Journal of Avian Medicine and Surgery 39(4):222–228, 2025

Clinical Brief

Delayed Clinical Onset of Congenital Heart Disease in a Geriatric Macaw (*Ara ararauna*)

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Abstract: An approximately 33-year-old male blue and gold macaw (*Ara ararauna*) was presented for postmortem examination after dying without premonitory signs at the owner's home. The bird had a recent history of a grade II/VI left-sided systolic murmur, feather-destructive behavior, was overweight, and had bilateral cataracts. Gross and microscopic postmortem examinations revealed a subaortic interventricular septal saccular defect most compatible with a diverticulum intimately associated with a multifocally fibrotic right coronary aortic semilunar cusp, and its distended sinus. The resulting congestive heart disease was morphologically characterized by concentric myocardial hypertrophy of the left ventricle and cardiogenic pulmonary edema. Reports of cardiac congenital disease in birds include ventricular septal defects, congenital aneurysm, persistent truncus arteriosus, aortic hypoplasia, duplicitas cordis, multiplicatis cordis, and ectopia cordis. To the best of the authors' knowledge, this is the first documentation of a subaortic interventricular septal saccular defect in an avian species. This case adds to the knowledge of cardiovascular disease and raises awareness of delayed-onset clinical disease linked with congenital heart anomalies in birds.

Key words: heart, congenital heart disease, subaortic interventricular septal saccular defect cardiac diverticulum, psittacine, *Ara ararauna*, avian

CLINICAL REPORT

A 1.22 kg, 33-year-old, male blue and gold macaw (*Ara ararauna*) was presented after dying acutely without premonitory signs in the owner's home. The bird had lived with this owner since it was a juvenile. The macaw's diet consisted of a commercial pelleted diet for parrots (Harrison's Bird Foods, Brentwood, TN, USA), fresh fruits and vegetables, and small amounts of grains and nuts. The bird was examined annually throughout its life, and no heart murmurs or arrhythmias had been noted until the exam 10 months before death. During that exam, the bird was found to be over-conditioned with a body condition score of 8 out of 9.

Additionally, a grade II/VI left-sided systolic heart murmur was auscultated using an infant stethoscope (Littmann Classic II Infant Stethoscope, Saint Paul, MN, USA); no arrhythmia was identified during auscultation. A cardiac workup, starting with sedated radiographs and possibly including echocardiography and an electrocardiogram, was offered to the owner at this visit, but was declined. The patient also had a clinical history of chronic feather-damaging behavior, obesity, and bilateral cataracts. Annual diagnostics consisting of a complete blood count, biochemistry panel, bile acids, and protein electrophoresis performed at the final visit were relatively unremarkable (Avian and Exotic Animal Clin Path Labs, Wilmington, OH, USA); values outside the reference intervals included a mildly elevated uric acid (12.8 mg/dL; reference interval 2.5–9.5 mg/dL) and mildly elevated triglycerides (232 mg/dL; reference interval 25–170 mg/dL). After the bird's death, it was presented to the veterinary clinic for pathologic examination; remains were sent to the Texas Veterinary Medical Diagnostic Laboratory (College Station, TX, USA) for postmortem examination and histopathology.

On postmortem examination, the carcass was considered in good postmortem condition but obese. The main gross findings were confined to the cardiovascular system. The left ventricle was enlarged, and its walls were thickened (free wall: 5-mm thick)

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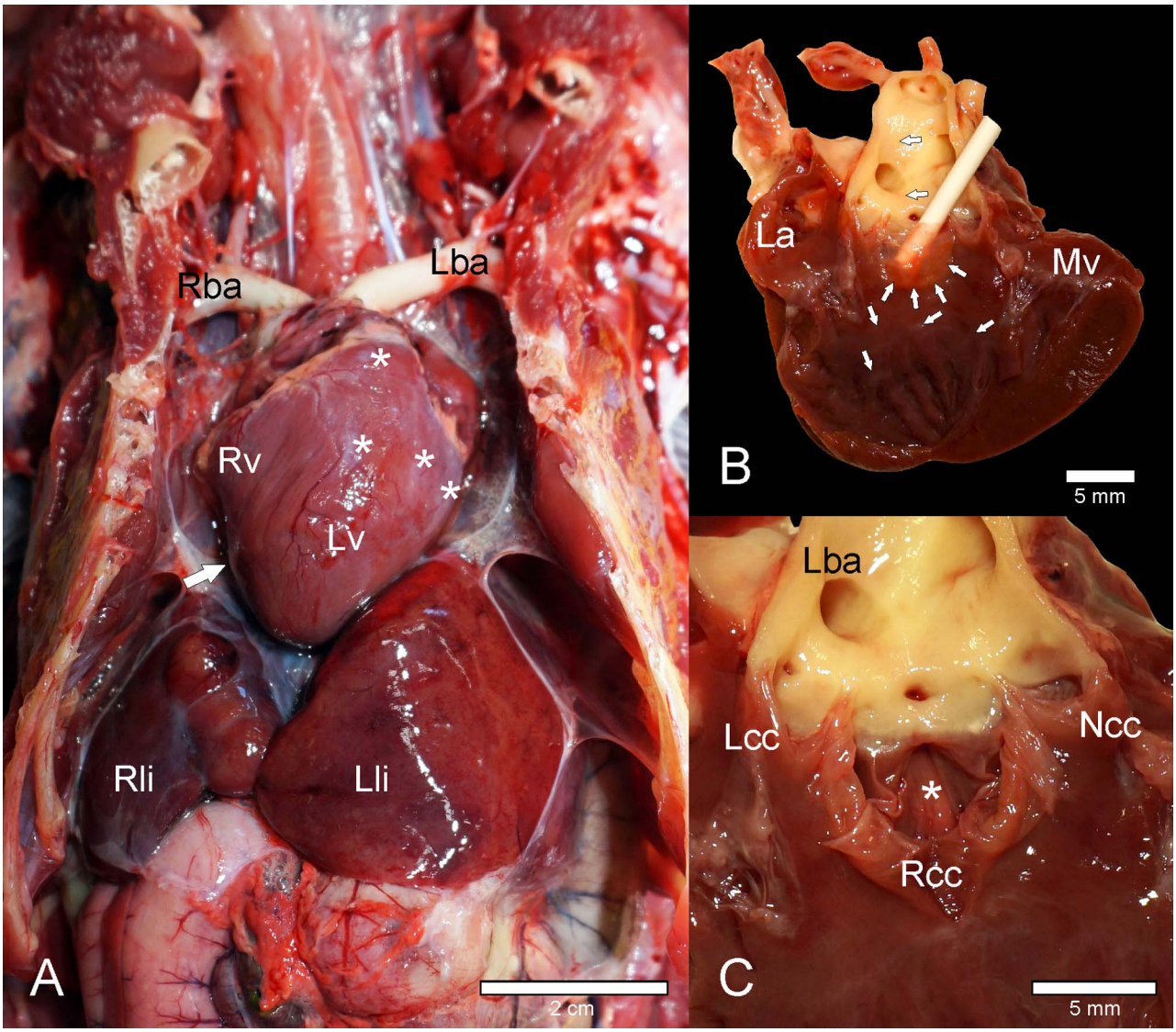

Figure 1. Macroscopic features of subaortic interventricular septal diverticulum in a blue and gold macaw (*Ara ararauna*). (A) The heart is enlarged with an elongated appearance, primarily in the left ventricle. Note the slightly raised demarcation between the right free wall and the interventricular septum (arrow). Multiple fibrotic patches are noted along the epicardium (asterisks). The left brachiocephalic artery is diffusely distended. Bar = 2 cm. (B) The right coronary aortic semilunar valve is distended, and a probe underscores the ventral extension of a distal saccular cavity (diverticulum). Fibroelastosis is noted as pale brown, rough patches or irregular streaks in the cusp of the right coronary cusp and the adjacent aortic outflow and endocardium (arrows). Bar = 5 mm. (C) The cranial wall of the defect (*), including the right coronary semilunar aortic cusp, has been dissected to expose the lumen of the subaortic interventricular septal diverticulum. Note the multiloculation of the saccular defect. Bar = 5 mm. Rba, right brachiocephalic artery; La, left atrium; Lba, left brachiocephalic artery; Lcc, left coronary cusp; Lli, left liver; Lv, left ventricle; Mv, mitral valve; Ncc, non-coronary cusp; Rcc; right coronary cusp; Rli, right liver; Rv, right ventricle.

(Fig 1A). The aortic outflow and the proximal aorta were mildly dilated. The right coronary aortic semilunar valve was distended (up to 3 times the size of the adjacent semilunar valves) and had multiple patches of fibroelastosis, primarily along the right ventral aspect, representing up to 75% of the inner luminal aspect (Fig 1B). Between the cusp of the right coronary semilunar aortic valve and the interventricular septum, there was a 6 × 6 × 5-mm multiloculated saccular cavity (diverticulum) that projected towards the right ventricle but did not communicate with its lumen (Fig 1C). There were scattered pale white foci in the endocardium (fibrosis) along the left ventricle, and a 1 mm in diameter, white, flat patch was present at the ventricular aortic

junction adjacent to the proximal right commissure; the intimal surface of the aorta was slightly roughened (fibroelastosis). The left auricle and atrium were mildly dilated. The left brachiocephalic artery was diffusely mildly distended. The epicardium over the right and left ventricles and atria had multifocal, irregular, white foci (fibrosis). Other relevant gross pathologic findings were marked feather loss throughout the lower neck, pectoral, middle and dorsolateral aspects of the wings, legs, and the mid and lower back; diffusely expanded, pale pink to reddened and wet lungs with scattered dark red foci along the dorsal and medial aspects; mild hepatomegaly with a nodular surface; mild to moderate crop and proventriculus distension with abundant ingesta; an enlarged left testicle; rare multisystemic petechiae; and bilateral cataracts.

Samples from the brain, spinal cord, tongue, trachea, esophagus, crop, proventriculus, ventriculus, small intestine, large intestine, cloaca, pancreas, liver, gall bladder, lungs, heart, great vessels, spleen, air sacs, thyroid gland, parathyroid gland, kidneys, testicles, adrenal glands, skeletal muscle, sciatic nerve, and bone marrow were collected and fixed in 10% neutral buffered formalin and processed for routine histopathologic assessment. Special histochemical stains (periodic acid-Schiff for mucopolysaccharides, Alcian blue for mucins, and Masson's trichrome for collagen) were used to further characterize the findings in the heart.

Microscopically, the main changes in the heart consisted of a localized subaortic interventricular septal saccular defect (SAISSD; Figs 2A and 2B). Specifically, the apical luminal (aortic outflow) surface of the defect, consisting of the right coronary cusp, had a large area with mild to moderate fibroelastosis on the right lateral aspect (noted grossly). In contrast, the remaining surface comprised an otherwise unremarkable right coronary cusp with ventricularis, spongiosa, and fibrosa layers. However, the abluminal (septal) aspect of the defect consisted of a circumferential fibrointimal band with variably preserved superficial endothelial cells and subendothelial spindle cells (fibroblasts/fibrocytes) with occasional interspersed cardiomyocytes that merged with collagen fibers and the underlying mural cardiomyocytes. Intimately associated with the septal defect, the adjacent myocardium exhibited localized cardiomyocyte atrophy, loss and disarray, hemosiderin, myxedema/mucin, and minimal myocardial fibrosis (Fig 2C).

Furthermore, there was mild, multifocal, chronic cardiomyocyte hypertrophy, multifocal hemorrhage, and minimal pleocellular infiltrates in the epicardium, and mild, multifocal mural arterial tunica media hypertrophy and hyperplasia with minimal intimal fibrosis. The left testicle had a seminoma with minimal capsular invasion. The changes in the skin were characterized by minimal to mild, multifocal, chronic dermal fibrosis and feather loss. In the lungs, there was moderate, diffuse congestion and edema, and rare perivascular lymphocytic infiltrates. In the liver, hepatocellular nodular hyperplasia was present, along with rare hepatocellular karyomegaly and mild, multifocal oval cell hyperplasia/bile duct hyperplasia. In addition to the above organs, congestion and acute hemorrhage were also noted in the thyroid glands, thymus, and spleen.

DISCUSSION

Histological examination confirmed the gross finding of a SAISSD, as well as fibroelastosis in the right coronary cusp and left ventricular myocardium in this geriatric blue and gold macaw. The myocardium adjacent to the SAISSD exhibited various localized findings, including cardiomyocyte atrophy, loss, and disarray, as well as hemosiderosis, myxedema/mucin deposition, and minimal to mild myocardial fibrosis. It is plausible that SAISSD could have contributed to aortic valve insufficiency and, concomitantly, led to the development of congestive heart failure. Eventual acute decompensation could have precipitated death in this bird.

The exact developmental stages of the cardiovascular system have been characterized in very few animal species, including birds.[1] In general, the main stages comprise the following: (1) gastrulation and formation of the primitive heart tube, (2) segmentation of the primitive heart tube, (3) looping, realignment of inflow and outflow segments, (4) septation of the atria, ventricles, and outflow segments, (5) formation of atrio-ventricular valves, and (5) development of aortic and pulmonary trunks and aortic arches.[1] Abnormalities at a given stage may result in impactful (eg, early embryonic death, still birth, delayed clinical onset) or subclinical consequences.[2] Available evidence suggests ventricular diverticula and aneurysms may start to develop in the endocardial tube within the first embryonic month.[3] Recognized mechanisms for such defects may include failure of the differentiation of the primitive intra-embryonic mesoderm into its splanchnic and somatic layers and inappropriate attachment of the primitive heart tube to specific structures of the yolk sac.[3] In chicken embryos, left ventricular aneurysms could be induced

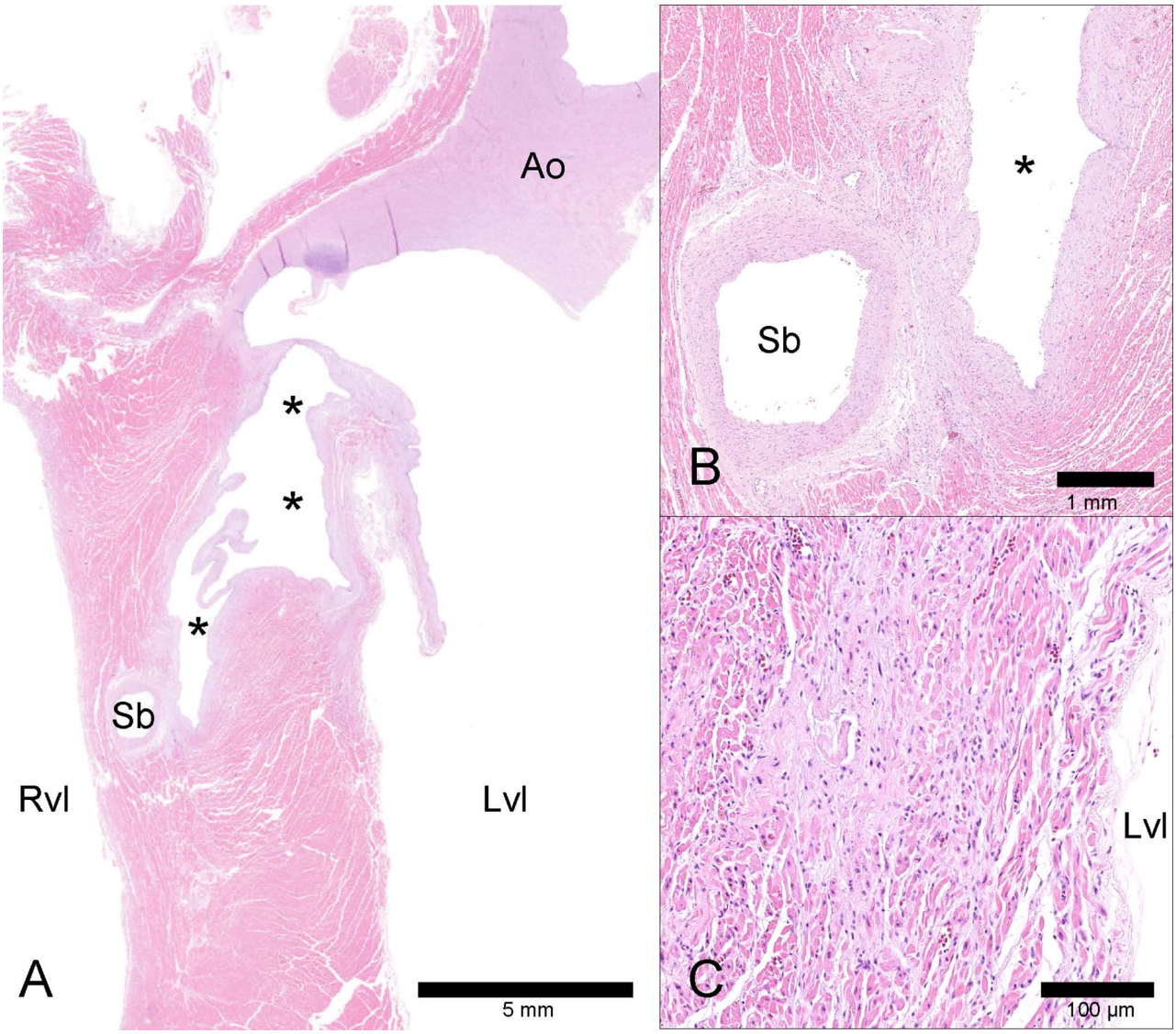

Figure 2. Microscopic features of a subaortic interventricular septal diverticulum in a blue and gold macaw (*Ara ararauna*). (A) The multiloculated diverticulum (*) extends deep into the interventricular septum. Bar = 5 mm. Hematoxylin and eosin stain. (B) The diverticulum (*) is lined by endothelium (not visible at this magnification) and a thin band of fibrous connective tissue. Multiple small and medium caliber interventricular mural arteries are close to the wall of the diverticulum. Bar = 1 mm. Hematoxylin and eosin stain. C) Focal myocardial fibrosis with cardiomyocyte atrophy and loss. Bar = 100 µm. Hematoxylin and eosin stain. Ao, aorta; Lvl, left ventricle lumen; Rvl, right ventricle lumen; Sb, presumptive septal branch of the left anterior descending artery.

by an amniotic band or a pericardial hole very early in embryonic development.[4]

Congenital heart disease (CHD) in avian species, excluding poultry, is rarely reported.[5,6] Reports of CHD in birds include ventricular septal defects and congenital aneurysms (mainly in psittacine birds),[7–10] persistent truncus arteriosus,[8] aortic hypoplasia,[8] duplicitas cordis, multiplicatis cordis, and ectopia cordis.[11] Ventricular septal defects prevail and have been reported in chickens (*Gallus gallus domesticus*), turkeys (*Meleagris gallopavo domesticus*), and a tundra swan (*Cygnus columbianus*).[12] Recently, a possible congenital coarctation-like arteriopathy of the right brachiocephalic artery was described in a Spix macaw (*Cyanopsitta spixii*).[13] A comprehensive search for CHD in birds, including key words "avian," "bird," "heart," "cardiac," and "cardiovascular malformation/anomaly/congenital defect" in the main academic search engines (Google Scholar, PubMed, ScienceDirect, Web of Science) and specialized journals and current main texts on avian medicine and pathology revealed that lesions comparable to the

SAISSD presented here have not been previously documented in avian species, and appear to be rare in humans and other animal species.[14,15]

Discrimination of cardiac outpouchings, including diverticula and aneurysms, relies on both morphologic features and contractility patterns, but it is often troublesome.[16,17] The lack of a widely established nomenclature has prevented the development of definite classification systems, and the historical interchangeability of these terms has resulted in reporting ambiguity.[18,19] The anatomic location (eg, ventricular apical vs proximal vs left ventricular outflow tract/aortic vestibule), etiopathogenesis, and duration of these saccular lesions may account for some of the variability encountered in the literature. Typical left ventricle diverticula have a narrow ostium and may contain cardiomyocytes that enable synchronous contractility, whereas left ventricle aneurysms have a wide ostium, largely consist of endocardial or transmural fibrosis, and tend to be akinetic or dyskinetic.[20] Other features, such as the presence or absence of concomitant heart or midline thoracoabdominal defects, may assist in their classification. The distinction becomes even more tenuous when diverticula subtypes, namely muscular and fibrous-type ventricular diverticula and pseudoaneurysms, are considered.[21] In the aortic outflow, another rare saccular defect to be considered is the aneurysm of the sinus of Valsalva (ASV), which consists of a dilatation of 1 or more of the aortic sinuses between the aortic valve anulus and the supra-aortic ridge. Aneurysms of the sinus of Valsalva may be acquired or congenital, progress into the interventricular septum,[22] and may coexist with ventricular diverticula and other aneurysms.[23]

In this case, the SAISSD consisted of a localized subaortic outpouching between the right coronary semilunar aortic valve and the interventricular septum that communicated with the aortic outflow and failed to communicate with either the left or the right ventricle. The lack of communication with the ventricles excluded a ventricular origin. Structurally, the inner walls of the SAISSD consisted of a circumferential fibrointimal band with variably preserved superficial endothelial cells and subendothelial spindle cells (fibroblasts/fibrocytes) that merged with collagen fibers and underlying mural cardiomyocytes. Based on these features, the inner wall of the SAISSD would most closely recapitulate features of a fibrous-type diverticulum; however, infallible distinction from an aneurysm would not be possible based on the current lack of consensus for such lesions.[21,24] In this regard, the saccular defect was structurally similar to an ASV, but the fibrous annulus of the aortic valve was largely preserved except for a focal area, coinciding with the dorsal edge of the septal defect, in which it was narrowed down to 1.5-mm thick. The latter differs to some degree, with the often more distal location of such a defect at the aortic annulus in humans.[22] Thus, the present case illustrates some converging features of 2 challenging and rare cardiac saccular defects.

Subaortic interventricular septal saccular defects in humans and other species have been linked to aortic regurgitation, thrombus, and arrhythmias, and are often associated with other cardiac, vascular, or thoracoabdominal abnormalities.[14] Diagnosis often requires imaging techniques (eg, echocardiography, computed tomography scanning, magnetic resonance imaging). The clinical presentation of SAISSD may range from asymptomatic (the SAISSD exhibits normal contractility) to high morbidity and mortality due to heart failure, rupture of the diverticulum, thromboembolism, and sudden cardiac death.[3,14,25] Similarly, ASV presentation severity may range from asymptomatic (intact ASV) to slowly progressive or sudden chest pain, dyspnea, and palpitations with eventual syncope and death. Heart murmurs and congestive heart failure are known to occur in ASV.[26] The murmur detected in the bird's latest reevaluation could have been associated with the SAISSD, valvular dysfunction, or a combination thereof. Fatal acute decompensation of chronic heart disease is most plausible. Additionally, the fibroelastosis noted in this case was confined to the right coronary cusp, as well as the adjacent aortic outflow and endocardium, and was interpreted as a secondary phenomenon resulting from turbulent blood flow. Other histopathologic changes in the heart of this bird (eg, cardiomyocyte atrophy, loss and disarray, hemosiderosis, myxedema/mucin deposition, and minimal myocardial fibrosis) were considered incidental and associated with the SAISSD based on their restricted location and extent. The minimal cardiac mural arterial/arteriolar changes noted were deemed most compatible with those of arteriosclerosis in aged individuals rather than the earlier stages of atherosclerosis. Atherosclerosis was not apparent in any of the organs examined histologically.

Testicular neoplasms identified in psittacine birds include Sertoli cell tumors, seminomas, interstitial cell tumors, lymphomas, leiomyosarcomas, teratomas, and undifferentiated neoplasms.[27] Sertoli cell tumors are the most frequently reported in captive

and free-ranging birds.[28] When small, these tumors are often asymptomatic, but as they enlarge, common clinical signs associated with testicular neoplasia include coelomic distension, ascites, dyspnea, anorexia, and lethargy.[29] In the case presented here, the seminoma was deemed an incidental finding, and no metastases were detected. Several previous studies have documented metastatic behavior in seminomas of psittacine birds.[27] Cardiovascular diseases (eg, atherosclerosis) and gonadal disease, among others, have been linked to feather-destructive behavior (so-called feather plucking or pterotillomania).[30] A causal association for feather-destructive behavior could not be determined. The histopathologic features of skin samples with feather-destructive behavior were like those reported previously[31] without any evidence of infectious pathogens.

In summary, this case report describes a 33-year-old blue and gold macaw with a delayed clinical onset of congenital heart disease. Specifically, SAISSD and aortic valvular dysfunction were believed to have resulted in CHD. This case contributes to the understanding of cardiovascular disease and raises awareness of delayed-onset clinical disease associated with congenital heart anomalies in avian species. The findings presented here may be of value in both antemortem and postmortem diagnostic schemes for avian patients with evidence of cardiac disease, such as heart murmurs, cardiomegaly, or pulmonary edema, or less specific clinical signs, including exercise intolerance or weakness.

Acknowledgements: We thank the histology technicians at Texas A&M Veterinary Medical Diagnostic Laboratory for their professionalism and commitment.

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