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Title : HISTOCHEMICAL CHANGES IN MALIGNANT HYPERTHERMIA SUSCEPTIBLE PATIENTS

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INTRODUCTION: Isaacs and Barlow[1] suggested in 1970 that malignant hyperthermia(MH) was always associated with a myopathic process which in most cases was subclinical. This was supported by others and Harriman[2] consolidated the association between susceptibility to MH and a variety of myopathic changes. In 1977 he presented data on the histology of muscle biopsies of 75 families, 35 of which were found by caffiene contracture to be susceptible to MH. Their conclusions were that the most common defect seen were internally situated nuclei. Other prominent findings were variation in fiber size fiber splitting, and TypeI(slow fiber)atrophy. Bradley[3] reported normal fiber types in one susceptible family.

METHODS: For the past three years we have gathered histological(hematoxylin-trichrome) and histochemical(Ca-Mg ATPase and NADH-NBT reductase) data on 51 patients suspected of being susceptible to MH. These patients are from a wide geographical area and represent not a concentration of family members but a number of individuals from various families throughout the U.S.A. Of 51 patients 9 are from family groups. 42 patients had either clinically diagnosed MH or were suspected family members of such a patient. Thin cryostat sections,8um thick,were cut serially from frozen biopsy samples and placed on a coverslip. Some samples were incubated for ATPase, others for oxidative enzymes. For distribution of Type I fibers, sections were preincubated at pH 4.3 and the reaction carried out at pH 9.4. Subtyping of Type II,fast twich, fibers was done by incubating the sections in a solution containing 10mM $CaCl_2$,5mM $MgCl_2$,1mM ATP,17% ethanol and 20mM Barbital,pH9.4. Oxidative enzymes were demonstrated by incubating sections with NADH-NBT reductase,pH 7.5.[4] Susceptibility to MH was determined by a reduction in sarcoplasmic reticulum Ca^{2+} uptake of 20% or more than normal from one of these sections.

RESULTS:

Defect in Fibers	Number of Patients
Type IIB Atrophy	26
Type I Atrophy	11
Type IIB Defiency	3
Type I Predominance	15
Normal Histochemistry	11

15 of 40 patients with abnormal fiber types also showed internal nuclei and/or "moth eaten" fibers. Where myopathy was present,family members showed similar abnormalities. Two family members shown not to be susceptible to MH by having normal Ca^{2+} uptake had normal fiber typing while their susceptible family members showed the presence of a myopathy.

DISCUSSION: Glycolytic fast twitchfiber (Type IIB) atrophy was the predominant abnormal histochemical finding(51%). Similar to the findings of Harriman[2] 22.5% of the patients demonstrated slow(Type I)fiber atrophy. Internal nuclei and "moth eaten" fibers were seen in 37.5%. Unlike previous authors we found a 22% incidence of normal histochemistry demonstrating that myopathy is not a universal finding in MH. We found myopathic changes in all age groups(2 patients under 5 years). Proportions of each fiber type varies from one muscle to another or at different sites in a given muscle as human muscles do not have a uniform fiber distribution. Therefore the site of biopsy is very important. All of our biopsies came from approximately the same location from the vastus lateralis muscle. A sub clinical myopathy is not unique to patients susceptible to MH. It is seen in patients with malignancy,after exercise training or experimental chronic stimulation and in several genetic disorders. It is also not unusual to find Type IIB atrophy in myopathic states as it appears to be the most susceptible of all fiber types to change.[4]

CONCLUSIONS: 51 patients susceptible to MH were studied for histochemical changes they demonstrated a wide variety of myopathic changes from very abnormal to completely normal. The most common abnormality was Type IIB atrophy which is common to many other myopathic states.

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