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Authors: MacLean, Robert A., Imai, Denise, Dold, Christopher, Haulena, Martin, and Gulland, Frances M. D.

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Persistent Right Aortic Arch and Cribiform Plate Aplasia in a Northern Elephant Seal (*Mirounga angustirostris*)

Robert A. MacLean,[1,4,7] Denise Imai,[2] Christopher Dold,[3,5] Martin Haulena,[3,6] and Frances M. D. Gulland[3]
[1] Environmental Medicine Consortium, Department of Clinical Sciences, North Carolina State College of Veterinary Medicine, 4700 Hillsborough St., Raleigh, North Carolina 27606, USA; [2] Anatomic Pathology Service, Veterinary Medical Teaching Hospital, University of California, One Garrod Dr., Davis, California 95616, USA; [3] The Marine Mammal Center, Marin Headlands, Sausalito, California 94965, USA; [4] Current address: The Audubon Nature Institute, 6500 Magazine St., New Orleans, Louisiana 70118, USA; [5] Current address: SeaWorld Orlando, 7007 SeaWorld Dr., Orlando, Florida 32821, USA; [6] Current address: Vancouver Aquarium, 845 Avison Way, Vancouver, British Columbia V6G 3E2, Canada; [7] Corresponding author (email: bmaclean@audubooninstitute.org)

ABSTRACT: A female weanling northern elephant seal (*Mirounga angustirostris*) presented to The Marine Mammal Center in Sausalito, California, USA, in poor body condition. An esophageal obstruction was diagnosed by contrast radiography and esophagoscopy, but despite extensive diagnostics and supportive care, the seal died 6 days later. On postmortem examination, the right aortic arch was persistent, forming a vascular ring anomaly with a patent ductus arteriosus that compressed the distal esophagus. Aplasia of the right cribiform plate and hypoplasia of the right olfactory nerve was also identified. A review of necropsy reports from January 1988 to December 2003 revealed 16 severe congenital anomalies in 454 juvenile northern elephant seals that stranded in northern California.

Key words: Cribiform plate aplasia, congenital anomaly, ligamentum arteriosum, *Mirounga angustirostris*, northern elephant seal, olfactory nerve hypoplasia, patent ductus arteriosus, persistent right aortic arch.

Congenital anomalies reported in juvenile northern elephant seals (*Mirounga angustirostris*; NES) have been reviewed recently (Trupkiewicz et al., 1997), and they include hydrocephalus, severe cardiac anomalies, hydronephrosis, focal pulmonary dysplasia, and congenital epidermal angiomatosis. In this article, we report a persistent right aortic arch (PRAA) anomaly and aplasia of the right cribiform plate in a juvenile NES, and we provide an update on congenital defects noted in this species at The Marine Mammal Center (TMMC; Marin Headlands, Sausalito, California, USA) between January 1996 and December 2003.

An approximately 4-mo-old, recently weaned female NES stranded in Monterey County, California, and the animal was transported to TMMC on 6 May 2004. This seal was emaciated (38.8 kg), mildly responsive, lethargic, and 5% to 10% dehydrated on presentation. Volunteers reported difficulty passing an esophageal tube intended for the administration of an electrolyte solution, and the animal subsequently regurgitated 15cc of blood and saliva along with several fish bones. A complete blood cell count (Vet ABC hematology analyzer, Heska Corp., Fort Collins, Colorado, USA), a manual 200-cell differential count, and a clinical chemistry profile (AU5200, Olympus America Inc., Melville, New York, USA) were performed on blood drawn the next day. Results, when compared with historical values obtained from apparently healthy NES (Bossart et al., 2001), indicated a mild neutrophilia with a degenerative left shift. Biochemistry values revealed elevations of serum γ-glutamyl transferase (340 U/l), lactate dehydrogenase (486 U/l), and alkaline phosphatase (247 U/l) concentrations, indicative of mild liver disease, and a mild azotemia with an elevated blood urea nitrogen (59 mg/dl) concentration. The animal was treated with lactated Ringer's solution (Burns Veterinary Supply, St. Paul, Minnesota, USA; 2 l intravenous [IV]), antibiotics (procaine benzathine penicillin G, G.

C. Hanford Mfg. Co., Syracuse, New York, USA; 1,200,000 IU intramuscular [IM] once daily (s.i.d.); and enrofloxacin, Baytril, Bayer Corp., Shawnee Mission, Kansas, USA; 200 mg IM s.i.d.), and an anti-inflammatory (flunixin meglumine, Banamine, Schering Plough Animal Health, Union, New Jersey, USA; 40 mg IM s.i.d.).

Thoracic radiography, including a barium esophogram, was performed on day 2 without sedation. A foreign body resembling fish bones was observed associated with an esophageal obstruction and moderate esophageal dilatation. An esophageal perforation proximal to the carina was evidenced by a curvilinear area of radiopacity extending laterally from the esophageal border. The following day the animal was premedicated with atropine sulfate (Atroject SA, Burns Veterinary Supply; 0.8 mg IM) in the gluteal muscles, sedated with diazepam (Valium, Hoffman-La Roche, Nutley, New Jersey, USA; 5.9 mg IV) in the extradural intravertebral vein, and induced with 5% isoflurane (IsoFlo, Abbott Laboratories, North Chicago, Illinois, USA) in 100% O_2 by mask for endoscopic evaluation. An esophageal obstruction of fish bones was observed, and the material was extracted using endoscopic and long-handled forceps. In this area, the esophagus was markedly dilated, and the mucosa was severely ulcerated. After removal of the obstruction, the endoscope passed easily into the stomach. Supportive therapy continued for 3 days. On day 5, the animal was force-fed two fish and later regurgitated one of the fish. The animal continued to decline despite supportive care, and it died on the morning of day 6.

On gross postmortem examination, the distal esophagus was entrapped and constricted between the trachea, pulmonary artery, and ligamentum arteriosum by a persistent right aortic arch (Fig. 1). The esophagus cranial to the stricture contained one intact fish, and the area was moderately dilated and diffusely thickened, the mucosal surface of which was markedly irregular and ulcerated. Multiple fish bones were embedded within the mucosa, often perforating through the wall. The esophagus, both extrathoracic and distal to the stricture, was unaffected. Several mites (identified as *Orthohalaranche attenuata*) and fish bones were present within the nasopharynx. The ductus arteriosus was patent. In the cranium, the right olfactory nerve and bulb were small and truncated. The right lateral aspect of the cribiform plate was absent. In this region, the ethmoid bone was intact, lacked foramina, and fused smoothly with the frontal, maxillary, and palatine bones.

Other findings included a markedly diminished amount of intra-abdominal, pericardial, and subdermal adipose tissue (blubber depth was 1.3 cm), with serous atrophy of the mesenteric fat. The liver was small (953 g; 2.5% of body weight) and soft, with sharp borders. There were multiple large volcanic ulcers within the pylorus and pinpoint shallow ulcers within the duodenum.

Representative tissue samples from multiple organs were fixed in 10% neutral buffered formalin, routinely processed, embedded in paraffin, sectioned at 5 μm, and stained with hematoxylin and eosin. Histologic examination revealed a severe chronic ulcerative esophagitis within the dilated segment just proximal to the stricture. The right olfactory nerve was morphologically and structurally normal but markedly diminished in size. Hepatocytes were atrophic and contained abundant hemosiderin, exocrine pancreatic zymogen granules were rare, and the mesenteric fat exhibited serous atrophy, all of which are indications of starvation. Acute congestion of the lung, kidney, and adrenal gland was interpreted as agonal, secondary to cardiovascular collapse. Other findings included gastric and duodenal ulceration and eosinophilic enteritis, which, in the absence of enteric parasites, may have resulted from debilitation and stress.

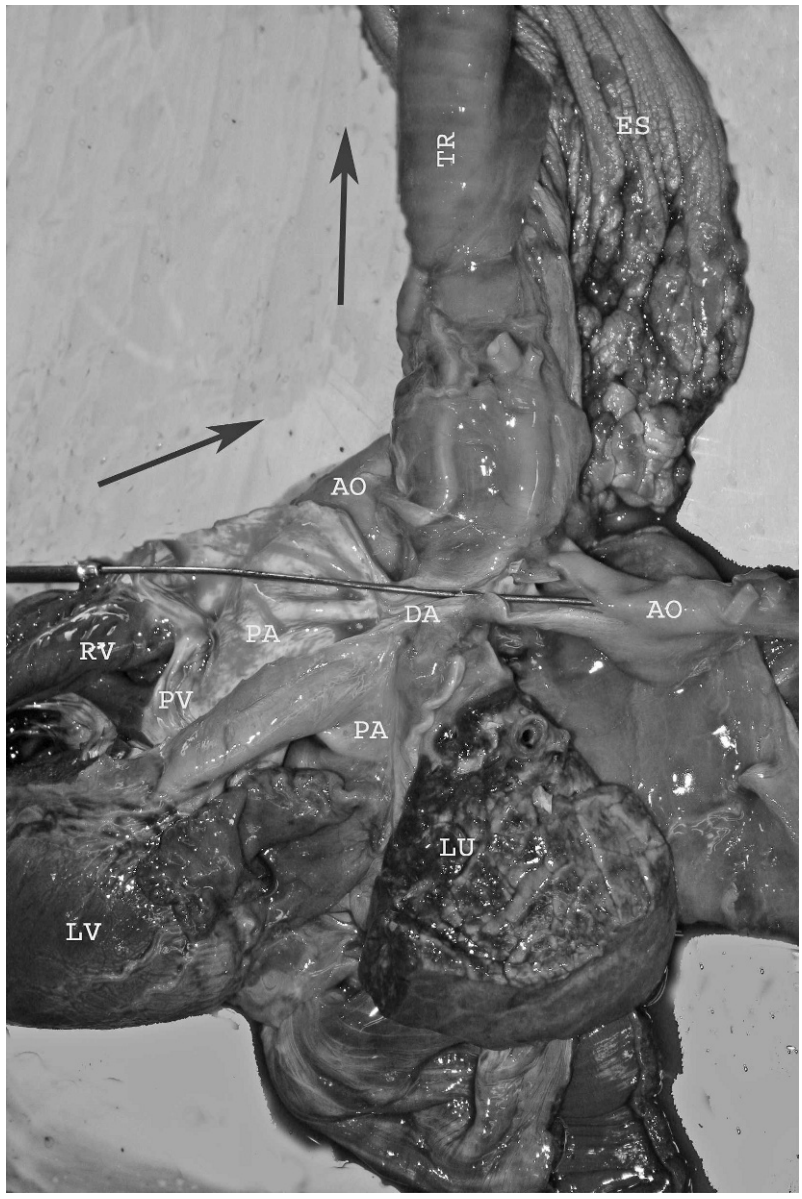

FIGURE 1. Persistent right aortic arch in a juvenile northern elephant seal (*Mirounga angustirostris*): aorta (AO), ductus arteriosus (DA), esophagus (ES), left ventricle (LV), lung (LU), pulmonary artery (PA), pulmonary valve (PV), right ventricle (RV), trachea (TR). Arrows indicate cranial for orientation.

The clinical history and course presented in this case were consistent with a weanling seal suffering from the complications of a PRAA. Upon the diagnosis of the esophageal obstruction, a PRAA was on the list of differentials, but it was considered rare and unlikely compared with a simple food impaction. After clearing the obstruction, the endoscope seemed to pass easily into the stomach, and no external constriction was evident. The fact that the animal regurgitated one of two force-fed fish should have raised suspicions of a PRAA; however, it was assumed that the other fish had been swallowed into the stomach. Had the

TABLE 1. Congenital abnormalities and patent ductus arteriosus in the elephant seal (*Mirounga angustirostris*) noted at The Marine Mammal Center between 1 January 1988 and 12 December 2003.

Congenital defect	No. animals from 1988 to 1995[a]	No. animals from 1996 to 2003[b]	Total animals from 1988 to 2003
Hydrocephalus	7	2	9
Malformation right atrium and/or ventricle	2	2	4
Angiomatosis	1	0	1
Pulmonary dysplasia	1	0	1
Hydronephrosis	1	0	1
Scapulo/humeral and elbow joint hypoplasia	0	1	1
Polydactyly	1	0	1
Patent ductus arteriosus	6[c]	10[d]	16

[a] Total necropsy records examined = 210 from 1 January 1988 to 31 December1995.

[b] Total necropsy records examined = 244 from 1 January 1996 to 31 December 2003.

[c] Total records specifically noting the status of the ductus arteriosus is unknown.

[d] Total records specifically noting the status of the ductus arteriosus is 111.

diagnosis of a PRAA been made antemortem, the animal would have been euthanized as an inappropriate candidate for rehabilitation. Although surgical repair is the definitive therapy in such cases, a successful outcome is uncertain, especially in a debilitated patient; moreover, the animal would be inappropriate for breeding due to likely heritable factors (VanGundy, 1989; Patterson, 1989).

Both the PRAA and the hypoplastic right olfactory bulb and nerve are congenital defects that were either hereditary or acquired during gestation. The vascular defect occurs with the formation of the aorta from the right fourth aortic arch instead of the normal left fourth aortic arch. As a result, the esophagus and trachea are encircled by the aorta on the right (which crosses to the left dorsally), the pulmonary artery and the base of the heart ventrally, and the ligamentum arteriosum on the left, all causing a constriction of the distal esophagus that manifests in weanlings in the regurgitation of solid foods (VanGundy, 1989).

The significance of the olfactory nerve and bulb hypoplasia is undetermined; however, in laboratory mice, it has been found that normal development of the olfactory bulb requires retrograde development of olfactory receptor neurons in the respiratory epithelium to the olfactory bulb (Gong, 2001). In this seal with its absent right cribiform plate and unilaterally imperforate ethmoid bone, it is possible that the olfactory nerve and bulb hypoplasia was not a primary defect but due instead to the impeded retrograde migration of neurons from the nasal cavity to the brain. One case report in the human literature describes a patient with bilateral optic nerve hypoplasia (septo-optic dysplasia), diagnosed at 6 mo of age, and olfactory bulb hypoplasia (Levine et al., 2001). The optic nerves seemed normal in this NES, and they were not further investigated.

In addition to a variety of toxins, congenital defects in some farm and laboratory animals are known to have a hereditary component (Szabo, 1989). The PRAA anomaly is known to be a complex hereditary trait in certain breeds of dogs, such as German shepherds and Irish setters (Patterson, 1989). In humans, the defect has been associated with a deletion on chromosome 22 (Momma et al., 1999). Some researchers have speculated that congenital defects in the NES may be caused by the severe genetic bottleneck of perhaps less than 10 individuals that occurred in the late 1800s after heavy hunting pressure (Trupkiewicz et al., 1997; Hoelzel et al., 2002). Studies of NES genetic material from both before

and after the bottleneck have indeed shown a historic loss in diversity in both allelic and mitochondrial DNA (Weber et al., 2000; Hoelzel et al., 2002). The cheetah is thought to be in an analogous situation after a proposed historical population bottleneck; however, similar increases in anomalies have not been observed in this species (O'Brien et al., 1985). Moreover, several other terrestrial carnivores have even lower genetic polymorphisms than the cheetah and also do not exhibit evidence of inbreeding depression in the wild (Merola, 1994; Amos and Harwood, 1998). Another possible etiology of the cardiac defect includes a congenital viral infection, because some viruses, such as morbillivirus in humans, can cause cardiac defects (Shoen, 1994). Congenital viruses, such as bovine viral diarrhea virus, can also cause central nervous system defects (Jubb and Huxtable, 1993).

In the previous report on NES anomalies, it was noted that six animals over 2 mo of age were observed with a patent ductus arteriosus, suggesting that closure of this vessel may be delayed normally in marine mammals compared with terrestrial species (Trupkiewicz et al., 1997). An examination of 111 necropsy records at the TMMC between January 1996 and December 2003, where the status of the ductus arteriosus was recorded, revealed 10 animals, averaging 4 mo of age (range 3–6 mo), that had either an open ($n=4$) or a partially closed ($n=6$) ductus with no other vascular abnormalities noted. Other congenital anomalies noted during this period are listed in Table 1.

Cumulatively, of the 454 juvenile NES necropsy records at TMMC between January 1988 and December 2003, 16 individuals (3.5%) had a significant congenital anomaly that was considered to have contributed to the animal's demise. In the previous report, the rate of NES congenital anomalies discovered on necropsy (5%) was extrapolated to represent the minimum rate likely present in the wild population. It is important to remember, however, that these data are generated from stranded juveniles and that more animals may be affected or unaffected that are either lost at sea or not terminal, making extrapolation inaccurate, at best. Continued reporting of congenital anomalies in wildlife is important, however, because it may provide valuable data for future investigations.

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