5-1-1964

Amyotonia congenita (oppenheim)

Thomas R. Laird
University of Nebraska Medical Center

AMYOTONIA CONGENITA (OPPENHEIM)

Thomas Richard Laird

Submitted in Partial Fulfillment for the Degree of
Doctor of Medicine

College of Medicine, University of Nebraska

February 1, 1964

Omaha, Nebraska

TABLE OF CONTENTS

AMYOTONIA CONGENITA (OPPENHEIM)

I. Introduction

Hypotonic infants were first described by Hoffmann in 1893. (38) He listed the symptoms as follows: The cases were usually familial. The onset occurred in a previously healthy infant during the first year of life. There was a gradual increase of symptoms. He found the proximal muscles to be more involved than the distal. Eventually bulbar and intercostal muscles were affected leading to death, usually within two years. Pathologic material was available to Hoffmannand he verfied that this was a disease of the anterior horn cell and ventral roots.

In 1900, Oppenheim described eight patients who had a nonfamilial disease present at birth and characterized by hypotonia, absent deep tendon reflexes, and muscular weakness that gradually improved with age. (28) Oppenheim postulated that this disease was the result of a temporary abnormality of muscle. Batten later (1903) presented three cases of infantile myopathy to the Royal Society of Medicine. (7) No histologic studies were available. However, Spiller (1905) presented the necropsy findings of a hypotonic infant thought by him to be an example of Oppenheim's disease. The tissue examined showed

no change within the central nervous system. The striated muscle fibers were universally small.

Collier and Wilson (1908) published their review on the subject of amyotonia congenita three years after Spiller's case. (14) They came to the conclusion that the syndrome described by Oppenheim was valid and that this represented a new disease. They listed seven criteria which in their opinion established the diagnosis: (1) There was no familial tendency in amyotonia; (2) no case of amyotonia had been reported in a myopathic family; (3) a large majority of cases of amyotonia were congenital; (4) the characteristic flaccidity of amyotonia was not present in myopathy; (5) local wasting was not present in amyotonia; (6) the course of myopathy was progressive, whereas the course of amyotonia was progressive amelioration; (7) the deep tendon reflexes returned. Again no biopsy or necropsy material was presented.

Reuben (1917) reviewed one hundred and thirty-six cases from the literature of what he termed amyotonia congenita. (36) In the majority of the cases which came to necropsy, disease was found in the anterior horn cell or ventral roots. Reuben added no biopsy or necropsy material of his own.

Greenfield and Stern (1927) on the basis of litera-

ture and of a family examined by them with detailed post-mortem and biopsy material came to the conclusion that the disease described by Werdnig and Hoffmann and the syndrome described by Oppenheim were actually one and the same. (22) They further emphasized that the criteria for diagnosis outlined by Collier and Wilson (1908) were not valid for the following reasons: (1) Sporadic cases of Werdnig-Hoffmann disease may be seen (2) infantile spinal atrophy may be noted on or about birth (3) characteristic adipose distribution of infancy would mark any local wasting (4) spontaneous periods of remission up to two years would occur in infantile spinal atrophy.

The majority of investigators agreed with Greenfield and Stern. An exception was noted, however, in the cases reported by Turner (1940). (43) Turner had the good fortune of examining the family originally presented by Batten (1909-1910) as infantile myopathy. The pathology in these cases was reviewed by Greenfield, and he and Turner came to the conclusion that these patients at that time represented a non-progressive myopathy. A further necropsy study of the same family was presented by Turner in 1949.

Werdnig, in 1891, and Hoffmann, in 1893, independently described the syndrome of progressive spinal (and bulbar) muscular atrophy that now bears their names. (23) This

disease entity is similar to amyotonia congenita except that progressive weakness and deterioration occur, usually leading to death in five years with post-mortem evidence of anterior horn cell degeneration.

II. Differential Diagnosis

Unfortunately, the term "amyotonia congenita" has become a "catch-all" diagnostic category for many hypotonic infants whose correct diagnosis is not apparent. A survey of the literature reveals a list of twenty-three possible causes of muscle hypotonia, occurring either congenitally or of insidious onset during early infancy. These probably may be best classified as diseases of the "Central Nervous System", of the "motor unit", and altered metabolism. See Table I. (30)

The term "amyotonia congenita" has been used by many to embrace all cases of early infantile hypotonia of whatever cause, while these, following Oppenheim's original description, have reserved this label for cases which show signs of spontaneous improvement. All too often this difference in usage has resulted in regrettable misunderstandings when one doctor has diagnosed amyotonia in a child with obvious spinal muscular atrophy, and has given a good prognosis, only to be proven hopelessly wrong by the course of events. The diagnosis of Werdnig-

TABLE I

Classification of Causes of Infantile Muscular Hypotonia

I. Central Nervous System Diseases (excluding AHC)

1. Brain damage (including cerebral palsy and mental deficiency
2. Mongolism
3. Degenerative Central Nervous System diseases
4. Cerebellar disease

II. Motor Unit Diseases

1. Werdnig-Hoffmann disease
2. Polyneuritis of insidious onset
3. Neonatal poliomyelitis
4. Muscular dystrophy
5. Polymyositis
6. Myasthenia gravis
7. "Benign Congenital Hypotonia" (Amyotonia congenita)

III. Metabolic

1. Cretinism
2. Scurvy
3. Rickets
4. Malnutrition
5. Storage diseases
6. Infantile acidosis
7. Infantile hypercalcemia
8. Adrenocortical hyperfunction
9. Arachnodactyly

Hoffmann, through common usage, is now generally taken to include all cases in which generalized weakness and hypotonia of the skeletal musculature is present at birth, or is noted within the first three months, and in which there is no clear evidence of any cerebral, skeletal, or metabolic disorder.

There are three main forms of Werdnig-Hoffmann disease recognized:

(1) A congenital or precocious form of spinal amyotrophy. This is the form seen in infants in whom the disease has commenced during the last month of pregnancy or during the first month of life. The picture is well known. The infant shows a generalized and symmetrical hypotonia; its lower limbs are lifeless, its upper limbs often show the "handle of basket" appearance; respiration is entirely abdominal, the cry feeble, tendon reflexes are absent. It is intelligent, smiles spontaneously. The contrast between the severity of the paralysis and the integrity of the psyche is one of the most valuable diagnostic signs.

(2) An infantile form of spinal muscular atrophy. The essential feature of this variety is that onset and further development of paralysis takes place after birth and can therefore be witnessed by observers. The paralysis

first affects the proximal muscles of the lower limbs, viz. the glutei, quadriceps, the long spinal muscles, extending to the nuchal and anterior cervical muscles, the muscles of the shoulder girdle, arms, forearms, and legs. Meanwhile, the muscles first affected become progressively more atrophied, while the foot and hand muscles are last to be affected. If the child is able to walk before the illness, he is soon incapable of doing so. The paralysis is flaccid, symmetrical, of greater or lesser severity and tendon reflexes are absent. There is a severe amyotrophy, though this is often marked by subcutaneous fat. The intercostals are often affected. In these cases intellectual development is normal.

(3) Forme frustes confined to the lower limbs are rare. The child cannot stand and is unable to walk. The wasting of muscle is moderate and symmetrical. An assessment of muscular power shows that the paralysis is not complete and is most marked in the proximal muscles and in the lumbar muscles. There are often contractures of tendons in the popliteal fossa. It is in this variety that one may still find feeble tendon reflexes in the same areas.

Signs of brain disease or metabolic defect, however, are notoriously difficult to elicit in the first few

months of life and this is why so many cases with hypotonia symptomatic of systemic disease are initially impossible to distinguish from others with a primary neuromuscular abnormality. A proportion of cases of the Duchenne or pseudohypertrophic type of muscular dystrophy may show signs of muscular weakness during the first year of life. In only a few of the cases observed has hypotonia with excessive mobility at the joints been a striking feature. As these grew older pseudohypertrophy of the calves appeared and progressive deterioration was apparent; but in the beginning, in the absence of a positive family history, accurate diagnosis is virtually impossible. Few cases of polymyositis in infancy have been described, although this condition may give generalized muscular hypotonia, signs of constitutional upset and of muscular tenderness and subsequent induration and fibrosis of muscles are generally apparent in cases occurring at this age and act as valuable distinguishing features. In myasthenia gravis, too, the ptosis and the evidence of involvement of the cranial musculature, signs which are usually apparent even in infancy, may - when added to evidence of general muscular weakness - be sufficient to demand a therapeutic test with Tensilon or Prostigmin. Polyneuritis in infancy appears to be a rare disease,

even though Adams, Denny-Brown, and Pearson (1953) considered that this condition may account for many recoveries from so-called amyotonia congenita.

One should imagine that in cases of this type, the muscular weakness and hypotonia would often show a relatively rapid onset, that there might sometimes be evidence of ascending paralysis, and that the cerebrospinal fluid protein would be raised.

In the various cerebral disorders which may be accompanied by severe muscular hypotonia any infant, which is found to have hypotonic musculature following prolonged cyanosis after a difficult labor, may be presumed to have a cerebral birth injury, particularly if other evidence of brain damage is present. The infant with cerebral palsy, too, may have remarkably limp and flaccid limbs, and may show a striking delay in the development of motor skills, while unusual posturing of the limbs with rather sinuous movements may herald the development of athetosis. Generally, in such cases the tendon reflexes are retained and even unusally brisk, and the plantar responses may remain unequivocally extensor long after the usual age. Similar features usually become evident in cases of cerebral lipidosis which may also be generally hypotonic in the beginning, but subsequently

epileptic manifestations and particularly myoclonus on startle usually develop. In kernicterus, too, there may be a history of prolonged neonatal jaundice, while associated deafness and evidence of rhesus incompatibility may be invaluable distinguishing features. Finally, in this group must be mentioned the mentally defective child whose limbs are often limp and unusually mobile on passive movement, and whose delay in motor development may be much more striking than his relatively slight mental backwardness. The diagnosis of minor degrees of mental defect in infancy can be a matter of the greatest difficulty and may call upon all the pediatricians reserves of skill and experience in assessing the infant's behaviour against a background of known variations in normal development.

When one cares to consider the various nutritional and metabolic disorders, it is almost possible to dismiss rickets as a disease which no longer occurs in this country, except in infants with renal disease. Usually it is apparent in this entire group of cases that the muscular weakness and hypotonia which the infant shows is a relatively secondary feature and is overshadowed by fever, wasting, or some other striking features of systemic disease. When generalized hypotonia develops after an acute illness, rapid recovery is usually the rule; but when the condition

is more prolonged, careful attention to the dietary history, urinalysis, examination of the stools, radiographs and biochemical studies, revealing perhaps hypercalcemia or urinary infection with nephrocalcinosis, may solve the problem. The diagnosis of cretinism, too, will rarely present much difficulty to the experienced pediatrician after a few weeks life. It is in the less common cases where muscular hypotonia is the presenting feature, overshadowing the evidence of general disease, that difficulty arises. Scurvy can often lead to such a picture. Glycogen storage disease can often lead to difficulty in diagnosis. In some cases of this type there is no hepatomegaly or splenomegaly as the disorder of glycogen storage is confined either to the muscles - when the diagnosis may only be made by histochemical studies of muscle removed by biopsy - or to the ganglion cells of the central nervous system.

Among the skeletal conditions which may be associated with muscular hypotonia is osteogenesis imperfecta. In late infancy this condition may present with flabbiness and undue mobility of the limbs but the family history and subsequent development of fractures will generally lead to the correct diagnosis being made. In arachnodactyly, muscular hypotonia is generally slight, though

the limbs may always seem to be unusually mobile. Here the diagnosis will be made on the appearance of the digits, on the family history, and the association of other defects such as arching of the palate or cardiac abnormalities. It should also be remembered that some infants with congenital heart disease (particularly the tetralogy of Fallot) may be limp and flabby, as may others with multiple congenital abnormalities of, say, heart and skeleton. The diagnosis of the rare spinal cord birth injury is not generally difficult to make as there is generally severe flaccid paralysis of the lower limbs only, often with sensory loss. And finally, in considering the causes of symptomatic hypotonia, the possibility of misinterpretation of physical signs should be remembered. In some cases of bilateral congenital hip dislocation, for instance, the comparative immobility of the lower limbs may be wrongly attributed to muscular weakness. In Table II are a number of points which may aid in the differential diagnosis. (46)

III. Etiology

The etiology of the condition is unknown. The disease is inherited as an autosomal recessive. Walton speculates that it may be the result of an abnormality of neuromuscular development - that is - the child may be

TABLE II

The Differential Diagnosis of the Causes of Infantile Hypotonia

Benign Congenital Hypotonia	Symptomatic Hypotonia	Spinal Muscular Atrophy	
++	+ -	+++	Muscular weakness and atrophy
++	+(+)	+++	Hypotonia and joint hypermobility
+ -	-	++	Respiratory muscle involvement
-	-	+	Fasciculation of tongue and bulbar involvement
+ -	+ -	++	Contractures and skeletal deformity
+ -	+	-	Tendon reflexes
-	+	-	FMG
Myopathic	Often Normal or else that of the primary disease	Neuropathic	Muscle biopsy
Normal		Denervation atrophy	Natural history
Improvement	That of the primary disease	Progressive	

born with immature motor units, or perhaps may have less than the normal number of muscle fibers. (45)

The thymus, the thyroid and the adrenals have been considered factors in causing the syndrome of amyotonia. Manifold congenital malformations have been observed in various cases of amyotonia and have led Lewey to postulate that the whole picture may be explained on the basis of a developmental retardation and malformation. Arthur (1954) believes that it is due to late maturation of the pathways controlling tone. (29) Gurdjian believes that this may be some toxic process. (27) He says that congenital types could be explained on such a theory. Under the influence of such a factor, the anterior horn cell and the muscle either degenerate or do not develop properly. On the toxic theory one may be able to explain amelioration of some cases. With cessation of toxic causes the anterior horn cell and the muscles recover function sufficiently to operate.

Grinker (1927) found the pathological changes entirely within confines of the lower motor neuron. (26) He found an absence of glial reaction, scar formation, or vascular change which suggested to him that this was not an active process and certainly not an inflammatory or toxic condition. Simple paucity of cells of anterior horn and pres-

ence of cells which were either small, rounded and poor in chromatin or long and fusiform, suggested a developmental defect.

Of the various theories which have been formulated, the most important are those which presuppose a premature halt, in the process of development, owing to which the nerve cells, nerves, and muscle fiber of the neuromuscular system remain in fetal condition. Pathologic evidence is altogether in favor of the disease being due to a degeneration of the neurons of the ventral horns, a process which may begin either before birth or within the first year of life, and which may be either rapid or slow in its progress or may cease to advance.

IV. Clinical Aspect

The outstanding features of amyotonia congenita is underdevelopment and hypotonicity of the skeletal musculature. These children are brought to the physician with varying complaints such as: "easy fatigability"; "frequent falls"; "legs are weak"; "loose joints and crooked gait"; and "inability to sit, stand or walk at the appropriate time".

Signs of hypotonia are: (a) Head drop phenomenon. If the shoulders of a supine patient are rapidly raised, the head drops (falls back). (b) Phenomenon of loose

shoulders. If the examiner places his hands under the armpits of the sitting patient and tries to raise the shoulders, the shoulder girdle gives in and the patient may slip through. (c) Frog belly. The abdominal wall of the supine patient protrudes further laterally than the thoracic cage. (d) Rag doll phenomenon. If the examiner shakes the hands or foot of the patient, they quiver like the extremities of a rag doll. (e) Pendulousness. If the patella tendon is tapped while the patient sits with his legs hanging free, the leg swings back and forth several times like a pendulum because of the decreased tone of the hamstrings and quadriceps. (f) Kyphosis. The back of a sitting child forms a kyphosis. (48)

The disease is first apparent in early infancy and there is evidence it antedates birth. The hypotonicity interferes with normal postural development. When the disease is severe, the infant is never able to hold up its head or to sit erect. When it is milder, these acts are achieved at an age considerably later than normal. In some cases, even walking with a peculiar waddling gait may become possible. For those persons in whom the hypotonicity involves the intercostal muscles, pneumonia is a frequent terminal complication before the end of the

first year of life. In those in whom the muscles concerned with respiration are spared, the disease is apt to run a longer course, sometimes marked with periods of apparent improvement; but most children afflicted with amyotonia congenita succumb to intercurrent infection before adult life is reached. (9)

A significant proportion of the patients recover completely without showing signs of any cerebral, metabolic or skeletal disorder. See Table III.

The condition of the musculature, as reported, have been found fairly uniform. Clinically, the muscles are weak, but not paralyzed. The disease produces progressive muscular weakness which early in its course involves the proximal muscles more severely than the distal. They show quantitative reduction or absence of electrical response. They do not show the reaction of degeneration. Tendon reflexes are weak or absent.

V. Musculature

(a) General

The condition of the affected muscles is one of complete tonelessness with preservation of some degree of voluntary power, though in severe cases this power may be insufficient in a proximal muscle to raise the limb against gravity. This condition has led to descriptions

TABLE III

The Clinical Features of Benign Congenital Hypotonia

(a) Cases with incomplete recovery	(b) Cases with complete recovery	
++	+	Muscular weakness and atrophy
+++	++	Hypotonia and joint hypermobility
+ -	-	Respiartory muscle involvement
Depressed or Absent	Normal or Depressed	Tendon reflexes
Persisting muscular weakness, atrophy and hypotonia particularly of proximal limb groups	Complete recovery 5-12 years	Prognosis

of complete paralysis in this disease, but careful investigation has shown that, however complete the apparent paralysis may be, every muscle when put into a favorable position as regards work involved contracts voluntarily.

With the extreme limpness of the muscles is associated also considerable relaxation of the ligaments, and the most fantastic positions of the limbs and trunk may be assumed. The relaxation of muscles and ligaments allows the most remarkable over-extension of the joints, and leads to a highly characteristic flail-like condition of the joints when shaken. The muscles are small, and impart a peculiar soft velvety sensation to the touch, quite different to the feel of normal muscles on the one hand, or to that of myopathic muscles on the other hand. The hard patches that are so often to be felt in the muscles of myopathy, even when there is no pseudo-hypertrophy, are never present.

Very striking and peculiar to amyotonia is the impossibility of distinguishing by touch between the skin, the subcutaneous tissue and the underlying muscle. One can make no separation between these structures, and from the skin down to the bone there seems to be but one soft homogeneous substance.

There is no local wasting of the muscles, although

the relatively smaller size of the proximal muscles of a limb, compared with the size of the peripheral muscles, may be conspicuous in a limb where the proximal muscles show a much higher degree of amyotonia; and conversely, where the amyotonia is more marked in the muscles of the periphery, these may be conspicuously smaller than the proximal muscles. Smallness in size of one individual muscle, or of part of a muscle, such as is so commonly met with in cases of myopathy, never occur in amyotonia.

(b) Electrical Reactions

Electromyography is a technique used for gaining information about the functional state of the motor unit; i.e., the lower motor neuron and the muscle fibers it supplies. (18) The equipment consists of a needle electrode, the pick-up device, an amplifying system, and both a loudspeaker and an oscilloscope as the indicating instrument.

During a normal strong contraction the many motor unit action potentials completely cover the oscilloscope screen and the sound is constant. This is called the normal interference pattern. A loss of motor units, due either to anterior horn cell disease or to peripheral neuropathy, results in fewer than the normal number of motor unit action potentials being seen and heard during

a strong contraction, so that there is not complete obliteration of the oscilloscope screen. The size of the individual potentials is approximately normal, however, since the amplitude and duration of the motor unit spike potential depends on the number of individual muscle fibers functioning in the motor unit. This is the neuropathic interference pattern. In diseases of the muscle fibers, the size of the motor unit action potential is decreased and the sound is of higher pitch, but there are a normal number of motor unit action potentials present during maximal contractions because all the lower motor neurons are intact. This is the myopathic interference pattern.

There are also abnormal types of discharges. The most important of these is the denervation fibrillation potential that is due to "spontaneous" activation of a single muscle fiber.

Walton has observed that the electromyographic tracings of seven cases of those without complete recovery are myopathic, meaning that the interference pattern on voluntary effort showed excessive polyphasic and short duration potentials, as seen in myopathic disorders. He believes that this may only mean that many motor units are populated with less than the normal number of muscle

fibers. He has observed normal tracings in five of eight cases with complete recovery.

VI. General Nerve Signs

There are no signs of lack of cerebral development or of mental deterioration. The special senses have been normal in all the reported cases. The cranial nerves have been found normal in all cases. Strabismus had not been noticed, and the ocular muscles have been free from affection in all cases. Sensibility seems to be normal. The Spincters are never affected. The deep tendon reflexes are invariably lost in the regions where amyotonia is marked. The superficial reflexes are intact.

VII. Treatment

No specific treatment for amyotonia congenita is known today. Alleged improvement, often considerable, has been described as a result of use of Vitamin E and its analogues (Bichnell, 1940; Stone, 1940; Rabinovitch, Gibson and McEachern, 1951). (33,40)

The treatment of the disease at present consists of symptomatic treatment. As these children are prone to develop pneumonia, every precaution must be used to prevent them from developing it. Of course with the development of pneumonia, the appropriate measures must be taken in treating the disease.

VIII. Pathology

At necropsy the muscles are observed to be small and pale, and sometimes they are thin enough to be described as transculent. Microscopically, the picture is that of embryonic muscle; most fibers are small, and some are of normal size. There is a decided increase in sarcolemma muscles. Both fat and connective within the muscles are increased, but there is practically universal agreement concerning the absence of signs of degeneration within the muscles. The pathologic changes found in the nervous system have not been as consistent as those in the musculature.

In a review of 28 cases, Greenfield and Stern found the following: (1) Atrophy and degeneration of anterior horn cells in the cord; (2) thinness and poor myelination of anterior roots; (3) slenderness and definite myelination of the peripheral nerves with, in most cases, a large proportion of very thin myelin sheaths; (4) atrophic changes in the muscle. According to these same authors, the amount of destruction or degeneration of the cranial nerve nuclei varies in different cases. In their cases the hypoglossal nucleus (somatic efferent cells) was always involved. Degeneration of similar types was described by Baudoin, Rothmann, Griffiths, Spiller, Buzzard, Kaumheimer and Slauck. Baudoin described chromatolysis

in the abducens nucleus and Rothmann described chromatolysis in the nucleus ambiguus. Kaumheimer found the cells of the spinal accessory nucleus to be atrophied. Archangelsky and Abskosoff, DeVilla, Foot, Bower and Schippers found the hypoglossal nucleus to be normal.

Conel thoroughly studied one case using as controls a 5 month old infant with intussusception, a 4 month old with meningitis, a 4 month old with congenital defect of the kidney. (15) Careful research revealed affected neurons in the following locations: Ventral anterior column of the gray matter (somatic efferent cells); the nucleus ambiguus (branchial efferent cells of the vagus and glossopharyngeal nerves); the motor nucleus of the facial nerve (branchial efferent cells); the nucleus of the oculomotor nerve (somatic efferent cells); the globus pallidus (efferent internucleated cells); the gyrus centralis anterior (giant pyramidal cells of Betz).

The cells of the nuclei resemble one another in the following respects: They are large, multipolar and efferent, and have coarse Nissl bodies; the axons of all but the Betz cells and the cells of the globus pallidus end on striated muscle. The axons of the Betz cells end in synapse with the somatic and branchial efferent cells of the cranial and spinal nerves.

The proportion of atrophied cells and cells in the late stages of involvement to cells in the early and intermediate stages was greater in the spine than in the brain stem; conversely, the proportionate number of affected cells in the early and intermediate stages increased from below upward. In the nucleus of the oculomotor nerve, the globus pallidus and the anterior central gyrus all the affected cells were in early or anterior stages. These facts suggest the disease progresses gradually from below upward. Support for this hypothesis is furnished by the ratio of normal and affected cells. Cells presenting a healthy appearance were present in all the nuclei. Proportion of affected to unaffected was least in the thoracic region of the spinal cord. Unaffected cells were least numerous in proportion to affected and atrophied cells in the medial part of the anterior column of the gray matter in the lumbar and cervical enlargements and in the upper cervical region.

Conel in 1940 in a 5½ month old child found involvement also of the trochlear nerve, the lateral vestibular nucleus and the spinal ganglions. (16)

In some cases no abnormality in the spinal cord has been detected, but in the majority a reduction in the number of cells in the anterior horns has been an out-

standing observation. Most workers have reported deficient myelination of the peripheral nerve fibers and of the anterior roots of the spinal cord. The two points on which there is relative agreement among those workers who have found a disorder in the nervous system is, first, its location within the lower motor neuron and, second, the absence of secondary degeneration.

Other parts of the body have been found abnormal, particularly the various endocrine glands.

IX. Conclusions

Amyotonia congenita (Oppenheim) is an autosomal recessive inherited disease which begins in infancy. A significant proportion of the patients recover completely without showing any signs of cerebral, metalbolic or skeletal disorder. If the disease persists, there is seen persisting muscular weakness, atrophy and hypotonia particularly of the proximal limb groups. The disease appears to have no effect on cerebral development. In general, the only significant neurological finding is loss of deep tendon reflexes. No paralysis of the musculature has ever been found to be present. No treatment is known at the present. Death is usually the result of pneumonia secondary to intercostal muscle involvement.

X. Summary

Hypotonic infants were first described by Hoffmann in 1893. In 1900 Oppenheim described eight patients who had a nonfamilial disease present at birth and characterized by hypotonia, absent deep tendon reflexes, and muscular weakness that gradually improved with age. Oppenheim postulated that this disease was the result of a temporary abnormality of muscle.

Benign congenital hypotonia (amyotonia congenita) must be differentiated from other causes of hypotonia in infants. Review of the literature reveals a list of 23 possible causes of hypotonia of infancy. Probably the most important and the most difficult to distinguish is Werdnig-Hoffmann disease.

The etiology of the disease is unknown. General theories have been proposed. These consist of: (1) abnormality of neuromuscular development; (2) endocrine; (3) toxic processes; (4) a premature halt in the process of development.

The disease is first apparent in early life. The hypotonicity interferes with normal postural development. In severe cases the child may never be able to hold the head up. In milder cases, they may even walk. Pneumonia is a severe complication due to involvement

of the intercostal muscles. Most succumb to intercurrent infection before adult life is reached. A significant proportion recover completely.

The muscles present with complete tonelessness with preservation of some degree of voluntary power. With extreme limpness of the muscles is associated also considerable relaxation of the ligaments, thus fantastic positions of the limbs and trunk may be assumed. No local wasting of muscles is seen.

In general, cerebral development is normal. There is no change in the special senses, cranial nerves, sensibility, superficial reflexes, sphincters. The deep tendon reflexes are invariably lost in severe cases.

To date, no specific treatment is known.

Bibliography

1. Batten, F.E., Case of Amyotonia Congenita. Proceedings of the Royal Society of Medicine, 10 (Neurology Section):47,1916-1917.

2. _____, Myopathy, Simple Atrophic Type. Proceedings of the Royal Society of Medicine, 86 (Neurology Section):69,1915.

3. _____, Progressive Spinal Muscular Atrophy of Infants (Werdnig-Hoffmann). Proceedings of the Royal Society of Medicine, 4 (Clinical Section): 115,1911c.

4. _____, Progressive Spinal Muscular Atrophy of Infants and Young Children. Brain, 33:433,1911a.

5. _____, Simple Atrophic Type of Myopathy: So-called "Myotonia Congenita", or "Amyotonia Congenita". Proceedings of the Royal Society of Medicine, 4 (Section on Diseases of Children):100,1911b.

6. _____, The Myopathies on Muscular Dystrophies. Quarterly Journal of Medicine, 3:313,1910.

7. _____, Three Cases of Myopathy, Infantile Type. Brain, 26:147,1903.

8. Benjamin, E.L., Amyotonia Congenita: Report of Two Cases in the Same Family. Archives of Pediatrics, 48:734,1931.

9. Burdick, W.F., Whipple, D.V., and Freeman, W., Amyotonia Congenita (Oppenheim): Report on Five Cases with Necropsy; Discussion of Relationship Between Amyotonia Congenita, Werdnig-Hoffmann Disease, Neonatal Poliomyelitis and Muscular Dystrophy. American Journal Diseases of Children, 69:295,1945.

10. Chambers, R. and MacDermot, V., Polyneuritis as a Cause of "Amyotonia Congenita". Lancet, 1:397,1957.

11. Collier, J.S., A Case of Amyotonia Congenita. Brain, 30:146,1907.

12. _____, Questionable Amyotonia Congenita. Proceedings of the Royal Society of Medicine, 68 (Neurology Section): 69,1915.

13. Collier, J.S. and Holmes, Gordon, The Pathological Examination of Two Cases of Amyotonia Congenita with the Clinical Description of a Fresh Case. Brain, 32:269,1909.

14. Collier, J.S. and Wilson, S.A.K., Amyotonia Congenita. Brain, 31:1,1908.

15. Conel, J.L., Amyotonia Congenita. Archives Neurology and Psychiatry, 40:337,1938.

16. _____, Distribution of Affected Nerve Cells in Amyotonia Congenita (Second Case). Archives Pathology, 30:153,1940.

17. Councilman, T. and Dunn, C.H., Myatonia Congenita: A Report of a Case with Autopsy. American Journal Diseases Children, 2:340,1914.

18. Eaton, I.M. and Lambert, E.H., Electromyography and Electric Stimulation of Nerves in Diseases of Motor Units. Journal American Medical Association, 163: 1117,1957.

19. Faber, H.K., Amyotonia Congenita: A Survey of the Known Cases with a Report of Three New Cases. American Journal Diseases Children, 13:305,1917.

20. Foot, N.C., Report of a Case of Amyotonia Congenita with Autopsy. American Journal of Diseases of Children, 5:359,1913.

21. Gowers, W.R., Myopathy and a Distal Form. British Medical Journal, 2:89,1902.

22. Greenfield, J.G. and Stern, R.O., Anatomical Identity of Werdnig-Hoffmann and Oppenheim Forms of Infantile Muscular Atrophy. Brain, 50:652,1927.

23. Greenfield, J.G., Cornman, T., and Shy, G.M., The Prognostic Value of the Muscle Biopsy in the "Floppy Infant". Brain, 81:461,1958.

24. Griffith, J.P.C., A Case of Amyotonia Congenita. Archives Pediatrics, 27:305,1910.

25. Griffith, J.P.C. and Spiller, W.G., Amyotonia Congenita: A Clinical and Pathological Study. American Journal Medical Science, 142:165,1911.

26. Grinker, R.B., The Pathology of Amyotonia Congenita. Archives Neurology Psychiatry, 18:982,1927.

27. Gurdjian, E.S., Myotonia Congenita with Past Reference to Pathology and Familial Tendency. Archives Neurology and Psychiatry, 24:52,1930.

28. Hardman, R., The Floppy Infant. American Journal Diseases of Children, 101:525-35,1961.

29. Holmes, J.B., Amyotonia Congenita (Oppenheim): Report of a Case with Full Histopathologic Examination. American Journal Diseases of Children, 20: 405,1920.

30. Jebsen, R.H., Johnson, E.W., Knobloch, H., and Grant, D.K., Differential Diagnosis of Infantile Hypotonia. The Use of Electromyography and the Development and Neurologic Examination as Aids. American Journal Diseases of Children, 101:17,1961.

31. Krabbe, K.H., Congenital Familial Spinal Muscular Atrophies and Their Relation to Amyotonia Congenita. Brain, 43:166,1920.

32. Macleod, J.G. and MacDonald, R.M., Infantile Muscular Atrophy of Spinal Origin: A Report of Two Cases. Archives Diseases of Children, 17:30,1942.

33. Nattrass, F.J., Recovery from Muscular Dystrophy. Brain, 7:549,1954.

34. Nielsen, J.M., Myotonia Congenita of Oppenheim: Report of a Unique Case. American Journal Diseases of Children, 35:82,1928.

35. Pearce, N.O., Amyotonia Congenita. American Journal Diseases of Children, 20:393,1920.

36. Reuben, M.S., Amyotonia Congenita of Oppenheim. Archives Internal Medicine, 20:657,1917.

37. Richter, R.B. and Humphreys, E.M., Unusual Myopathy: Presentation of Two Cases with Muscle Biopsy. Archives Neurology and Psychiatry, 73:574,1955.

38. Shy, G.M. and Magie, K.R., A New Congenital Non-Progressive Myopathy. Brain, 79:610,1956.

39. Sly, M., Horner, F.A., Boyarsky, L.L., and Packer, J.T., A Hypotonic Infant. Clinical Pediatrics, 2:127-31,1963.

40. Stone, S., Vit Ein the Treatment of Muscle Disorders of Infancy and Childhood. Journal Pediatrics, 18: 310,1941.

41. Thieffry, S., The Muscular Hypotonias of Infancy. American Journal Physical Medicine, 38:231,1959.

42. Turner, J.W.A., An Amyotonia Congenita. Brain, 72: 25,1949.

43. _____, The Relationship Between Amyotonia Congenita and Congenital Myopathy. Brain, 63:163,1940.

44. Tuthill, C.R. and Levy, M.G., Amyotonia: Report of Case with Histologic Observation. American Journal Diseases of Children, 41:591,1931

45. Walton, J.N., Amyotonia Congenita: A Follow-up Study. Lancet, 1:1023,1956.

46. _____, The Amyotonia Congenita Syndrome. Proceedings of the Royal Society of Medicine, 50:301,1957.

47. Wohlfart, G., Muscular Atrophy in Diseases of the Lower Motor Neurons. Archives Neurology Psychiatry, 61:599,1949.

48. Zellweger, H.U., Smith, J.W., and Cusminsky, M., Muscular Hypotonia in Infancy: Diagnosis and Differentiation. Review Canadian Biology, 21:599,1962.