ALTERED TRABECULAR MICROARCHITECTURE IN BRACHIAL PLEXUS BIRTH PALSY: A RAT MODEL STUDY

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INTRODUCTION

Brachial plexus birth palsy (BPBP) is a peripheral nerve injury affecting about four in 1,000 births annually [1], leading to impaired function of the neonatal upper limb. The resulting denervation of muscles often causes gross morphological changes in surrounding bone structures, exacerbating limb impairment that is observed clinically [2]. Effects to bone due to altered musculoskeletal loading require an in-depth understanding of changes in bone mineralization and microstructure in developing joints, which is currently not well understood. Examining changes in bone will provide clinicians with additional information to optimize treatment plans and minimize or circumvent onset of permanent shoulder deformity.

The purpose of this study was to determine whether changes in cancellous bone mineralization and microarchitecture of the proximal humerus occur with the altered musculoskeletal loading characteristic of BPBP injuries using a rat model.

METHODS

Sixteen male Sprague-Dawley rat pups were separated into two groups (n=8 each). Group 1 (neurectomy) underwent neurectomy of the left brachial plexus upper trunk, representative of the C5 and C6 nerve root injuries most commonly observed in clinical cases of BPBP [3]. Group 2 (sham) received a sham surgery including division of the left pectoralis major with no injury to the nerve. Surgical interventions were applied five days after birth and approved by the Institutional Animal Care and Use Committee. Animals were sacrificed eight weeks post-operatively, and the left (affected) and right (control) humeri were excised and imaged using micro-computed tomography (micro-CT) (SCANCO µCT 80). One animal from each group was excluded from analyses due to specimen damage following excision.

Micro-CT scans were reconstructed at a 10-µm isotropic voxel size, and a global threshold of 441 mg/cm³ of calcium hydroxyapatite (HA) (3891 Hounsfield units, or HU) was applied. A region of interest (ROI) equal to 5% of the overall humeral length was selected in the proximal metaphysis immediately distal to the growth plate. The ROI was evaluated using the SCANCO proprietary software to assess tissue mineral density (TMD) and 3D trabecular thickness (Tb.Th), separation (Tb.Sp) and number (Tb.N), as well as trabecular connectivity and orientation. Two-tailed t-tests (α=0.05) were used to compare bone mineralization and microstructure between groups (SAS 9.4).

RESULTS AND DISCUSSION

The affected limbs in the neurectomy group experienced trabecular thinning with a tendency for reduced tissue mineral density relative to sham affected limbs (Fig. 1). Tb.Th was reduced by 12% (p=0.046) in the neurectomy group (Fig. 2).

Figure 1: Sagittal view of the proximal metaphyseal region (bottom half of the bone profile, separated from the top by the dark curvature representing the growth plate) shows reduced trabecular thickness with neurectomy (left) compared to sham (right).
Clinically, radiographic evidence of muscle atrophy in all rotator cuff muscles following BPBP injury has correlated with anterior humeral head subluxation and changes in glenoid shape [5]. Prior analyses using the same animals from our study showed postural (reduced external rotation) and osseous (glenoid declination, inferior humeral head translation) deformity of the glenohumeral joint for animals experiencing neurectomy. Deformity was significantly correlated with reduced optimal fiber length for muscles, including teres major and subscapularis, thereby simulating mechanical conditions capable of altering normal bone growth [4]. Other studies have also suggested that impairment to the longitudinal growth of muscles can induce postural constraints, causing increased passive forces of muscles crossing the glenohumeral joint [6].

In addition to gross changes in bone morphology, altered musculoskeletal loading with disuse has been associated with trabecular thinning in mice [7]. The present study suggests that altered mechanobiological effects on bone following peripheral nerve injury, compounded with the resulting changes in load transferred from paralyzed muscle to bone, may disrupt normal bone remodeling processes. We are currently examining bone cell activity in histologic sections from these humeri. Simulations of load distribution in cancellous bone have shown that changes in trabecular microarchitecture lead to reduced stiffness [8]. Likewise, changes in bone tissue mineralization represent significant alterations in cancellous bone tissue that are associated with large changes in bone elastic modulus and resistance to loading [9]. While not a direct indicator of bone strength, reduced bone mineral density has been associated with higher fracture risk clinically [10]. Currently, we are analyzing the right (control) humeri to assess trabecular differences between the unaffected (right) and affected (left) limbs in the same animal. Future computational and animal model studies are necessary to isolate the extent of changes in trabecular mineralization and microarchitecture associated with limited use of the affected limb alone and in the presence of denervated muscle. While the etiology of osseous deformity in BPBP remains unclear, understanding changes in bone microstructure resulting from injury may present a foundation for understanding the progression of deformity and offer targets for interventions and treatments.

REFERENCES


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