Early Observations on Duchenne-Meryon Muscular Dystrophy

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Duchenne muscular dystrophy is an X-linked recessive, progressive muscle-wasting disease affecting all world populations equally, with an incidence of about 1 in every 5,000 live male births.

Duchenne made use of his invention, the ‘harpoon’ that he employed to perform percutaneous muscle biopsies; not surprisingly, this aroused hostile criticism of its ethical propriety, in the local press. The discovery of pseudohypertrophic paralysis, or mysclerotic paralysis in 1868 [1], was however, a remarkable and important contribution [2], dependent on and illustrated by pictures of histology obtained by harpoon biopsy.

In 1858, he studied the case of a 9-year-old boy who could not walk because of muscle wasting. He had suspected the existence of this disease from the concurrence of the characteristic symptoms, and in the second edition of *De l'Electrisation localisée* [3] he published his first description, and proposed the name ‘hypertrophic paraplegia of infancy’.

His first case crystallised the essential features:

‘Paralysie pseudo-hypertrophique; début dans la première enfance, par la faiblesse des membres inférieurs; grossissement considérable, à l’âge de 7 ans, des muscles moteurs des membres inférieurs et des extenseurs de la colonne vertébro-lombaire; généralisation progressive de la paralysie et abolition complète de tous les mouvements, à 13 ans et demi; intelligence obtuse; mort phthisique, à 15 ans’.

He described the male predominance, progressive course, waddling gait, pseudo-hypertrophy of calf mus-

Fig. 1. Edward Meryon.

cles, loss of ambulation by adolescence, and early death. His harpoon muscle biopsies established the loss of muscle fibre striation, hyperplasia of fibrous connective tissue with replacement by granular matter and fat vesicles, and fascicular atrophy of the muscles and destruction of the muscle as essential features. Duchenne wrote [4]:

‘This disease is mainly characterised: (1) By feebleness of movement, usually situated at first in the muscles

of the lower extremities and of the lumbar spine, ultimately spreading progressively to the upper limbs, and increasing in intensity till all movement is lost; (2) by increase in size of most of the paretic muscles; (3) by increase of the interstitial connective tissue of the paretic muscles, and in the more advanced stages by an abundant production of fibrous tissue or of fatty globules.

The name I have given to this disease pseudo-hypertrophic muscular paralysis ... has reference to the symptoms ... It may be called myosclerotic paralysis, a name which is more scientific and justified by pathological anatomy. But the significance of the fatty infiltration was uncertain'.

Griesinger described muscular dystrophy with pseudo-hypertrophy, elaborating the histology in 1865 [5]; hence, the common eponym 'Duchenne-Griesinger disease'. This contribution Duchenne acknowledged, and used the term 'myosclerotic paralysis' based on hyperplasia, and 'pseudo-hypertrophic paralysis' based on the symptoms that he explicated in a long, illustrated account of the disorder [4]. From 1861 to 1866, 15 cases of 'pseudo-hypertrophic paralysis' had been published. In 1868 Duchenne mistakenly claimed that Meryon had confused his cases with progressive muscular atrophy [6], an error corrected by Meryon [7] himself and by Gowers.

Edward Meryon (1807–1880, fig. 1) presented a paper to the Royal Medico-Chirurgical Society on 9 December 1851, which described two typical 'Duchenne' families and one with what we might now call Becker type dystrophy [8]. He recognised them as primary diseases of muscle [9] and in another important paper showed post-mortem the typical 'granular degeneration' [10]. He showed that the disease was familial and only affected boys; importantly, he showed at autopsy that the cord was normal. His histological examinations indicated that the sarcolemma was broken down and destroyed, a point now known to be fundamental in pathogenesis:

'The striped elementary primitive fibers were completely destroyed. The sarcous element being diffused, and in many places, converted into oil globules and granular matter, whilst the sarcolemma or tunic of the elementary fibre was broken down and destroyed'.

Gowers [11] proposed the hereditary basis described in his 1886 text:

'The disease is thus transmitted by women who are not themselves its subjects, thus the congenital tendency is exclusively due to the maternal element in the embryo. This is also shown by another fact, that the chil-

dren of the same women, by different husbands, have been affected'.

According to Gowers, Charles Bell had written the first clinical description of Duchenne dystrophy in his text, *The Nervous System of the Human Body* (1830).

Meryon was of Huguenot stock. He studied medicine at University College, London, [12] and in Paris. He obtained the London MD degree in 1844. His chief appointments were as physician to the National Hospital for Nervous Diseases and lecturer in comparative anatomy at St Thomas's Hospital. 'A man of wide learning, as well as an accomplished and single-minded physician' [13], he published one volume of a history of medicine (1861), *Practical and Pathological Researches on the various forms of paralysis* (1864) and a work *On the Functions of the Sympathetic System of Nerves* (1872). In a communication to the Royal Medical and Chirurgical Society in December 1851, which was published in the Transactions of the Society the following year, he described in detail eight boys in three families with a disease later to be associated with the name of Duchenne. He was particularly impressed by the exclusive affection of males and its familial nature. It is often said that he was the first physician to make a systematic study of the disorder before Duchenne [14, 15]. However, the historical roots lie in the 19th century papers of Conte, Bell, Partridge, and Meryon through the classic monographs by Duchenne and Gowers [16].

Moreover, in 1982 Dubowitz [17] suggested that two brothers, described by Coste and Gioja in 1838 and recorded by Karl Christian Schmidt (1792–1855) in his *Jahrbücher der in- und ausländischen gesammten Medicin* (1839), were the first reported cases.

The term 'pseudo-hypertrophic dystrophy' was firmly established by 1879 when Gowers gave a series of lectures to the students of University College Hospital, describing 21 personal cases and reviewing 139 from the literature.

Peter Emil Becker and Franz Kiener [8] examined five affected family members with late onset and more benign course; six of the kindred had reproduced. Because Duchenne patients do not reproduce they asserted an independent syndrome¹. Precisely one century after Gowers' observations, Kunkel identified the DMD gene [18] on

¹ Namely 'Becker muscular dystrophy'. Reported characteristics: progressive symmetrical muscle weakness and atrophy, proximal to distal, often with calf hypertrophy; weakness of quadriceps may be the only sign. Wheelchair dependency, if present, after 16 years of age. Preservation of neck flexor muscle strength in Becker muscular dystrophy differentiates it from Duchenne muscular dystrophy.

the X chromosome Xp21.2, 12q21, which encodes the protein dystrophin.

Dystrophin-associated muscular dystrophies range from the severe Duchenne muscular dystrophy to the milder Becker muscular dystrophy. Both result from mutations in the huge dystrophin gene. Dystrophin links the

actin filament of the contractile apparatus to a complex series of linking proteins in the cell membrane, and hence to the extracellular matrix. Defects in the dystrophin-associated glycoprotein complex underlie other forms of muscular dystrophy.

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