Dermatomyositis: Ultrastructure of Abnormal Mitochondria in the Skeletal Muscle *

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ABSTRACT

The mitochondrial anomalies observed in the skeletal muscle of a patient with dermatomyositis included paracrystalline inclusions, dense bodies and stacks of lamellae. Virions were not found. These anomalies are similar to those noted in other myopathies.

Introduction

Ultrastructural alterations of muscle mitochondria have been observed in several forms of myopathy, polymyositis and in animal experiments which induced degeneration and regeneration of myofibers. Luft and associates described the occurrence of altered mitochondria containing densely packed crystals in a severely hypermetabolic euthyroid patient. Shy et al demonstrated enlarged and numerous mitochondria referred to as “megaconial” and “pleoconial”, respectively, in two cases of clinical myopathies. In a review of muscular dystrophy, Price stated that in certain forms of myopathy the mitochondrial aberrations seem to be unique. He suggested that such derangement may represent the primary defect in these disorders which he referred to as “mitochondrial myopathies.”

This communication presents an ultrastructural study of mitochondrial abnormalities in skeletal muscle from a patient with dermatomyositis. Some anomalies resemble those reported previously as occurring in individuals with various other clinical disorders. Other mitochondrial aberrations here described have not been reported before.

Case History

This 54 year old white male presented to the hospital with a chief complaint of weakness, weight loss, chest pain and violaceous skin rash of six months’ duration. Contributing laboratory data included a sustained elevation of serum creatinine phosphokinase. Muscle and skin biopsies from the region of the left deltoid revealed pathologic changes which substantiated the clinical diagnosis of dermatomyositis (figs. 1 & 2). A portion of muscle was submitted for electron microscopic examination, the results of which are discussed in the body of this paper. One week after this biopsy, the patient experienced progressive dysphagia. Radiologic examinations showed irregular filling in the lower half of the esophagus. The endoscopy and biopsy of esophagus revealed an adenocarcinoma of the gas-
troesophageal junction. The patient's general poor condition precluded operative treatment of the malignancy. One day prior to initiation of radiation therapy for the esophageal lesion the patient experienced sudden onset of dyspnea and hypotension. Despite the resuscitative efforts, the patient expired. The autopsy findings confirmed the diagnosis of esophageal carcinoma which had metastasized to the adrenal glands, vertebral bodies and to the cerebrum. The immediate cause of death was numerous thromboemboli in the branches of the right pulmonary artery. The thromboemboli originated from thrombosed veins of the legs.

Materials and Methods

Small pieces of muscle tissue were fixed in a 4 percent phosphate buffered glutaraldehyde for two hours, then postfixed in 1 percent phosphate buffered osmium tetroxide for one hour. After dehydration, tissues were embedded in Epon 812. Sections were stained with uranyl acetate and lead citrate.

Results

Alterations of the fine structure of mitochondria were observed mostly at the intermyofibrillar and subsarcolemmal spaces, especially in the latter area. Changes of mitochondrial structure will be considered in terms of paracrystalline inclusions, dense spherical bodies and degenerative.

Paracrystalline Inclusions

Some mitochondria contained stacks of delicate parallel lamellae replacing the whole matrix (figure 4). Elsewhere mitochondria contained rectangular in-
Figure 3. Subsarcolemmal accumulation of mitochondria with paracrystalline inclusion: two or three groups of four lamellae, each one enveloped in the membranes of cristae (→), vacuoles in mitochondria (V), and dense spherical bodies (D). × 36,000 Insert: Two rectangular inclusions with four lamella in the mitochondria (→). Dense spherical bodies (D). × 37,500.
Inclusions made of groups of four parallel lamellae. Each lamella measured about 75 Å in thickness. These inclusion bodies were bound by the membranes of mitochondrial cristae. In some cases, more than one of these inclusions were surrounded by the membranes of the mitochondrial cristae (figure 3 and inset). The number of inclusions in one mitochondrion varied between two and ten (figure 4). The lamellae exhibited focally a curvilinear appearance in addition to complicated micro-hobnailed surfaces which interdigitate with each other. The variegated appearance of the paracrystalline inclusions may be due to differences of angle of section through the lamellae.

**Dense Spherical Bodies**

Dense spherical bodies measuring from 0.1 μm to 0.3 μm were found in a few of the mitochondria (figures 3 and 4). They were not bound by limiting membrane. These bodies were possibly the precursors of the paracrystalline inclusions.

**Degenerative Changes**

In some muscle fibers, homogenous osmiophilic substances and degenerated...
condensed form of mitochondria filled the subsarcolemmal spaces (figure 4, inset). Interruption of mitochondrial membranes were common in these degenerated mitochondria.

In the same specimen, accumulation of glycogen granules at the subsarcolemmal and intermyofibrillar spaces were observed in certain muscle fibers (figure 4). Careful scrutiny of sarcolemmal nuclei, sarcoplasm and interstitium did not reveal microtubular filaments or spindle-shaped crystalline arrays. A diligent search was made for the two last structures because Chou observed them in patients with polymyositis and postulated a viral pathogenesis for this illness.2

Discussion

In this report the ultrastructural anomalies of muscle mitochondria of a patient with dermatomyositis are documented and compared to other mitochondrial anomalies reported primarily in journals dedicated to the neurosciences. Mitochondria in normal skeletal muscle fibers are located either in the subsarcolemmal or in the intermyofibrillar space along the I-bands of the sarcomeres. It has been noted that type I muscle fibers have more mitochondria per square micrometer than the type II fibers.15 In our patient, the increased concentration and enlargement of the mitochondria are obvious in the illustration and cannot be attributed to just a normal structural difference of the muscle fibers. The simplest explanation for the abnormal concentration of mitochondria is that the loss of myofibrils was not accompanied by a loss of these organelles. Tandler and Hippel19 have annotated the conditions in which abnormal number and shapes of mitochondria in various tissues occur. In any event, the mechanism of this remarkable mitochondrial alteration eludes us.

Another feature to be mentioned is the association of gastrointestinal carcinoma with dermatomyositis which has been noted to occur in about one-third of all cases.7 The question of whether or not these two diseases are related has been the subject of various publications and reviewed recently.1

A topical negative finding in our study was the absence of so-called viral particles in the sarcoplasm and sarcolemmal nuclei. Some investigators have reported cytoplasmic and nuclear anomalies (viruses?) in the muscle of patients with inflammatory myopathies.3–10 Our negative finding should in no way imply disproof of a viral etiology.

In conclusion, the present authors emphasize the nonspecific character of the ultrastructural changes in the mitochondria of muscle occurring in a patient with dermatomyositis. Since such changes are not specific for any particular primary muscular disorder, it seems inappropriate to us to label a given form of muscular disease according to the morphology of the abnormal mitochondria.

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References