester for the first patient, and a twin-to-twin transfusion syndrome at 25 gestational weeks leading to a fetal death of the twin.<sup>5</sup> No information about cerebral imaging was available.

The mechanism of brain lesions in our observation can be interesting to discuss with the questionable respective part of carbon monoxide poisoning and circulatory impairment in the generation of the fetal injury. Carbon monoxide binds to hemoglobin with an affinity estimated 200 times superior than oxygen, leading to hypoxia.<sup>7,8</sup> Maternal hypoxemia due to carbon monoxide poisoning also participated in fetal hypoxia. Moreover, carbon monoxide has 2.5 times more affinity for fetal hemoglobin than adult hemoglobin. The fetus accumulates carbon monoxide, exposed to higher rates of carbon monoxide-hemoglobin for a longer period of time than his or her mother. Carbon monoxide has direct cellular toxicity. Fetal neurological consequences of the carbon monoxide poisoning depend on the severity of maternal intoxication and the gestational age occurrence of this insult. Fetal and postnatal magnetic resonance imaging in the present observation showed mostly deep gray matter mimicking severe term hypoxic-ischemic magnetic resonance imaging patterns.<sup>9</sup> In this observation, 2 intricate mechanisms led to fetal hypoxia, namely, direct carbon monoxide toxicity and maternal hemodynamic

compromise. Deep gray matter is the most vulnerable region requiring the highest energy resources and has the highest concentration of excitatory amino acid receptors in fetus and neonates. During gestation, thalami and brain stem are also areas of great metabolism activity because of the ongoing myelination. The magnetic resonance imaging appearances of brain lesions after acute carbon monoxide intoxication were reviewed in 19 adult patients. Globus pallidus was reported as the commonest site of injuries.<sup>10</sup>

In our case report, ischemia was also responsible for decreased cerebellar growth without evidence of cortical atrophy, demonstrating the peculiar cerebellar vulnerability during the third trimester of pregnancy.<sup>3</sup> In another cohort, 2 infants exposed to intrauterine ischemic event presented microcephaly and cerebral atrophy.<sup>5</sup>

In conclusion, acquired in utero ischemic corticospinal tracts and basal ganglia injuries can be a cause to consider in infants with arthrogryposis multiplex congenita, requiring a focused reading of magnetic resonance imaging.

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### Author Contributions

PVV and PV are first authors and have equally contributed to this work. NB and GL contributed to the organization, execution, review and critique. PM, NB, AA, JPB and GM were involved in the patient's care. All authors approved the final version of the paper for publication.

### Authors' Note

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### Ethical Approval

Authors waived the requirement to obtain institutional review board approval.

### References

1. Volpe JJ. *Neurology of the Newborn*. 5th ed. Philadelphia, PA: Elsevier Health Sciences; 2008.
2. Kalampokas E, Kalampokas T, Sofoudis C, Deligeoroglou E, Botsis D. Diagnosing arthrogryposis multiplex congenita: a review. *ISRN Obstet Gynecol*. 2012;2012(3):1-6.

3. Garel C. *MRI of the Fetal Brain*. Berlin, Heidelberg: Springer; 2004.
4. Charollais A, Lacroix C, Nouyrigat V, Devictor D, Landrieu P. Arthrogryposis and multicystic encephalopathy after acute fetal distress in the end stage of gestation. *Neuropediatrics*. 2001; 32(1):49-52.
5. Darin N, Kimber E, Kroksmark AK, Tulinius M. Multiple congenital contractures: Birth prevalence, etiology, and outcome. *J Pediatr*. 2002;140(1):61-67.
6. Vuopala K, Leisti J, Herva R. Lethal arthrogryposis in Finland - a clinico-pathological study of 83 cases during thirteen years. *Neuropediatrics*. 1994;25(6):308-315.
7. Prockop LD, Chichkova RI. Carbon monoxide intoxication: an updated review. *J Neurol Sci*. 2007;262(1-2):122-130.
8. Bothuynne-Queste E, Joriot S, Mathieu D, et al. Ten practical issues concerning acute poisoning with carbon monoxide in pregnant women [in French]. *J Gynecol Obstet Biol Reprod (Paris)*. 2014;43(4):281-287.
9. Barkovich AJ, Westmark K, Partridge C, Sola A, Ferriero DM. Perinatal asphyxia: MR findings in the first 10 days. *AJNR Am J Neuroradiol*. 1995;16(3):427-438.
10. O'Donnell P, Buxton PJ, Pitkin A, Jarvis LJ. The magnetic resonance imaging appearances of the brain in acute carbon monoxide poisoning. *Clin Radiol*. 2000;55(4):273-280.