International Journal of Pediatric Otorhinolaryngology, 16 (1988) 45–53
Elsevier

POR 00531

Arthrogryposis multiplex congenita: otolaryngologic diagnosis and management

Donald R. Paugh [1], Charles F. Koopmann, Jr. [1] and John W. Babyak [2]

[1] *Department of Otolaryngology, University of Michigan Medical Center, Ann Arbor, MI 48109 (U.S.A.)* and [2] *Department of Otolaryngology, St. Joseph Mercy Hospital, Ann Arbor, MI 48106 (U.S.A.)*

(Received 14 January 1988)
(Revised version received 9 June 1988)
(Accepted 21 June 1988)

Key words: Arthrogryposis multiplex congenita

Abstract

Arthrogryposis multiplex congenita (AMC) is an uncommon congenital disorder characterized by multiple fixed joint deformities and non-progressive neuromuscular dysfunction. A small fraction of these infants will present with otolaryngologic problems resulting from cranial nerve weakness, muscle dysplasia, or structural dysharmony of the head and neck. The charts of 50 patients with AMC were reviewed to determine the incidence of these findings. A summary of the literature is presented discussing the etiology, pathophysiology, diagnosis and management of this interesting clinical problem.

Introduction

Since first described by Otto in 1841, the syndrome known as arthrogryposis multiplex congenita (AMC) has been discussed in the orthopedic, neurologic, and pediatric literature. In 1976, Cohen and Isaacs [5] reviewed their experience with the otolaryngologic signs and symptoms associated with AMC, since then no further contributions have been made in our literature. This paper serves a dual purpose. First, we wish to clearly define AMC, briefly discussing the many diverse etiologies and the associated neuromuscular pathology. Second, the incidence and clinical significance of head and neck involvement are explored. A case report, retrospective chart review and review of the literature are presented.

Correspondence: D.R. Paugh, Department of Otolaryngology, University of Michigan Medical Center, 1500 E. Medical Center Drive, 0312, Ann Arbor, MI 48109-0312, U.S.A.

Arthrogryposis multiplex congenita is not a specific disorder, but rather complex of symptoms of congenital joint contractures associated with both neurogenic and myopathic disorders [1]. Any process which limits fetal mobility in utero can result in AMC. More selective diagnostic criteria include the following: (1) joint contractures at birth in at least two different areas of the body; (2) evidence of muscle wasting with fusiform joint configuration; and (3) no evidence of progressive neurologic disease [8]. One of the many possible etiologies for AMC is a loss of muscle mass with imbalance of muscle power at the joints [16]. The result is decreased motion, provoking a collagenic response which replaces muscle volume and causes thickening of joint capsules. Dysfunction of the temporomandibular and cricoarytenoid joints, as well as the more classic limb deformities, can also be ascribed to the above pathogenic model.

Potential causes for decreased fetal movement in utero can be divided into two groups: (1) disorders of the developing motor system at any level (Table I); and (2) conditions associated with decreased intrauterine volume, such as twinning, oligohydramnios or bicornuate uterus [9,15,18]. The entities listed in Table I serve only as a brief outline, a complete listing of neurologic and myopathic factors linked to congenital contractures is beyond the scope of this report. Retrospective analysis by many authors [2,8] have demonstrated neurogenic AMC to be a much more common entity than primary myopathy. Electromyography (EMG), muscle biopsy, and autopsy have confirmed these results. The primary pathology most often demonstrated is loss of anterior horn cells at all levels of the spinal cord, including analogous (brainstem motor nuclei) cranial nerve lesions [2,3,6,16]. Agenesis of the corpus callosum has been demonstrated in a few severely afflicted children [14]. Fenichel [7] has demonstrated abnormal muscle maturation in brain-damaged children. Mental retardation has been documented by many in-patients with 'central' AMC. Fortunately, these occurrences are uncommon, most children afflicted with AMC are of normal intelligence and respond to surgical correction and rehabilitative therapy [17].

Many congenital anomalies, involving all the organ systems, have been associated with AMC. Those of interest to the otolaryngologist include the ones listed in Table

TABLE I

Disorders of neuromuscular development

– Loss of anterior horn cells (patients 6 and 7)
– Amyoplasia congenita [11]
– Non-progressive myopathy
Disorders of brainstem development
Disorder of brain development

TABLE II

Congenital anomalies associated with arthrogryposis multiplex congenita

Cleft palate
Hyperostosis frontalis
Glaucoma
Esophageal atresia
Mandibular hypoplasia
Laryngeal dysphasia [15]
Pulmonary hypoplasia [13]
Hypertelorism

II. These anomalies may occur sporadically or as phenotypic syndromes associated with AMC. The Pierre Robin sequence is the most common of these syndromes. Although relatively uncommon, many of these dysmorphisms and syndromes involved with AMC may cause difficulties with respiration, deglutition, and speech, warranting otolaryngologic evaluation and treatment. Since most of these children are of normal intelligence, and our orthopedic colleagues are often very successful in rehabilitating these patients, long-term management is indicated.

Materials and Methods

The case history of an arthrogrypotic infant presenting with multiple congenital contractures and progressive stridor is presented. To determine the incidence of otolaryngologic manifestations of AMC (including laryngopharyngeal involvement and dysmorphic features), all charts of patients diagnosed with AMC at the University of Michigan Medical Center, from 1975 to the present, were reviewed. Fifty patients fulfilled the criteria for AMC as proposed by Fischer et al. [8]: joint contractures in at least two different areas of the body (patients with only talipes equinovarus (club feet) being excluded); no evidence of progressive neurologic disease; evidence of muscle wasting with fusiform joint configuration; and absence of skin creases with or without joint webbing [4]. Dysmorphic features, cranial nerve examinations, and relevant diagnostic studies were tabulated in each patient with an abnormal head and neck evaluation.

Case report

J.C., a Caucasian male, presented as a breech vaginal delivery at 38 weeks gestation. Apgar scores were 4 and 5 at 1 and 5 min respectively. Examination revealed remarkable flexion contractures at the wrists, knees, hips, and ankles. Deep tendon reflexes were absent. The patient had normal facial muscle tone and grimace, a high, arched palate without cleft, hyperostosis frontalis, and micrognathia (Fig. 1). Progressive stridor required intubation at 24 h. Extubation at 5 days failed, secondary to persistent stridor and aspiration. Because he was 'failing to thrive', the patient was re-intubated and a nasogastric feeding tube was placed. Direct laryngoscopy and bronchoscopy confirmed paralysis of the right true vocal cord and laryngomalacia. After tracheostomy and jejunostomy were performed, the infant began to gain weight and was weaned from the ventilator in a short time. After 6 weeks of hospitalization, he was discharged to be followed-up by the Orthopedics and Otolaryngology Services. The motor denied use of tobacco or other drugs during pregnancy. Amniocentesis at 19 weeks gestation showed an elevated α-fetal protein level and a normal karyotype. Ultrasound at 19 weeks gestation demonstrated decreased fetal movement and a bicornuate uterus. Torch screening and other viral studies were negative.

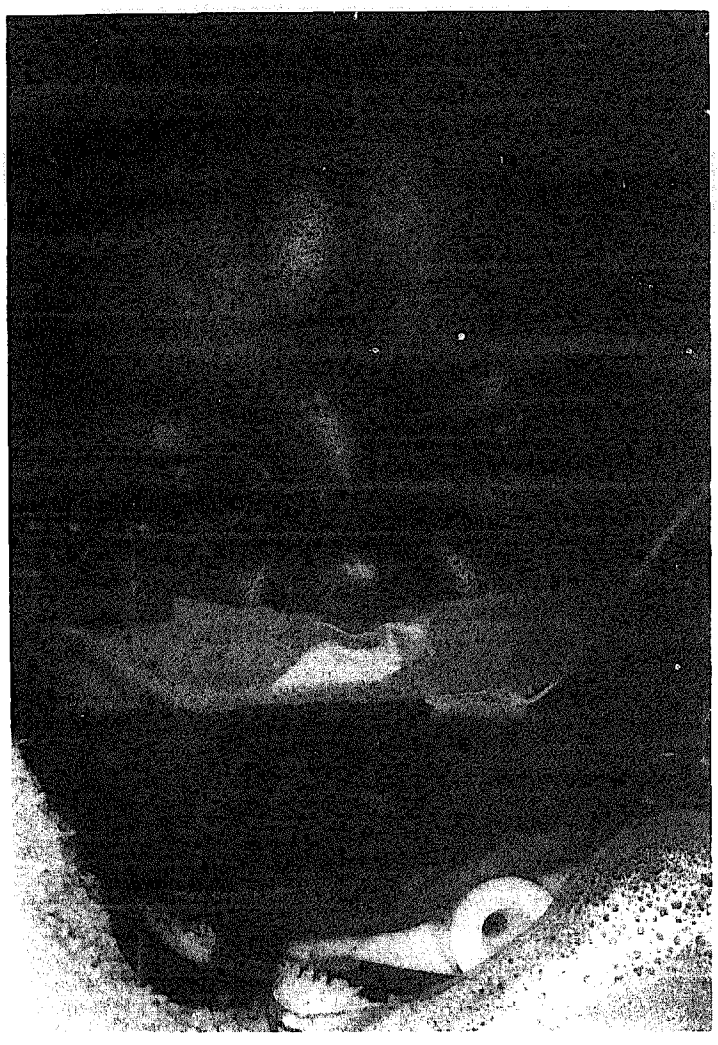

Fig. 1. Mandibular hypoplasia and hyperostosis frontalis in this patient with arthrogryposis.

EMG demonstrated a denervation process consistent with primary neuropathy. Muscle biopsy showed immature skeletal muscle infiltrated with fat and fibrous tissue. An auditory brainstem response (ABR) indicated prolonged absolute and interpeak latencies bilaterally. Brain CT scan and chest X-ray were within normal limits.

Results

Including the index case above, 50 patients were diagnosed with AMC. Ten of these patients manifested otolaryngologic abnormalities. Pertinent obstetric history, clinical findings, diagnostic procedures, and electromyographic diagnoses are summarized in Table III. Three patients (1,2,10) presented with progressive stridor

TABLE III

Patients with otolaryngologic expression of clinical AMC

Patient	*Obstetric history*	*Otolaryngologic clinical findings*	*Diagnostic procedures*	*Electromyographic diagnosis*
1	Polyhydramnios Fetal movement Breech Bicornuate uterus	Micrognathia (unilateral TVC paralysis) Progressive stridor Laryngomalacia Hyperostosis frontalis	Direct laryngoscopy EMG (neuropathic) Muscle biopsy (fibrosis, fat infiltration) Karyotype (normal)	Neurogenic
2	Oligohydramnios Fetal movement	Bilateral TVC paralysis Progressive stridor Laryngomalacia Micrognathia	Direct laryngoscopy EMG (neuropathic) Muscle biopsy (fibrosis)	Neurogenic
3	No abnormalities noted	Bilateral VII paresis	EMG (neuropathic)	Neurogenic
4	Polyhydramnios Breech	Glossoptosis Absent gag Tongue movement Dysphagia	Oropharyngeal videofluoroscopy	–
5	NL gestation	Profound sensorineural hearing loss Epicanthal folds Low set ears	EMG, NCV (normal) (normal)	Normal
6	Polyhydramnios	Cleft palate Glossoptosis Micrognathia Aspiration	Reflux scan (gastro-esophageal) EMG (neuropathic)	Neurogenic
7	Polyhydramnios	Absent gag reflex Low-set ears Dysphagia Macrognathia	EMG (neuropathic) Muscle biopsy (agenesis of striated muscle) Karyotype (normal) Oropharyngeal videofluoroscopy	Neurogenic Myopathic
8	Oligohydramnios Fetal movement	Flattening of occiput Cleft palate	Fetal ultrasound	No EMG diagnosis
9	Fetal movement Polyhydramnios	Cleft palate Low-set ears Generalized hypotonia	Fetal ultrasound (patient expired before antenatal testing)	No EMG diagnosis
10 *	34 week gestation fetal movement	Microcephaly Micrognathia Laryngomalacia Blindness Progressive stridor	Direct laryngoscopy CT scan (agenesis of corpus callosum)	No EMG diagnosis

* Associated with profound multisystem organ failure; this patient was treated with supportive care only. EMG, electromyogram; NCV, nerve conduction velocity.

requiring intubation and subsequent tracheostomy. Direct laryngoscopy confirmed bilateral true vocal cord paralysis in one patient, unilateral vocal cord paralysis and laryngomalacia in another, and laryngomalacia with glossoptosis in a third infant. Abnormal subglottic or tracheobronchial findings were not recorded in these infants. Direct laryngoscopy and bronchoscopy were not performed in the other 7 patients. Decreased tongue mobility and failure of the oral phase of deglutition were diagnosed in two patients (4,7) by videofluoroscopy. Each of these two patients demonstrated an absent gag reflex.

The most common dysmorphic feature was mandibular hypoplasia, seen in 5 patients. One patient (6) exhibited the classic Pierre-Robin triad of micrognathia, cleft palate, and glossoptosis. Cleft of the secondary palate (without alveolar or lip involvement) was seen in two other patients (8,9). Facial diplegia was noted as an isolated cranial nerve finding in one patient (3). Severe sensorineural hearing loss, documented by audiometric screening and ABR, was confirmed in one patient. In one other severely affected infant with multiple systemic anomalies, CT scan confirmed agenesis of the corpus callosum (10).

The elucidation of a primary pathophysiology for AMC requires EMG and muscle biopsy. EMG findings were recorded in 6 patients, confirming primary neuropathology in 5 and showing no such deviation in one patient with multiple contractures of all extremities and profound sensorineural hearing loss (5). Muscle biopsy in this patient was normal. In two other patients muscle biopsies were consistent with a denervation pattern consistent with primary neuropathy. In

TABLE IV

Otolaryngologic findings in 50 patients with AMC

	Number of patients
Laryngeal, oropharyngeal (presenting with stridor, aspiration, or dysphagia)	
Vocal cord paralysis (1 bilateral and 1 unilateral)	2
Absence of gag reflex	3
Laryngomalacia	3
Retracted, hypomobile tongue	3
Dysmorphic features	
Cleft palate	3
Micrognathia	6
Low set ears	4
Microstomia	1
Expressionless facies	1
Flattening of occiput	1
Other neurologic findings	
Severe sensorineural hearing loss	1
Agenesis of corpus callosum	1
Microcephaly	1
No visual tracking	1

TABLE V

Cranial nerve dysfunction in 10 patients with AMC

II	1 (blindness)
VII	1 (facial diplegia)
VIII	1 (profound sensorineural hearing loss)
IX	3 (absent gag)
X	2 (true vocal cord paralysis)
XII	3 (paresis)

patient no. 7, EMG diagnosis was consistent with a neuropathic process. However, muscle biopsy demonstrated agenesis of striated muscle (total replacement with fibrofatty tissue), consistent with a rare autosomal recessive myopathy known as amyoplasia congenita. This was the only patient in which a diagnosis of primary myopathy was entertained.

Table IV lists the clinical otolaryngologic findings found in 50 patients with AMC. The glossopharyngeal, vagus, and hypoglossal nerves were most frequently affected in the patients reviewed (Table V). One patient (9), born with generalized hypotonia, cleft palate, and auricular hypoplasia (associated with multiple congenital contractures), expired prior to EMG testing; necropsy was not permitted.

Discussion

AMC is a syndrome clinically characterized by congenital contractures at multiple joints. A number of other developmental defects of the central nervous system (CNS) and other viscera have been described in association with these joint deformities. Hence, AMC is clinically a very heterogeneous syndrome with two common features: onset during fetal development and dysgenesis of some portion of the neuromuscular pathway. Many authors [1,2,5,6,8] have observed neurogenic AMC to be far more common than primary myopathic AMC. Of our 10 patients, only one patient (10) was diagnosted to have a primary myopathic process, without showing evidence of motor cranical nerve weakness. Banker et al. [1] autopsied 53 patients with a diagnosis of neurogenic AMC. Disorders associated with dysgenesis of the anterior horn cells were the most common pathologic type. This pattern was seen with or without concurrent decreased numbers of neurons in the cerebral cortex and brainstem motor nuclei. Thus, in these patients, AMC can be ascribed to decreased organization and numbers of motor nuclei in the brainstem and anterior horns. Consequently, affected muscle is hypoplastic and becomes fibrotic according to the law of connective tissue [16]. The non-progressive nature of these lesions can be explained by cessation of proper neuronal migration during embryogenesis. Of interest, one patient with Pierre-Robin sequence was studied in this group: the nucleus ambiguus and the hypoglossal nucleus were hypoplastic and contained very few neurons. Hence, the relatively common Pierre-Robin phenotype seen in AMC may herald decreased neuronal population in the brainstem motor nuclei.

Although laryngeal involvement can be attributed to a hypoplastic nucleus ambiguus, definitive clinical pathologic correlation has not been demonstrated. Technically, laryngeal electromyography and muscle biopsy are difficult to perform. These studies were not obtained in our two patients diagnosed with vocal cord paralysis. There is one report [14] of documented neuromyopathic changes in the larynx of a two-month-old female with arthrogryposis who died of aspiration and respiratory insufficiency. Severe fibrosis of the intrinsic musculature was associated with congenital absence of the left arytenoid. The nucleus ambiguus was normal in appearance. Our two patients with true vocal cord paralysis had normal laryngeal morphology and EMG findings (in the extremities) consistent with a neurogenic process.

Arthrogryposis (multiple congenital contractures) occurs one in every 3000 live births [10]. Congenital contractures associated with progressive or non-progressive neuromuscular affliction (multiple sclerosis, muscular dystrophy, etc.) must be ruled out for the diagnosis of AMC. Our retrospective study showed that 3 of 50 patients diagnosed with AMC had laryngopharyngeal involvement requiring intubation and tracheostomy. These results compare well with those of Cohen and Isaacs who found 3 of 37 patients with AMC requiring tracheostomy [1]. They reported a total of 9 patients, all with neurogenic AMC. Our patient (3) had isolated bilateral facial paresis (Möbius syndrome), which is associated with AMC [9].

To summarize, approximately 10% of all patients with AMC will present with upper airway or other cranial nerve abnormalities. The otolaryngologist at a tertiary care center may be asked to evaluate one or two of these patients a year. Diagnostic studies which may be helpful include direct laryngoscopy, oropharyngeal videofluoroscopy, and CT scanning to rule out abnormal CNS morphology. CNS abnormalities, fortunately uncommon, are associated with mental retardation, multiple systemic anomalies, and a poorer prognosis. EMG and muscle biopsy are usually completed by the time of referral; these tests are the corner stone of physiologic diagnosis and prognosis in these patients. Our Orthopedic colleagues have reported excellent rehabilitative results with surgery, serial splinting, prosthetics, and therapy. Prospective follow-up in patients with these otolaryngologic problems has not been well doccumented. These studies are necessary to assess the long-term management strategies for dysphagia, dysarthria, dysphonia, and facial weakness in patients with AMC and non-progressive congenital lesions of the head and neck.

References

1 Banker, B.Q., Neuropathologic aspects of arthrogryposis multiplex congenita, Clin. Orthop. Relat. Res., 194 (1985) 30–42.

2 Baracha, E.P., et al., Arthrogryposis multiplex congenita Part 1: Clinical and electromyographic aspects, J. Neurol. Neurosurg. Psychiatry, 35 (1972) 425–434.

3 Brandt, S., A case of arthrogryposis multiplex congenita, Acta Paediatr. 34 (1947) 365–381.

4 Brown, L.M., et al., The pathophysiology of arthrogryposis multiplex congenita neurologica, J. Bone Jt. Surg., 62 (1980) 291–296.

5 Cohen, S.R. and Isaacs, H., Otolaryngological manifestations of arthrogryposis multiplex congenita, Ann Otol., 85 (1976) 484–490.
6 Drachman, D.B. and Bauker, C.A., Arthrogryposis multiplex congenita, Arch. Neurol., 5 (1961) 77–93.
7 Fenichel, G.M., Abnormalities of skeletal muscle maturation in brain damaged children: a histochemical study, Dev. Med. Child Neurol., 9 (1967) 419–426.
8 Fischer, et al., Arthrogryposis multiplex congenita: a clinical investigation, J. Pediatr., 76 (1970) 225–261.
9 Hageman, G. and Willemse, J., Arthrogryposis multiplex congenita: review with comment, Neuropediatrics, 14 (1983) 6–11.
10 Hall, J.G., Genetic aspects of arthrogryposis, Clin. Orthop. Relat. Res., 194 (1985) 44–52.
11 Hall, J.G., et al., Twinning in amyoplasia – a specific type of arthrogryposis with an apparent excess of dicordantly affected identical twins, Am. J. Med. Gen., 15 (1983) 591–599.
12 Moerman, P.H., et al., Multiple ankyloses, facial anomalies, and pulmonary hypoplasia associated with severe antenatal spinal muscular atrophy, J. Pediatr., 103 (1983) 238–241.
13 Parrish, M.L., et al., Agenesis of the corpus callosum: a study of the frequency of associated malformations, Ann. Neurol., 6 (1979) 349–354.
14 Schmitt, H. P., Involvement of the larynx in a congenital 'myopathy', unilateral aplasia of the arytenoid, micrognathia, and malformation of the brain – a new syndrome? Virchows Arch. A, 381 (1978) 85–96.
15 Sul, Y.C., et al., Neurogenic arthrogryposis in one identical twin, Arch. Neurol., 39 (1982) 717–718.
16 Swinyard, C.A. and Bleck, E.E., The etiology of arthrogryposis (multiplex congenital contracture), Clin. Orthop. Relat. Res., 194 (1985) 15–27.
17 Thompson, G.H., et al., Comprehensive management of arthrogryposis multiplex congenita, Clin. Orthop. Relat. Res., 194 (1981) 6–11.
18 Wynne-Davies, R., et al., Arthrogryposis multiplex congenita: search for prenatal factors in 66 cases, Arch. Dis. Child, 51 (1976) 618–623.