Diagnostic Exercise
From The Davis-Thompson Foundation*

Case #: 118 Month: April Year: 2019

Answer Sheet

Title: Sternal Segment Dislocation and Epicardial Fibrosis in a C57BL6 Mouse

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Figure 3. Sternal segment dislocation (SSD); 16-week-old mice; H&E. A) Normal sternum from non-affected mouse. B) SSD at the fourth intersternebral joint (arrow) is enveloped by a periosteal bridging callus.
Figure 4. Higher magnification of sternal segment dislocation. 4A) Close up of Fig. 3B. 4B) Higher magnification of yellow inset in Fig. 4A showing the dislocated joint with amorphous material and degenerative changes. 4C and 4D) Higher magnification of the callus (black inset) in Fig. 4A. Note orderly maturation of cartilage zones.

Figure 5. Epicardial and subepicardial fibrosis, right ventricle; 16-week-old mouse. A) Epicardial and subepicardial fibrosis from the base to the middle aspect of the right ventricle (boundaries outlined by arrow heads). B) Higher magnification of inset in Figure A (H&E) - A plaque of
fibrosis and fibroplasia expands the epicardium and the subepicardium. Low numbers of mainly mononuclear cells are notable at the deeper aspects of the plaque of fibrosis (arrow). Figure C (Masson’s trichrome stain) - Serial section from Figure B; collagen deposition is evident within the inner and middle aspect of the lesion. LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle.

**Figure 6.** Near mid-sagittal section of thorax from non-affected mouse. A – Macroscopic. B – Microscopic, HE. S1-5 (Sternebrae 1-5); M-manubrium. Consider some degree of tissue retraction secondary to tissue fixation (Adissu HA, unpublished).

**Figure 7.** Early degenerative changes within the fourth intersternebral joint; 16-week-old mouse; H&E. Figure 7A) Early degenerative lesion within the fourth intersternebral joint is evident by a fissure along the joint line (box). Figure 7B) Higher magnification of inset in Figure 7A; degenerative changes within the joint are characterized by cleft-like fractures and fissures (arrows), multifocal loss of matrix and chondrocytes resulting in cysts containing fibrous material (arrow heads), and clusters of proliferating chondrocytes (yellow arrow).
Morphologic Diagnoses:

1. Sternum, 4th intersternbral joint: Dislocation, segmental, with periarticular nodular fibrocartilaginous hyperplasia (fibrocartilaginous callus).

2. Heart, Right Ventricle: Epicardial fibrosis, focally extensive

Potential relationship between the sternal and cardiac lesions: The right ventricular fibrosis was likely caused by abrasion or laceration of the right ventricle by the cartilaginous callus that protruded into the thoracic cavity (see discussion for additional evidence).

Potential etiology/cause and Comparative pathology significance - See discussion.

Discussion: This case is one of the cases with concomitant sternal segment dislocation (SSD) and focally extensive right ventricular epicardial fibrosis (RVEF) in C57BL/6N mice that have undergone a high throughput phenotyping screen (from Week 4-16). Occasional cases of xyphoid protrusion were documented in this facility previously and retrospective analysis of the thoracic X-rays showed dislocation of the fourth intersternbral joint. The dislocated ends of the fourth and fifth sternebrae were often displaced into the thoracic cavity while the xiphisternum (XS) protruded ventrally (outward). Gross findings consisted of a thick fibrous adhesion between the sternum and the right ventricular pericardium, a cartilaginous callus on the inner surface of the sternum, and a focal pallor on the right ventricular epicardium (Figure 2F). On histopathology, there was sternal segment dislocation with an enveloping (bridging) intrathoracic and extrathoracic callus (Figure 3B). The intrathoracic part protruded 500 μm into the thoracic cavity while the extrathoracic part extended into the pectoral muscle. The cartilaginous callus was enveloped by fibroplasia/fibrosis and was well organized with zones of proliferation, hypertrophy, and degeneration (ruling out a neoplastic process) (Fig 4 B-D). Low numbers of mononuclear inflammatory cells were present within the fibrous envelope and overlying pleural lining. The RVEF was characterized by an up to 2000 μm wide and 50 μm to 250 μm deep plaque of fibrosis/fibroplasia on the epicardium and subepicardium of the right ventricular free wall (Figure 5A-B). Inflammation was invariably minimal and limited to small numbers of mononuclear inflammatory cells and rare neutrophils within the outer aspect of the fibrous plaque (Fig.5B). Collagen deposition was evident within the superficial aspect of the lesion whereas immature/fine collagen fibers were seen within the deeper aspect of the lesion by Masson's-trichrome staining (Fig. 5C).

This case is one of the 51 cases with SSD described in a paper published in Veterinary Pathology (1). We showed that the presence of an intrathoracic callus, the size of the callus, and displacement/misalignment of the dislocated sternal segments were highly correlated with RVEF. The underlying cause of sternal dislocation was not determined (please see Ref. 1 for a discussion on potential causes/contributing factors). Interestingly, SSD almost exclusively
occurred at the fourth intersternebral joint, suggesting an underlying predisposition of this joint for dislocation. Indeed, we found early degenerative changes in this joint in approximately 30% of the wild type C57BL/6N mice at 16 weeks of age (Figure 7).

In humans, traumatic injuries to the chest are associated with sternal fracture or sternal segment dislocation. Sternal fracture involves disruption of the cortex of the sternum and most commonly results from motor vehicle impact and less commonly from falls and direct violence. Insufficiency sternal fractures secondary to osteoporosis have also been described in elderly women. Serious complications of sternal fracture include various cardiothoracic injuries such as pulmonary contusion, myocardial contusion and laceration, and aortic injury. The right ventricle is more frequently involved since the sternal boundary of the heart consists of the free surface of the right ventricle. The cardiac lesion we described shares significant similarity to the “collagen plaques” that are commonly present over the anterior surface of the right ventricle in humans (2). These collagen plaques, also called milk spots or soldiers’ patches, represent focal epicardial fibrosis consisting of dense collagen occasionally accompanied by low numbers of underlying mononuclear cells (2). They are typically associated with right ventricular enlargement and they presumably arise from the impact of the beating heart with the subjacent surface of the sternum (2).

In contrast to sternal fracture, sternal segment dislocation (SSD) involves separation of the sternebrae at the intersternebral cartilaginous joint/junction. Similar causes as those of sternal fractures are implicated in SSD. It is an extremely rare pathology in humans and mostly reported in children. The sternum is less susceptible to fracture in children since the sternum and associated structures are more elastic and the ribs are more flexible than in adults. Further, the sternebrae in early childhood are joined by primary cartilaginous joints (synchondrosis) while they are fused by synostosis in adulthood. Unlike humans, the sternebrae in rats and mice do not fuse and remain separated by intersternebral cartilaginous joints/junctions. Sternal fracture or dislocation had not been reported previously in laboratory rodents. Reported sternal lesions had been limited to degenerative disease of the intersternebral cartilaginous joints in aging rats and mice (3, 4).

References and Recommended literature:


*The Diagnostic Exercises are an initiative of the Latin Comparative Pathology Group (LCPG), the Latin American subdivision of The Davis-Thompson Foundation. These exercises are contributed by members and non-members from any country of residence. Consider submitting an exercise! A final document containing this material with answers and a brief discussion will be posted on the CL Davis website (http://www.cldavis.org/diagnostic_exercises.html).

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