FEMORAL HEAD DEFORMITY IN PIGLET MODEL OF ISCHEMIC NECROSIS: RELIABILITY AND PATHOGENESIS

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Introduction: The piglet model of ischemic necrosis of the capital femoral epiphysis (CFE) was originally reported in an abstract by Salter in 1966 as an experimental model of Legg-Calve-Perthes disease. The experimental model involves placing a non-absorbable ligature tightly around the femoral neck to disrupt the blood supply to the CFE. The animal model is thought to be a clinically relevant model in that piglets have similar vascular hip anatomy as humans and that the model was used to develop the concept of surgical containment using Salter’s innominate osteotomy in Legg-Calve-Perthes disease. Although the model has been shown to produce femoral head deformity (FHD), the reliability of the model to produce ischemic necrosis and FHD has not been investigated. Such information will be invaluable when planning pre-clinical studies to determine the effectiveness of therapeutic interventions to prevent FHD. In addition, the biological processes associated with the development of FHD in the model have not been investigated. Understanding the pathogenesis of FHD in the piglet model will allow better understanding of the pathogenesis of FHD in pediatric patients following ischemic necrosis. The purpose of this experimental investigation was to determine the reliability of the piglet model to produce FHD and to define the biological processes involved with the development of FHD in the piglet model.

Methods: The experimental investigation was approved by the Local Animal Care and Use Committee. Ischemic necrosis was induced in 20 piglets (aged 4-8 weeks) by placing a non-absorbable ligature tightly around the femoral neck. Four additional animals served as sham controls. All the animals were killed at 8 weeks to determine the reliability of the model. The proximal femora were dissected out and radiographed as a whole and after being sectioned (4 mm, coronal plane). The sections were then processed for histologic assessment. Hematoxylin/eosin or safranin O/fast green stains were used on histologic sections. The degree of FHD observed on radiographs was quantified by using the epiphyseal quotient. The epiphyseal quotient was calculated by dividing the maximal bony height by the maximal bony diameter measured on the central sections of femoral head radiographs. Statistical analysis was performed using Statview Software (2-sided, unpaired t-test with p<0.05 being considered significant).

Results: None of the sham operated animals showed any evidence of ischemic necrosis. Nineteen out of 20 experimental animals showed radiographic and histologic changes consistent with ischemic necrosis. Varying degrees of FHD were observed in the 19 animals, ranging from no deformity to severe deformity. On the non-operated side, there was a relatively narrow range of epiphyseal quotient (0.39 to 0.48) with the mean of 0.43±0.03 compared to the infarcted side which had a wider range (0.18 to 0.42) with the mean of 0.31±0.07 (Figure 1). The difference was significant (p=0.0001). Interestingly, the normal epiphyseal quotients observed on the operated side (i.e. infarcted heads with no or minimal deformity) were from younger animals operated at 4 weeks of age in comparison to 6-8 weeks old.

Radiographic and histologic assessments of the 19 infarcted femoral heads revealed two common patterns of revascularization and bone resorption (Figures 2-A, B and 3-A, B). In Pattern I, an extensive revascularization and osteoclastic bone resorption were observed mainly within the secondary center of ossification. Instead of new bone formation, fibrovascular tissues invaded the areas of bone resorption. The pattern was demonstrated in seven animals with a moderate to severe femoral head flattening (mean epiphyseal quotient = 0.27±0.05) in which the physis was normal in all but one. In Pattern II, revascularization and bone resorption were observed mainly around the physis with evidence of fibrovascular tissue invading towards the secondary center of ossification. The pattern was observed in six animals which displayed less flattening of the femoral head (mean epiphyseal quotient = 0.32±0.02). The physes in these femoral heads were abnormal in all but one. A significant difference in epiphyseal quotient was observed between Pattern I and II (p=0.04).

Discussion: The piglet model reliably produced ischemic necrosis and FHD; however, the degree of FHD varied depending on the age of the animal and on the location and the extent of revascularization and bone resorption. The location of revascularization (i.e. in the physis region) had an important bearing on the involvement of the physis. Revascularization of necrotic marrow space and resorption of necrotic trabecular bone in the secondary center of ossification played an important role in the pathogenesis of FHD. Femoral heads with extensive revascularization and bone resorption within the secondary center of ossification showed greater femoral head flattening. It is important to note that, unlike normal bone remodeling, resorption of necrotic trabecular bone was not replaced by new bone but by fibrovascular tissue. Identification of factors that modulate these biological processes may lead to development of specific treatment strategies to minimize the FHD and to stimulate the repair process.