American Journal of Surgical Techniques and Case Reports

ISSN: 2694-4901

Case Report

Muscle Biopsy Techniques for the Evaluation of Weakness, Screening for Malignant Hyperthermia, and Detection of Biochemical Disorders: Two Case Reports

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Abstract

The muscle biopsy procedure is a valuable clinical approach for obtaining muscle samples for laboratory analyses, with the selection of the appropriate techniques depending on the indication for the biopsy. We describe three techniques tailored to specific analytical needs. Consideration must be given to both biopsy acquisition and specimen handling to ultimately ensure sample viability and analysis accuracy. Significant differences in the surgical technique are compared with evaluating weakness, potential malignant hyperthermia, or biochemical disorders.

Keywords: Muscle biopsy; Vastus lateralis; Malignant hyperthermia; Dermatomyositis; Case report

Abbreviations

MH: Malignant Hyperthermia; DMS: Dermatomyositis; MW: Muscle Weakness; EMG: Elecromyography

Introduction

This report outlines surgical techniques for muscle biopsies used to diagnose weakness compared with those for muscle biopsies for evaluating susceptibility to malignant hyperthermia. Biopsies for a diagnosis of weakness require an atraumatic surgical approach to obtain a small sample, while those for contraction studies need larger segments for the isolation of viable muscle fascicles. Various symptoms and findings necessitate histologic and chemical muscle tissue analyses. Although treatable diagnoses primarily include inflammatory myositis, correct identification of muscle disorders remains crucial. Despite improved survival with $ETCO_2$ monitoring and dantrolene therapy, Malignant Hyperthermia (MH) mortality remains high [1,2]. The caffeine halothane contracture assay diagnoses MH susceptibility in patients lacking a genetic marker, necessitating high-quality muscle samples for the *in vitro* contracture testing. In this study, we present two cases where patients underwent vastus lateralis muscle biopsies: one for assessing Muscle Weakness (MW) and the other to test for MH susceptibility. We also outline the minimally invasive percutaneous muscle biopsy technique applicable for patients needing analyses of muscular microanatomy, biochemical, and genetic factors. We highlight the distinctions among these three surgical approaches.

Citation: Palzer B, Jadhav A, Ikramuddin S, Manousakis G, Chompoopong P, Karachunski P, et al. Muscle Biopsy Techniques for the Evaluation of Weakness, Screening for Malignant Hyperthermia, and Detection of Biochemical Disorders: Two Case Reports. Am J Surg Tech Case Rep. 2024;4(1):1028.

Publisher Name: Medtext Publications LLC

Manuscript compiled: Jun 03rd, 2024

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Material and Methods

Retrospective case reviews were performed. Both patients provided written consent for publication. The 2020 SCARE guidelines were followed for the publication of case reports [3].

Case 1 - Evaluation for muscle weakness

A 22-year-old woman presented with progressive, symmetric muscle weakness over 2 months, accompanied by bilateral proximal upper extremity edema, jaw pain, and reduced mandibular range of motion. Physical examination revealed symmetric muscle weakness (4/5) in deltoid, biceps, and quadricep muscles, with weakened bilateral hand grip. Additionally, bilateral hypopigmented patches were observed over the extensor surfaces of her fingers. To evaluate for malignancy, computed tomography of the chest, abdomen, and pelvis was obtained which indicated no abnormalities. Magnetic resonance imaging of the lower extremities revealed diffuse intramuscular edema and enhancement in pelvic girdle and lower extremity muscles bilaterally. IgG anti-nuclear antibody was positive at 1:1,280 (titer reference range<1:40), along with positive anti-SSA and anti-RNP

antibodies. The antibody panel for polymyositis and dermatomyositis was positive for Nuclear Matrix Protein 2 (NXP-2) antibody. High-dose steroid and broad-spectrum antibiotic administration resulted in only minimal improvement in the patient's weakness and associated symptoms. A suspected diagnosis of dermatomyositis was made, but because of her atypical presentation, which included the absence of a rash, a vastus lateralis muscle biopsy was performed.

Bedside ultrasound was used in the operating room to locate an optimal incision site directly over the left vastus lateralis muscle. Ultrasound prior to biopsy is useful in avoiding fat tissue, and for identifying any focal lesions present to further increase diagnostic yield of the biopsy. After the site was selected, instillation of 1% lidocaine was confined to the skin level. A longitudinal incision was made to access the muscular fascia, which was then incised to reveal the muscle fibers that were delicately mobilized. Silk ties were employed to isolate and retract the proximal and distal muscle fibers (Figure 1A). A muscle biopsy sample measuring 2 cm × 1 cm × 1 cm was collected using a #11 blade. Two muscle biopsy segments were placed on a sterile wooden tongue depressor (Figure 1B) for standard fixation. A smaller portion was stretched over a wooden tongue depressor using 5-0 Prolene sutures to avoid contraction after submersion in glutaraldehyde fixative for electron microscopy. All muscle biopsy material was submitted to the neuromuscular laboratory. Hemostasis was attained with electrocautery, and a 50:50 mixture of 1% lidocaine and 0.25% Marcaine was instilled above and below the fascia only after the muscle biopsy was obtained. Subsequently, the fascia and skin were reapproximated using 3-0 Vicryl, 4-0 Monocryl suture, and skin sealant. Histologic examination revealed perifascicular atrophy, muscle fiber degeneration with vacuolar changes, and fibrosis (Figure 2A). These findings were consistent with a diagnosis of dermatomyositis. Following a course of Methotrexate and Plaquenil, the patient regained full muscle strength. Clinical evaluation confirmed that the patient's disease remained well-controlled 3 years post-operation with routine follow-up with rheumatology and daily immunosuppression.

Case 2 - screening for malignant hyperthermia susceptibility

A 17-year-old woman with a family history of Malignant Hyperthermia (MH) presented for clinical exclusion of MH susceptibility due to her intention to enter military service. Genetic markers were not identified in her family. A left vastus lateralis muscle biopsy was performed to conduct contraction studies and evaluate for MH susceptibility. Ansthesia equipment was cleaned and prepared using an ansthesia protocol for MH- susceptible patients.

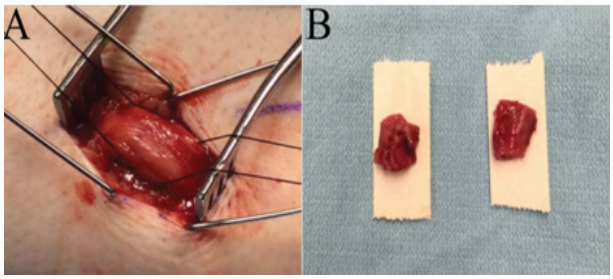

Figure 1: A) Vastus lateralis muscle fibers mobilized and retracted with 0 silk ties before removal using a #11 blade. B) Muscle biopsy samples on a sterile tongue depressor;smaller samples approximately 1/5 the size are stretched over wooden tongue depressors with 5-0 Prolene to prevent contraction when fixed in glutaraldehyde for electron microscopy.

Succinylcholine was blocked off in the Pyxis MedStation, and sedation was induced using propofol. Instillation of 1% lidocaine was limited to the skin level. Bedside ultrasound optimized the placement of a longitudinal incision over the left vastus lateralis muscle, providing access to the muscular fascia, which was incised to reveal normal-appearing muscle fibers. Zero silk ties were used to isolate and retract the proximal and distal muscle fibers. A muscle biopsy sample measuring 5 cm × 2 cm × 2 cm was collected using a #11 blade. The biopsy specimen was divided: the larger portion promptely immersed in krebs solution sourced from the MH Muscle Diagnostic Laboratory, which had pre-alerted prior to the biopsy procedure and the smaller portion (1 cm × 1 cm × 1 cm) was sent to pathology for histologic examination. Members of the MH Diagnostic Laboratory confirmed the specimen's viability and adequacy to the operating room. Hemostasis was attained by electrocautery, followed by infiltration of a 50:50 mixture of 1% lidocaine and 0.25% Marcaine into the site. Closure involved approximating the fascia and skin using 3-0 Vicryl, 4-0 Monocryl, and skin sealant. Histological assessment revealed increased variation in fiber size as a nonspecific finding (Figure 2B), with otherwise normal results. A caffeine halothane contracture assay, employing 3% halothane and escalating caffeine concentrations was performed [4]. Contraction studies yielded normal results, ruling out MH susceptibility with a sensitivity of 97% and specificity of 78% [5]. Subsequently, the patient successfully enlisted in military service.

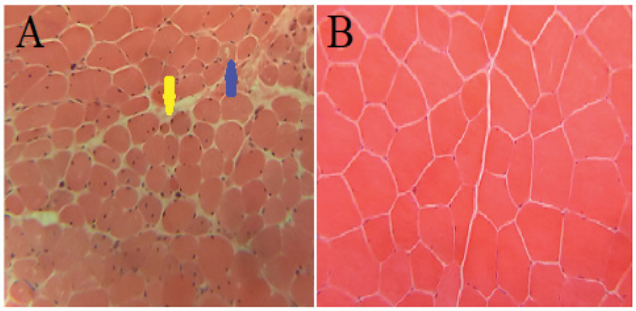

Figure 2: A) Case 1 - Perifascicular atrophy and fibrosis (yellow arrow), muscle fiber degeneration with vacuolar changes (blue arrow). B) Case 2 - Mild fiber size variation.

Percutaneous muscle biopsy-evaluation for biochemical and genetic analysis

Percutaneous muscle biopsy [6] is suitable for biochemical and micro-anatomic analyses, although the potential for sampling errors is significantly increased due to the small sample sizes obtained. To perform the procedure, the patient is placed supine, and the biopsy site is prepared and draped in a sterile manner. The underlying muscle is identified using handheld sterile ultrasound, and the biopsy site is marked. The site is then infiltrated with 1% lidocaine and 0.25% marcaine. A skin incision is made down to the fascia over the muscle using a #11 blade. A suction catheter biopsy needle is connected to suction tubing using a three-way stopcock. The percutaneous muscle biopsy device (Bergstrom Muscle Biopsy Needle, Millennium Surgical, Bala Cynwyd, PA) includes the biopsy needle and an inner cannula. The biopsy needle has a lateral window that allows intrusion of muscle fibers when suction is applied. After suction has been applied, the sharp inner cannula is used to obtain small muscle biopsy fragments (Figure 3). Multiple passes are made to obtain muscle tissue, usually yielding an aggregate sample of 250 mg. The muscle biopsy samples should be either immediately placed on moistened gauze for analysis or flash-

frozen with liquid nitrogen for future analysis. Direct firm pressure is applied to the patient's biopsy site for 20 minutes. An additional local anesthetic agent can be instilled into the soft tissues surrounding the muscle biopsy site following the procedure. Steristrips are applied over the muscle biopsy site to reapproximate the skin at the incision, followed by the application of a folded 2 cm × 2 cm gauze pressure dressing.

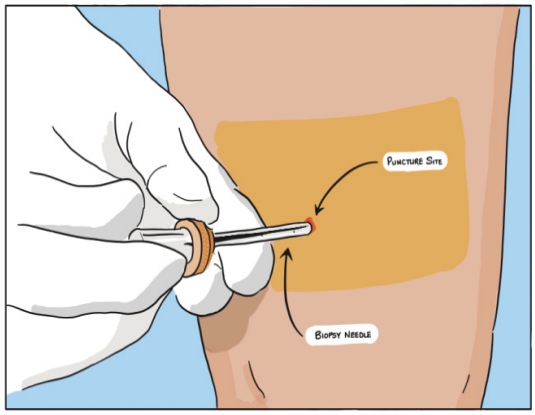

Figure 3: Percutaneous muscle biopsy device being used to obtain a biopsy of the left vastus lateralis muscle at bedside.

Discussion

Muscle biopsies can be clinically valuable to provide insights for patients experiencing muscle weakness, susceptibility to malignant hyperthermia, or the detection of biochemical or genetic disorders. While the vastus lateralis muscle is commonly utilized for biopsies, our team has performed biopsies on various other muscles, including those in the neck, deltoid, biceps, triceps, and leg. In all cases, a coordinated plan for delivering muscle samples to appropriate laboratories is essential before surgery. For patients undergoing analyses for malignant hyperthermia, careful anesthesia management in the operating room is crucial, following guidelines available on the Malignant Hyperthermia Association of the United States website (https://www.mhaus.org/). Before prepping and draping, a handheld bedside ultrasound can aid in locating the skin incision site overlying the desired muscle biopsy area. Ensuring adequate specimens and careful specimen handling are critical for quality evaluations. Preserving specimens for electron microscopy requires fixation with glutaraldehyde and securing muscle fibers over a sterile wooden tongue depressor fragment can prevent contractures during fixation. Avoiding local anesthetic and electrocautery prior to sample collection minimizes artifacts for these laboratory analyses. Understanding the significance of muscle biopsies is essential for assessing various muscle-related conditions. This extends to selecting appropriate candidates based on clinical presentation, imaging, and Electromyography (EMG) findings. EMG testing may cause artifacts such as changes in muscle texture and contraction. It is best to avoid obtaining muscle biopsies from sites where EMG testing has been performed.

Indication for biopsy

Muscle biopsies are indicated when other clinical and/or imaging studies fail to establish conclusive causes for presenting muscle weakness or when genetic markers for malignant hyperthermia are absent. Familiarity with indications, surgical techniques, and pathologic evaluations should be known in both academic and certain neurological institutions. Patient consultation and informed consent should cover the diagnostic likelihoods, possible complications, and the choice of the surgical approach tailored to individual clinical presentations.

Types of muscle biopsy

Several surgical techniques have been utilized to obtain muscle samples for various clinical analyses, including percutaneous needle biopsy, closed muscle biopsy techniques, and open biopsy; each with specific benefits, advantages and disadvantages. Minimally invasive techniques such as needle biopsy or closed biopsy offer the advantage for in clinic-based procedures and allow patients to resume activities with minimal postoperative pain. On the other hand, open biopsies, while more invasive, enable the retrieval of selected muscle fibers with gross abnormalities and larger samples suitable for in vitro contracture testing, biochemical study, light microscopy, as well as electron microscopy. The open muscle biopsy technique for evaluating muscle weakness or myopathies is typically conducted in an operating room under sterile conditions. Muscle fibers are identified, selected, and acquired without causing trauma through an open incision. This procedure necessitates surgical closure and postoperative monitoring. An open biopsy technique is used to obtain an adequate sample size to perform *in vitro* contracture studies and evaluate susceptibility to malignant hyperthermia. Noteworthy differences exist in surgical techniques between open muscle biopsy for analyzing muscle weakness in myopathies and those for suspected malignant hyperthermia cases [7-9]. The open biopsy for muscle weakness entails a 2 cm incision, yielding approximately 2 cm × 1 cm × 1 cm of muscle fiber bundles for microscopy and additional investigations. Alternatively, an incision up to 3 cm in length is used to obtain muscle bundle fibers suitable for *in vitro* contracture studies, with fibers being as long as 3 cm to 5 cm, and with dimensions of 1 cm in width and depth. These fibers are then sent to the contraction laboratory in a pre-oxygenated buffer for careful dissection and preparation for studying malignant hyperthermia susceptibility.

Benefits of muscle biopsy

The utility of muscle biopsy lies in diagnosing specific conditions that cannot be discerned without examining isolated muscle tissue. Certain muscle conditions have tailored treatments that can result in complete recovery. For example, accurate diagnosis is crucial for implementing year-long steroid therapy, preventing the inappropriate treatment of patients with undiagnosed conditions, and sparing those who wouldn't benefit from steroid exposure. For individuals being assessed for potential malignant hyperthermia susceptibility, ruling out this trait can be challenging. Confirming those at risk of malignant hyperthermia allows for the absolute avoidance of inhaled anesthetics during subsequent clinical procedures. Surgery and open muscle biopsy should only be undertaken when the benefits outweigh potential adverse events and consequences.

Complications

Postoperative complications linked with muscle biopsy encompass: wound infection, seroma, hematoma, and chronic pain. Wound infections are typically diagnosed through clinical examination and microbiological cultures. Treatment involves reopening the incision, irrigating with saline, applying antibacterial topicals, and allowing secondary intention wound closure with regular dressing changes. Seroma evaluation may entail handheld ultrasound, CT scans, and

clinical assessment. Fluid aspiration and bacterial culture submission are occasionally necessary. Wound seromas typically resolve without additional treatment, but aspiration can be performed. Persistent need for aspiration may warrant the use of sclerotic agents like tetracycline to resolve seromas around surgical incisions. Incision hematomas usually resolve on their own, but evacuation may be necessary in some cases. Patients experiencing chronic pain after muscle biopsy may benefit from local anesthetic instillation combined with steroid injection. Referral to a pain specialist might be necessary for some patients. Specialists may recommend additional injections or ultrasound treatments alongside oral pain medication therapy, often including gabapentin or Neurontin for chronic nerve pain post-surgery.

Conclusion

Muscle biopsy should be conducted based on clinical indications. The sample size requirements should align with the patient's issues, such as muscle weakness, susceptibility to malignant hyperthermia, and biochemical disorders. Appreciation of the precise indication for muscle biopsy facilitates tailoring surgical techniques, ensures high-quality investigation, and results in accurate diagnoses.

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