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Infantile Spinal Muscular Atrophy at the Albert Royer National Children's Hospital Center in Dakar

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Abstract

Introduction: Infantile spinal muscular atrophy (ISA) is an autosomal recessive disease caused by primary degeneration of cells in the anterior horn of the spinal cord, leading to muscle weakness and hypotonia. Its incidence is estimated at 1 in 6000 births worldwide. In Africa, particularly in Senegal, there are few studies interested on this pathology. We therefore deemed this study necessary, which set itself the objective of describing the diagnostic, therapeutic and progressive aspects of infantile spinal muscular atrophy at the Albert Royer National Children's Hospital Center in Dakar (CHNEAR). **Methodology:** We conducted a retrospective descriptive study over a period of two (2) years from December 2020 to December 2022. Included were all hospitalized patients in whom the diagnosis of spinal muscular atrophy was made with or without genetic confirmation. The data were collected on a pre-established form then entered and analyzed with the following software: Excel 2013 and R version 4.1.3. **Results:** During our study period, 2100 children were hospitalized, the annual incidence was 0.76%. The average age of our patients was 9 ± 9 months with a range of 3 months to 32 months and the median was 6.5 months. The sex ratio was 7. The notion of family consanguinity was found in 62.5% of cases and the notion of ISA in the family in 25% of cases. Hypotonia and respiratory distress were found at the forefront in equal proportions (50% of cases). Electromyogram (EMG) was performed in 3 patients (37.5%). Symptomatic medical treatment was administered in 100% of patients, 04 patients had benefited from respiratory physiotherapy, *i.e.* 50% of cases, and genetic counseling was carried out in one patient (12.5%). The evolution was immediately favorable in 2 patients or 25% of cases, unfavorable in 75% of cases with a death rate of 50% and the average age of death was 5.5 months ± 1 with extremes ranging from 3 to 7 months.

Conclusion: The number of Infantile spinal muscular atrophy cases remains low in hospitals in Dakar. Diagnostic means are still difficult to access. The course is difficult to predict and is often marked in the long term by respiratory difficulties which can be fatal.

Keywords

Spinal Muscular Atrophy, Child, Hypotonia, Dakar

1. Introduction

Infantile spinal muscular atrophy (ISA) is an autosomal recessive disorder [1]. It is due to primary degeneration of cells in the anterior horn of the spinal cord, leading to muscle weakness and hypotonia [2]. It is a serious condition, it is the most common cause of genetic death in children with an incidence of 1 in 6000 live births [3]. Although classified as a "rare disease", the incidence of ISA reaches 1 in 10,000 births in the United States and up to 2 in 10,000 births per year in France [1]. In France, around 120 new cases are diagnosed each year, and there are around 1500 patients, all types combined. In Africa, myopathies are very rarely reported due to difficulties in diagnostic confirmation. The disease is marked by great clinical variability [4]. Among proximal spinal muscular atrophies, there are four types (two infantile types, one juvenile type and one adult type):

- **Type I** called Werdnig-Hoffmann disease or severe infantile spinal muscular atrophy.
- **Type II** or intermediate infantile spinal muscular atrophy.
- **Type III** also called juvenile spinal muscular atrophy or Kugelberg-Welander disease.
- **Type IV** or adult spinal muscular atrophy.

The evolution of this condition seems difficult to predict. It appears to be a disabling pathology, requiring multidisciplinary care [5]. This pathology currently benefits from advances in molecular biology making possible a precise diagnosis which could lead to genetic counseling.

In order to better approach this pathology, we carried out this study with the main objective of describing the diagnostic, therapeutic and evolutionary aspects of infantile spinal muscular atrophy. The specific objectives were to determine the particularities of the management of the pathology in our context.

2. Methodology

This was a retrospective, descriptive study in the pediatric department of the Albert Royer National Children's Hospital Center in Dakar from December 2020 to December 2022. We included children in whom the diagnosis of infantile spinal muscular atrophy was made with or without genetic confirmation. Incomplete or non-usable files as well as patients whose parents had not signed

consent were excluded from the study. The data was collected on a pre-established form. They were entered and analyzed with Excel 2013 and R version 4.1.3 software.

During the descriptive analysis, we studied the sociodemographic data with the age of onset, the history, the clinical presentation as well as the proposed treatment. The qualitative variables were described by frequency tables and by bar and pie charts. The quantitative variables were described by the mean, median, standard deviation and extremes. A value of $p < 0.05$ was considered significant.

The diagnosis was made based on hypotonia in a suggestive context associated with electromyographic abnormalities with or without genetic confirmation.

3. Results

3.1. Sociodemographic Results

During the study period, 2100 children were hospitalized in the pediatric pulmonology department of the Albert Royer children's hospital. Among them, 08 cases of spinal muscular atrophy were collected, representing an annual incidence of 0.76%. The average age of our patients was 9 ± 9 months with a range of 3 months to 32 months. The median was 6.5 months. The sex ratio was 7. Among the patients, 50% were from Dakar.

3.2. Antecedents

The notion of spinal muscular atrophy in the family was found in 25% of cases and family consanguinity in 62.5% of cases.

The vaccination status of patients was up to date in 6 cases according to the extended vaccination program of senegal (PEV).

A delay in psychomotor development was found in 100% of the children. Vaccination was up to date in 75% of children according to Senegal's expanded vaccination program. In our study, severe malnutrition was found in 12.5% of cases.

3.3. Reasons for Consultation

Hypotonia and respiratory distress were found in 50% of cases.

3.4. Neurological Examination

Consciousness was preserved in 5 patients, a proportion of 62.5%. Normal voluntary motor skills were found in 6 patients (75%), a bilateral motor deficit of both limbs and flaccid paraplegia associated with paresis of the limbs were noted in 12.5% of cases. Superficial and deep sensitivity was preserved in 3 patients (37.5%).

3.5. Lung Examination

Examination of the respiratory system revealed paradoxical breathing in 75% of

cases. Respiratory distress, condensation syndrome and congestion were noted in 62.5% of patients. Figure 1 shows the distribution according to respiratory signs.

3.6. Classification

In 75% of cases the age of onset of symptoms was before 6 months (75% of cases).

However, in 12.5% of cases, it can be less or more than 18 months as shown in Table 1.

3.7. Paraclinic

Electromyogram (EMG) was performed in 3 patients (37.5%) including

- The 2 cases concluded that there was a severe peripheral neurogenic process in all four limbs with damage to the axial muscles (sternocleidomastoid) where a large, poor, accelerated tracing with giant potentials was found in favor of infantile progressive spinal muscular atrophy type I (WERDNIG HOFFMAN).
- The other showed an axono-myelin sensory-motor polyneuropathy of the four limbs.

In our study, no cases benefited from genetic and molecular biology studies.

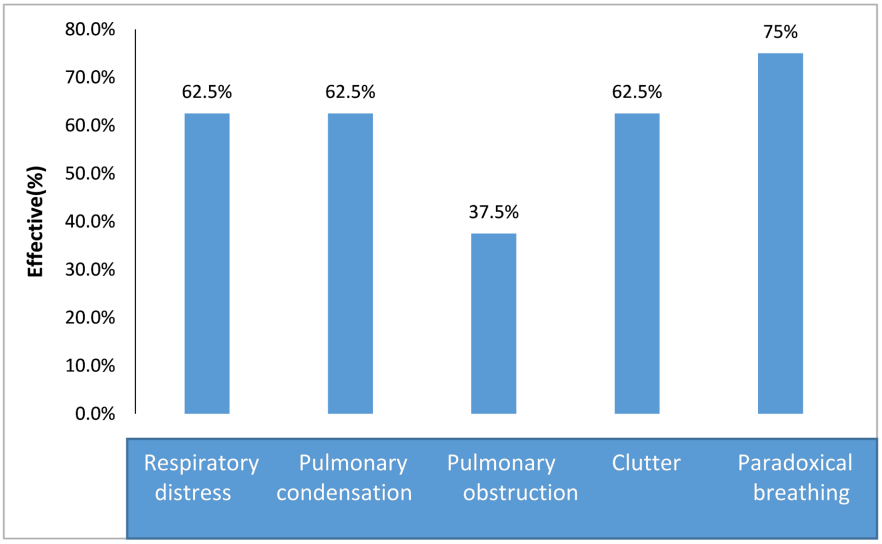

Figure 1. Distribution according to respiratory signs.

Table 1. Classification according to age of onset.

Age of onset	Effective	(%)
0 to 6 months	6	75%
Less than 18 months	1	12.5%
Greater than 18 months	1	12.5%
Total	8	100%

3.8. Diagnostic data

The average age of diagnosis was 8.5 months ± 8 with extremes ranging from 3 months to 30 months. According to the classification of the international ASI consortium we retained 6 cases of infantile spinal muscular atrophy type I and 2 cases of infantile spinal muscular atrophy type III.

3.9. Therapeutic Data

Medical treatment was administered in 100% of patients. Four patients had benefited from respiratory physiotherapy, *i.e.* 50% of cases. Genetic counseling was carried out in one patient (12.5%). Gene therapy was not prescribed in our patients.

3.10. Evolution

The outcome was immediately favorable in 2 patients or 25% of cases. Unfavorable outcome in 75% of cases with a death rate of 50%. The average age of death was 5.5 months ± 1 with extremes ranging from 3 to 7 months.

Long term was difficult to assess due to the loss of vision in several of the patients.

4. Discussion

4.1. Epidemiological Aspects

In our study, the average age of our patients was 9±9 with extremes of 3 months to 32 months. The median was 6.5 months, which is close to the study done in Morocco [6] and that in Chile [7]. On the other hand, the study carried out in Portugal [8] reported that the age of diagnosis was between 0 and 2 years. The age at diagnosis of spinal muscular atrophy varies and depends on the type and severity of the disease.

Furthermore, in our study, due to the fact that practitioners do not think early about the diagnosis, especially neonatal screening, and that parents are concerned late by the signs linked to this disease, the diagnosis is often made late. Consanguinity, as in all recessive diseases, is an important contributing factor in the emergence of spinal muscular atrophy. The consanguinity rate is significantly higher among couples who have given birth to children with ASI compared to couples without sick children. The figures range from 2.5 to 7.7% for marriages between relatives to 0.2% for a standard population [9]. In the Pearn series [10], the difference was even more significant (5% to 0.1%). In our work, consanguinity was found in 5 cases or 62.5%, which matches the figures reported by the study carried out in Egypt [11] and that of the Constantine University Hospital [12] which were respectively 46% and 47 %.

Spinal muscular atrophy is a genetic disease with serious consequences. It is important to look for the presence or absence of similar cases in the family.

The survey by the French Association against Myopathies carried out in France [13] cited that 22% of patients had one or more people in their family af-

fected by spinal muscular atrophy. This could be explained by the fact that in the case of a history of direct family ASI, the risk of developing ASI is increased. Therefore, early detection of at-risk cases is necessary in order to be able to implement appropriate measures to prevent the risk of having an ISA.

4.2. Diagnostic Aspects

The most frequent reasons for consultation were hypotonia in 4 type I cases (50%) and respiratory distress present in 4 type I and III cases. According to SHAWKY [11], the most common complaints were recurrent respiratory infections, hypotonia and muscle weakness in all type I patients (67.5%), followed by inability to walk in all type I patients. type II (27.3%), and functional impotence and difficulty walking in all type III patients (5.2%). Hypotonia is often the first clinical sign found in type I spinal muscular atrophy. Muscular paralysis progresses to affect the respiratory muscles such as the diaphragm, causing the paradoxical breathing found in certain cases of ISA. Respiratory muscle damage remains a poor prognosis criterion.

The genetic test makes it possible to obtain a definitive diagnosis in a very short time. It is often done straight away. However, in the literature it is reported that, in some cases, the doctor initially prescribes additional tests to guide the diagnosis: muscle enzyme measurements, electromyogram. Muscle biopsy is no longer necessary these days unless the result of the genetic test is ambiguous. [14]. In proximal spinal muscular atrophy linked to SMN1, the measurement of muscle enzymes shows CPK (creatine phosphokinase) generally low, indicating a process of loss of muscle fibers that is not very active. This examination thus makes it possible to rule out other neuromuscular diseases (muscular dystrophies, congenital myopathies, inflammatory myopathies, etc.), particularly in cases of type III spinal muscular atrophy and atypical forms of the disease [14].

In people suffering from proximal spinal muscular atrophy linked to SMN1, the electromyogram, if carried out, shows that it is the nerve, in this case the motor neuron, which is primarily affected, explaining the muscular weakness found [14]. In our study, only EMG was performed in 3 patients (37.5%).

This is explained by the fact that its examinations are more available and accessible in industrialized countries than in our context and by the fact that the socio-economic level is low in our countries where patients have difficulty taking care of themselves.

The age at diagnosis in our series was before 6 months in 75% of cases.

In the Ge series [15], the age of onset of the disease was between birth and the age of 9 months with an average of 3.1 months for type 1, and it varied between 2 to 18 months. With an average of 8.7 months for type 2 and he was between the age of 2 months to 5 years with an average of 21 months for type 3. Neonatal screening could help in early diagnosis and management adequate treatment of cases before symptoms set in. In our contexts the predominance of type I of the disease explains the fact that the age at diagnosis is before the acquisition of the sitting position.

4.3. Therapeutic Aspects

Symptomatic medical treatment was administered to all patients. The symptomatic treatment consisted to respiratory physiotherapy and oxygene therapy.

Genetic counseling was carried out in one patient (12.5%). The management of infantile spinal muscular atrophy is multidisciplinary and must be started as early as possible. There is no treatment that can permanently cure patients. However, medical treatment is symptomatic [16] [17]. However, innovative therapies have been available for several years in developed countries and are considered as basic treatment in ISA [14]. Gene therapy can increase the life expectancy of patients, especially if it is started early. However, it does not completely cure the disease. This difference in care can be explained by the financial difficulties encountered by our patients in our countries, unavailability and inaccessibility of these innovative therapies.

4.4. Evolutionary Aspects

The progression of proximal spinal muscular atrophy is specific to each person.

However, early and appropriate medical care can improve the quality of life of these patients [14]. However, infantile spinal muscular atrophy is a chronic disease, and in the absence of adequate care, there is a tendency at worsening, the evolution is not predictable. Serious complications can occur, even life-threatening. In this context our study showed an unfavorable evolution in 75% of cases with a death rate of 50%. The average age of death was 5.5 months ± 1 with extremes ranging from 3 to 7 months. In the long term, the evolution was difficult to assess due to the loss of sight of several of the patients.

5. Conclusions

Infantile spinal muscular atrophy is a rare but serious genetic disease.

Efforts must be made in early diagnosis and adequate management of cases. Genetic counseling should be mandatory for all families with confirmed cases.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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