

An Infant with Congenital Nemaline Myopathy and Hypertrophic Cardiomyopathy

Mizue Nakajima¹, Yoshio Shima¹, Sakae Kumasaka¹,
Kentaro Kuwabara², Makoto Migita² and Yoshitaka Fukunaga²

¹Department of Pediatrics, Japanese Red Cross Katsushika Maternity Hospital

²Department of Pediatrics, Nippon Medical School

Abstract

We describe an infant with nemaline myopathy accompanied by hypertrophic cardiomyopathy. The patient required long-term, intermittent positive-pressure ventilation after birth owing to muscle weakness, and cardiac failure developed during infancy. We diagnosed hypertrophic cardiomyopathy with outflow tract obstruction, and treated the heart failure with β -adrenergic and angiotensin II receptor blockers. We discuss the prognosis of nemaline myopathy combined with hypertrophic cardiomyopathy.

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Key words: nemaline myopathy, hypertrophic cardiomyopathy, early infancy

Introduction

Shy et al¹ first described nemaline myopathy as a congenital nonprogressive skeletal muscle disorder with rod body formation in the muscle fibers. Generalized muscle weakness and hypotonia involving respiratory and facial muscles are present in most patients with nemaline myopathy^{2,3}. However, cardiac muscle is usually not involved^{3–5}. Here, we describe an infant with nemaline myopathy complicated by hypertrophic cardiomyopathy, which is extremely rare.

Case Report

A 34-year-old woman (gravida 2, para 2) gave birth to a male infant weighing 2,486 g. Her family history did not include neuromuscular disease, but her first pregnancy ended in stillbirth. The

ultrasonography revealed polyhydramnios at 36 weeks of pregnancy which required emergency caesarian section because of the onset of membrane rupture and fetal distress.

At delivery the neonate had dyspnea, bradycardia, cyanosis, and generalized muscle hypotonia. The Apgar scores at 1 and 5 minutes after birth were 2 and 7, respectively. An endotracheal tube was immediately placed because of severe asphyxia. Typical clinical features of congenital myopathy, including muscle hypotonia, weakness, and a myopathic facies, were observed in our case. The results of hematological and chest X-ray examinations were normal. The karyotype of the patient was 46, XY. The biopsy of the right quadriceps femoris muscle revealed moderate variation in fiber size from 5 to 15 μ m in diameter, and ATPase staining revealed type I fiber atrophy. Modified Gomori trichrome staining showed that some fibers contained nemaline body-like inclusions

Correspondence to Mizue Nakajima, Department of Pediatrics, Japanese Red Cross Katsushika Maternity Hospital, 5–11–12 Tateishi, Katsushika-ku, Tokyo 124–0012, Japan
E-mail: s4019@nms.ac.jp
Journal Website (<http://www.nms.ac.jp/jnms/>)

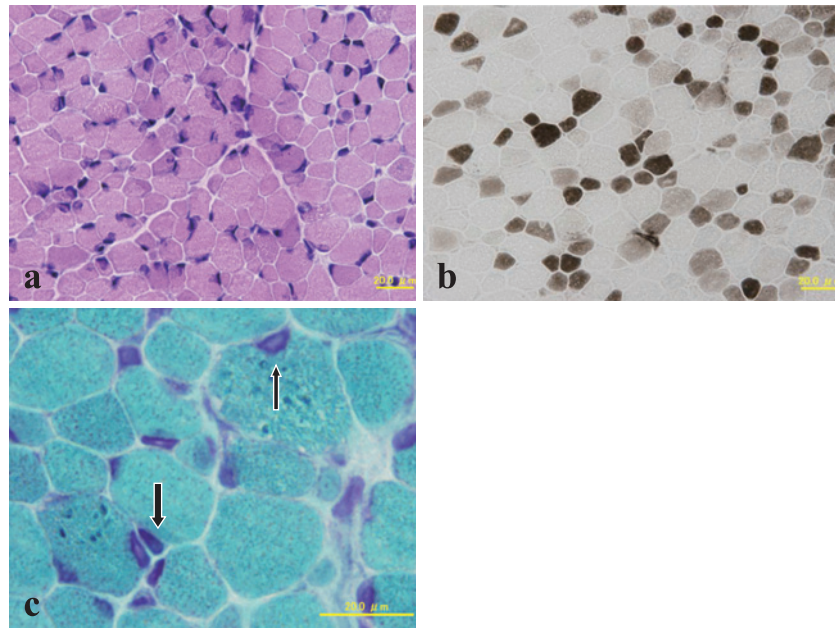


Fig. 1 Biopsy of right quadriceps femoris muscle.

- a: Staining with hematoxylin and eosin shows that fibers vary in size from 5 to 15 μm in diameter.
- b: Staining with ATPase shows type I fiber atrophy.
- c: Modified Gomori trichrome staining shows nemaline body-like inclusions (**arrow**) in some fibers.

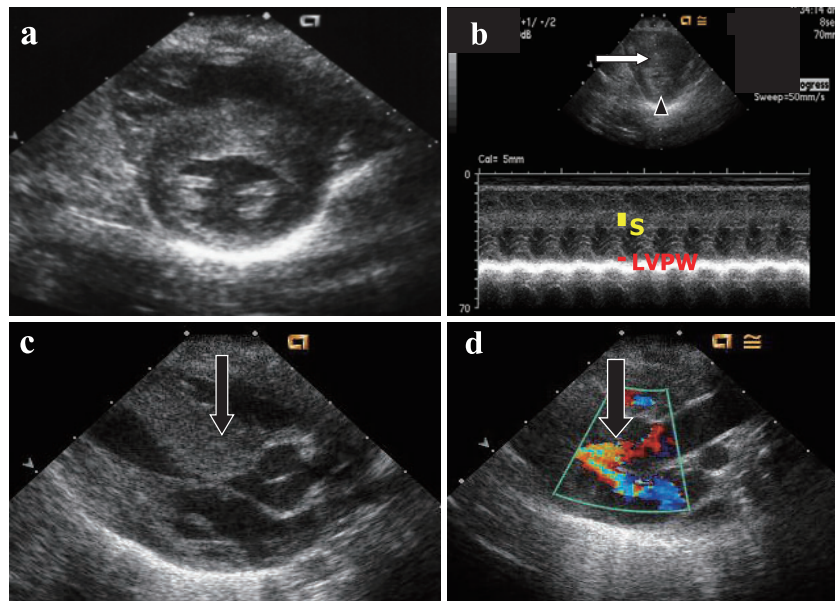


Fig. 3 Two-dimensional and color Doppler echocardiography.

- a: Short-axis view at systole shows hypertrophy of the septum and the left ventricular posterior wall.
- b: M-mode echocardiography shows a septal (S; **arrow**) thickness of 10.6 mm and a left ventricular posterior wall (LVPW; **triangle**) thickness of 3.7 mm.
- c: Long-axis view shows the systolic anterior motion of the mitral valve against the hypertrophied septum (**arrow**).
- d: Color Doppler echocardiography demonstrated turbulent, accelerated flow signals at the left ventricle outflow tract (**arrow**).

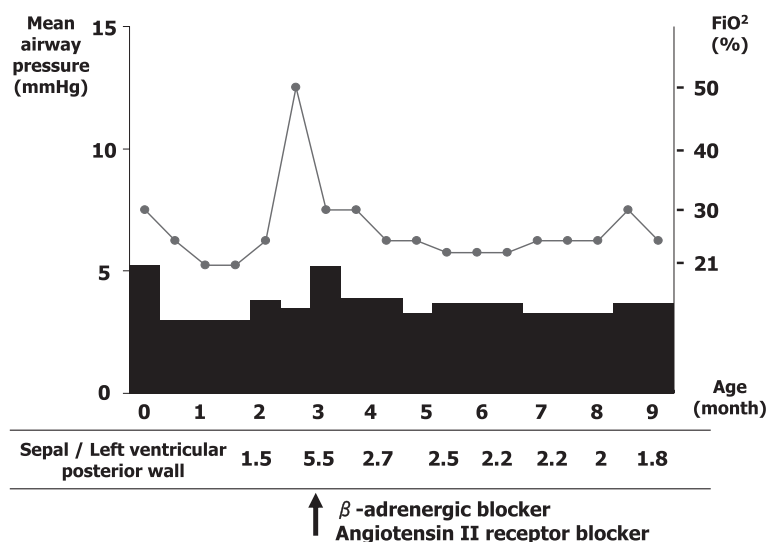


Fig. 2 Status of a neonate with nemaline myopathy. The patient was dependent on intermittent positive-pressure ventilation immediately after birth. At 3 months of age, increasing respiratory distress necessitated a high mean airway pressure and a high oxygen concentration because of heart failure. The ratio of the septum to the left ventricular posterior wall was 5.5. Heart failure was treated with β -adrenergic agents and angiotensin II receptor blockers.

(Fig. 1). Nemaline myopathy was thus diagnosed.

The infant remained dependent on intermittent positive-pressure ventilation.

At 3 months of age, respiratory distress had worsened, necessitating a higher airway pressure and a higher concentration of supplemental oxygen for mechanical ventilation (Fig. 2). At this time, we recognized a cardiomegaly on a radiographic examination. Marked hypertrophy of the interventricular septum and the posterior wall of the left ventricle was observed. The left ventricle cavity was small (Fig. 3a). The two-dimensional echocardiography demonstrated asymmetrical septal hypertrophy with a septal thickness (10.6 mm) nearly 3 times that of the left ventricular posterior wall (3.7 mm) (Fig. 3b). The left ventricular systolic function was impaired. The systolic anterior motion of the mitral valve against the hypertrophied septum was created by the high outflow velocities (Fig. 3c). A color and pulse Doppler echocardiograms also demonstrated a turbulent and accelerated flow signal at the outflow tract of the left ventricle (Fig. 3d). No cardiac malformations, such as aortic valvar stenosis, that would explain the left ventricular hypertrophy, were found. We concluded that the respiratory distress was caused by heart failure with hypertrophic cardiomyopathy. Treatment with β -

adrenergic and angiotensin II receptor blockers improved the left ventricular function.

The echocardiography of the patient at 1 year of age revealed persistent biventricular hypertrophy with a septum to left ventricular posterior wall ratio of 1.8. The heart failure remains controlled with medication.

Discussion

The hallmarks of nemaline myopathy are severe muscle weakness and nemaline rod bodies in skeletal muscle fibers⁶. The diagnosis of nemaline myopathy is a histopathological classification of congenital myopathy.

The clinical classification of nemaline myopathy into subtypes has been attempted on the basis of clinical features such as the pattern of weakness and age of onset⁶.

A few patients with nemaline myopathy accompanied by cardiomyopathy have been documented, but the combination of nemaline myopathy and hypertrophic cardiomyopathy is extremely rare. To our knowledge, only 11 patients with nemaline myopathy and cardiomyopathy have been described in the literature⁷⁻¹⁵. Table 1 shows that 7 patients with nemaline myopathy had

Table 1 Review of patients with nemaline myopathy accompanied by cardiac involvement

Case	Age (yr)	Skeletal myopathy	Nemaline rods in skeletal muscle	Cardiomyopathy	Nemaline rods in cardiac muscle
1 ⁷	2	+	+	HCM	Not examined
2 ⁸	3	+	+	DCM	+
3 ⁹	5	+	+	HCM	Not examined
4 ¹⁰	4	+	+	HCM	Not examined
5 ¹¹	46	+	+	DCM	-
6 ¹²	29	-	+	DCM	+
7 ¹²	37	-	Not examined	Sudden death	+
8 ¹³	69	-	+	DCM	+
9 ¹³	53	-	Not examined	DCM	+
10 ¹⁴	22	+	+	DCM	Not examined
11 ¹⁵	50	±	+	CHF	-
12 ^{our case}	0	+	+	HCM	Not examined

Abbreviations: HCM, hypertrophic cardiomyopathy; DCM, dilated cardiomyopathy; CHF, congestive heart failure.

cardiomyopathy in adulthood and that 4 patients had nemaline myopathy complicated by cardiomyopathy in infancy. An unusual feature of our patient was that cardiac failure developed during early infancy.

Although it is believed that involvement of cardiac muscle is unusual in nemaline myopathy in previous reports^{11,15}, some exceptional cases with nemaline rod bodies have been reported^{8,12,13} (**Table 1**). The historical incidence might have been underestimated because most patients with severe nemaline myopathy die in early infancy and few cardiac muscle biopsies have been performed.

Recently, a possible link between nemaline myopathy and hypertrophic cardiomyopathy has been reported, as has a common gene mutation^{7,16}. We speculate that cardiac involvement in nemaline myopathy may be more frequent than has previously been recognized, and further clinical study is needed.

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