CHAPTER 4

The Muscular Dystrophies

SEVERE X-LINKED RECESSIVE MUSCULAR DYSTROPHY (DUCHENNE-TYPE)

The best known and most frequently encountered of the dystrophies is the severe X-linked recessive variety. Initially described in 1868 by Guillaume Duchenne, the disease is characterized by rapidly progressive generalized muscle weakness and "pseudohypertrophy" of certain muscle groups. Death during the 2nd or 3rd decade is the inevitable outcome in all cases. Duchenne muscular dystrophy (DMD) is not an uncommon disorder. From 20 to 33 cases per 100,000 live male births are reported annually. Since the disease is inherited in an X-linked recessive manner, one-half of the male offspring of a relatively unaffected mother (carrier) will manifest the illness. Previously it was believed that up to one-third of cases resulted from spontaneous mutation either in the patient or his mother. However, with improved methods of carrier detection, it appears that such mutations are relatively uncommon.

It is known that some X-linked recessive disorders can manifest in females with normal karyotypes by inactivation of the paternal X-chromosome or lyonization. Despite this, Duchenne's dystrophy in females of normal karyotype is a rare event. Most female carriers are asymptomatic or have minimal non-progressive weakness. However, the typical clinical and laboratory features of Duchenne dystrophy have been described in a 9-year-old girl who appeared to be a manifesting heterozygote (Gomez et al, 1977). Her identical twin was normal, but the mother's brother had DMD and both the mother and the twin sister in question were identified as carriers by CPK tests. An additional case of a young girl with progressive muscle disease in a family with an extensive history of DMD has been reported by Olson and Fenichel (1982).
Clinical Presentation: Signs and Symptoms

The infant with Duchenne’s dystrophy attains all the early motor milestones on time and initially appears quite normal. Lack of apparent abnormalities in the earlier periods is probably due to the crudity of our observations. At about age 2½ however, it becomes obvious that there is something wrong with the child. He is observed to walk with his heels slightly raised off the ground and he is unable to keep pace with his peers. Falls are common, and the child is seen to rise from the floor by placing his hands on his knees and virtually “walking” his hands up his thighs (Gowers’ sign). By age three or four waddling, lordotic gait is noted, and the child complains of difficulty climbing stairs and rising from a seated position. As the strength of the normal child increases, so the strength of some Duchenne patients may appear to increase up to the age of ten, only to decline later. With time, progressive disability ensues so that in most cases by the end of the first decade, there is generalized muscle weakness and wasting (with sparing of the bulbar structures) and a wheelchair is required. Once the wheelchair is used, kyphoscoliosis and fixed joint contractures are likely to occur. Obesity, impaired circulation to the lower extremities with dependent edema, and mental and emotional problems are further complications of a wheelchair existence. Recurrent pulmonary infections secondary to mechanically impaired ventilatory effort are common at this stage. By the end of the second decade, the majority of patients have succumbed to pneumonia and/or cardiac disease.

Muscle pseudohypertrophy is seen in 85 to 90 percent of cases. This varies from minor degrees of muscle enlargement to gross hypertrophy. When present, it is most commonly seen in the calves, but it may involve the quadriceps muscle and shoulder and hip girdle musculature as well.

Many of the affected boys are mentally dull and almost 30 percent have IQs under 75 (Poser et al, 1969). This mental subnormality is present from birth and is nonprogressive.

Although the heart at autopsy frequently shows extensive damage, symptoms of congestive heart failure are surprisingly uncommon in Duchenne’s dystrophy. Electrocardiographic evidence of myocardial dysfunction is noted at an early stage, and includes tall R waves in the right precordial leads (V1 and V2) and deep Q waves in the left precordial leads (V5 and V6). Lethal arrhythmias may occur. Echocardiography frequently reveals contraction abnormalities in the left ventricular wall (Goldberg et al, 1982).

Laboratory Studies

While cases of DMD can frequently be recognized on the basis of the patient’s history and clinical signs, further laboratory evaluation is mandatory to confirm the diagnosis. Other neuromuscular disorders may be confused with DMD, and