”Sudden” Death in Pet Birds

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Summary

Although often presented with a history of sudden death, not all birds are acutely ill. At necropsy, the birds with chronic disease may have lesions referable to specific organ systems, particularly the gastro-intestinal system. In addition, the birds with chronic disease are usually thin and have inadequate muscle mass and fat deposits. A variety of chronic disease syndromes are seen. With acute disease, and death with no premonitory signs, muscle mass and adipose deposits are usually normal. Careful examination of the body must be done in order to rule out disease infecting the central nervous system, respiratory system, pancreas, endocrine glands, and heart. In particular, diseases involving the adrenal glands and heart may result in no gross change and minimal histological changes, and careful examination of appropriate portions of these tissues is necessary to try and establish a diagnosis. In some birds, there may be true cardiac sudden death, as a result of ventricular fibrillation in previously apparently healthy birds. Many of these will have microscopic heart lesions; however, with some, no pre-existing lesion is seen.

Introduction

Many cases are presented to the pathologist with a history of “sudden” death. This discussion will cover some of the conditions that cause a true acute/sudden death, and contrast these with cases that are actually chronic unrecognized disease. Due to the large number of conditions that could be included, only a few examples of each are presented. Gross and histologic lesions needed to make the diagnosis, and the protocol for proper tissue selection is important.

Results

I. General considerations.

- A. Birds with chronic disease are usually thin, with inadequate muscle mass.
- B. There is often poor feather quality or loss of feathers. fecal staining at the mucocutaneous junction of the vent.
- C. Chronic respiratory disease leads to exudate and possible plugging of the nares or enlargement of the sinuses.
- D. Chronic intestinal disease often results in fecal staining of the vent and surrounding feathers.

II. Specific disease problems.

- A. Chronic disease involving any organ can lead to a thin, wasted bird with no specific signs seen.

1. Lesions that may be noted include neoplasia, abscesses or granulomas and visceral urate deposits.
2. Particular attention should be directed to the gastro-intestinal system and associated glands.

B. Inadequate nutrition is a factor in many cases of "sudden" death.

1. Affected birds are thin and may have minimal ingesta, although nutrition can be inadequate even though the GI tract appears full.
    a. Usually no other lesion will be noted at necropsy. The problem may be inadequate amounts, caloric intake, lack of essential nutrients or inability to absorb/digest food.

C. Common chronic gastrointestinal disease in pet birds is often infectious or neoplastic.

1. In psittacine birds, proventricular dilatation syndrome is a frequent problem.

    a. Caused by a virus. There are usually (but not always) gross lesions including thinning and/or dilatation of the wall of one or more portions of the GI tract. Histologically, the diagnosis is made by finding ganglioneuritis in affected organs.

2. Avian mycobacteriosis is characterized by thickening of the small intestine with or without nodules. The liver and spleen may be enlarged and discolored. Histologically, there is a chronic histologic enteritis with numerous organisms present. Intestinal villi are usually atrophied/fused.

3. Chronic liver disease can lead to a variety of gross changes, from enlargement to atrophy.

    a. Affected organs may be smooth or nodular and are often discolored.
    b. Chronic liver disease is not uncommon in several psittacine genera and the exact cause is often not determined.

        i. Inflammation, toxins and nutritional problems all may play a part in the pathogenesis. Histologically, in most cases, there is variable inflammation, fibrosis, bile duct hyperplasia and hepatocellular degeneration.

4. Common neoplastic diseases that should be considered include gastric or intestinal carcinoma, as well as hepatic and pancreatic neoplasia.

    a. Gastric carcinoma is often found at the proventricular-ventricular junction, and may occur as a flattened, slightly thickened area which can be difficult to appreciate grossly. In some cases there may be ulceration/perforation. Intestinal carcinoma and smooth muscle neoplasia are less common.

    b. Bile duct carcinoma is the most common hepatic neoplasm, and may be associated with internal papillomatosis. These tumors are often multicentric, firm and grey-white or yellow. Pancreatic carcinoma is usually nodular and may vary from cream/white to red. It usually will

efface much of the pancreas and possibly the duodenal loop of the small intestine.

D. Acute conditions. When presented with a bird that died with no premonitory signs and which may have no apparent gross lesions, several organs must be carefully examined histologically.

1. Central Nervous System: The possibility of trauma must be ruled out.

   a. There may be no external trauma, but meningeal or brain hemorrhage will be noted. Post-mortem patterns of congestion in the bones of the skull should not be confused with true traumatic hemorrhage.

   b. Hemorrhage and necrosis may also follow thrombosis, which, in turn, can be associated with generalized cardiovascular disease; however, vascular lesions are not always obvious. In female birds with a history of egg laying, yolk embolus must be ruled out. This can usually only be done histologically.

2. Respiratory System: Acute blockage of the trachea or syrinx leads to collapse and sudden death.

   a. Common causes are seed inhalation, and chronic inflammation, usually due to fungal infection. Lesions may be confined to the syrinx, which must be opened in order to make a diagnosis in many cases. Food inhalation, particularly in young hand-fed chicks, may not be visible grossly, although it can be responsible for pulmonary collapse and acute death.

   b. Acute allergic pneumonitis is another cause of sudden death. It is most commonly reported in Blue And Gold Macaws. Histologic examination is necessary to differentiate the condition from infection or inhaled toxin exposure.

   c. A variety of inhaled gases or sprays can lead to sudden air capillary collapse, congestion and hemorrhage. The histologic lesion is suggestive, but a careful history is necessary for confirmation of the diagnosis.

3. Pancreas: Acute pancreatitis/necrosis is a cause of sudden death in pet birds, particularly quaker parakeets1. the cause of the condition is not known, but it may be related to high-fat diets. Acute necrosis may also be secondary to chronic conditions such as pancreatic neoplasia.

4. Endocrine Glands:

   a. In some cases of acute death, the only lesion found was thyroid hyperplasia and/or degeneration. The inference is that the birds were hypothyroid, although no supportive clinical chemistry data was available and no overt signs of hypothyroidism were seen. Thyroiditis, possibly autoimmune, has been seen in african grey parrots. Morphologically it is similar to the disease in chickens.

b. Hyperplastic or neoplastic parathyroid glands may lead to hypocalcemia and sudden death, particularly in african grey parrots. Enlargement of the parathyroid gland is usually obvious at necropsy.

c. The avian adrenal gland has no defined cortex or medulla. The cortical analogue is referred to as the interrenal cells, and the medullary analogue as chromaffin cells. Lesions involving either may lead to sudden death.

i. Lesions of the interrenal cells results in hypofunction (Addison's Disease). The underlying mechanisms can be infectious such as mycobacteriosis, chronic exhaustion due to stress or auto-immune disease. The latter has not been proved in avian species at this time.

Other than sudden death, hypofunction can lead to electrolyte imbalance or hyperpigmentation. Viral infections, particularly proventricular dilatation syndrome, affect nerves and nerve ganglia, and in some cases, the chromaffin cells of the adrenal gland.

5. Heart: A variety of cardiac lesions result in sudden death.

a. Myocarditis may be a sequela of bacterial septicemia, and can occur some time after the initial condition is thought to be resolved.

i. Bacterial dermatitis, enteritis or upper respiratory infection are all possible primary insults.
ii. Experimentally, Chlamydia makes a peptide that mimics a portion of heart muscle protein, leading to autoimmune myocarditis.
iii. Myocarditis, degeneration and/or inflammation of the cardiac conduction system can be due to polyomavirus infection, the virus causing proventricular dilatation syndrome, and paramyxovirus infection.

b. Non-inflammatory myodegeneration may be nutritional (Vitamin E/Selenium Deficiency) , toxic or secondary to athlerosclerosis.
i. Conditions such as endocardial fibrosis are infrequently seen, but must be ruled out in cases of sudden death.

c. Lesions of the conduction system can result in sudden collapse and death.

i. May be secondary to myocardial inflammation or degeneration; however, many cases are less obvious, have no apparent cause, and are found only by careful examination of several areas of the heart. In cases of sudden death, submission of the entire heart is preferred when practical.

d. Oculocardiac reflex reported in a bird. Can lead to sudden death.

i. There may be shared patterns of autonomic activation between heart and eye.
ii. Bradycardia and faintness result from stretching of ocular muscles or pressure on/within the eyeball.
iii. Trigeminal nerve is afferent limb of reflex and vagus to the heart is the efferent.
iv. Can occur during surgery, manipulation of lids, or restraint

6. Liver. Both herpesvirus and polyomavirus infections can cause diffuse severe hepatic necrosis leading to sudden death with few premonitory signs.

a. These conditions should be suspected if there is flock involvement, young birds dying, or other signs suggestive of infections. Both conditions can be diagnosed histologically in most cases.

III. Conclusions

"Sudden death does not necessarily imply an extension of a process, but it is within itself a disease entity which possibly may be avoided by proper therapy". Lown, A. Am. J. Med. 72:117-180 1982. A variety of chronic diseases that affect pet avians have either no observable signs, or the signs and physical changes are not appreciated by the owner, leading to a history of "sudden death". Regardless of the specific underlying problem, most of these birds have weight loss with depletion of adipose tissue and reduction in muscle mass, both of which are observable at necropsy. In many cases, no specific underlying cause is found, but the same changes are noted at necropsy[2]. The end result is cachexia which may be the actual cause of death. When the above described changes are seen it can be determined that the "sudden" death was only apparent; not real. The finding of obvious chronic lesions due to underlying disease, as well as hepatic and/or pancreatic atrophy[2], also indicates the true chronic nature of the disease process.

One definition of sudden death is that the individual died suddenly and unexpectedly, either instantaneously or within 24 hours of the onset of signs[3]. In such cases the changes described previously will not be present. The bird will have good muscle mass and adipose tissue and
often no gross lesion will be present.

The determination of the cause of sudden death depends on good gross observations and proper tissue selection for histopathology. Brain, heart, lung, adrenal gland, thyroid gland, pancreas and liver all should be carefully examined. In many cases lesions suggestive of inhalation and pulmonary collapse, acute pancreatitic necrosis and hemorrhage, vascular disease and thrombosis[5], or infectious disease[6] will be present grossly and/or histologically.

There are birds, however, in which few or no lesions will be found, and the cause of death will be speculative. In many of these cases, disease involving the heart or adrenal may be the cause, emphasizing the need for careful examination of these organs, preferably in their entirety.

The mechanism leading to acute death is often the creation of ventricular fibrillation or asystole[3]. There may be frequent premature complexes leading to tachycardia and fibrillation. Factors influencing fibrillation include a long QT interval, hypokalemia, acidosis, imbalance in sympathetic/parasympathetic stimulation with a sympathetic dominance, and emotion. With sympathetic dominance there is an exaggerated catecholamine reaction, reduced oxygen supply to the myocardium and muscle spasm. The cardiac conduction system has been described as anaerobic where every cell functions in an all-or-nothing capacity[3]. Since only a few cells are required for functioning, problems can persist for years until some insult leads to sudden death. In some mammals, n-6 and n-3

polyunsaturated fatty acids prevented ischemia-induced ventricular fibrillation due to a reduction in electrical excitability caused by partitioning of the free polyunsaturated fatty acids into the phospholipid membranes of the cardiac myocytes. Reflex nerve impulses associated with manipulation of the eye may lead to bradycardia and death[4]. Pretreatment with atropine may help to reduce the effect.

In humans, sudden cardiac-death is reported in 1,000 people each day in the United States[7]. Most incidents involve ventricular fibrillation, usually, but not always, in diseased hearts. Some of the changes reported in humans include trauma, tumors, fatty infiltration of the A-V node, mineralization of the bundle of His, sclerosis of bundle branches, genetically abnormal bundle branches and myocarditis. Many of the same lesions have been seen in birds, and the others probably exist, and will be found with thorough examination of hearts from more avian necropsies. The recent finding that Chlamydia peptides can result in an autoimmune myocariditis[8] suggests that the possible relationship between birds with chlamydiosis and later sudden death needs to be investigated.

In some cases in humans, spontaneous lethal fibrillation occurs, with no detectable underlying cardiac abnormalities[7]. In these cases the cause may be biochemical, particularly electrolyte (K/Mg) imbalance, or possibly associated with physical or mental stress, the latter leading to a prolonged Q-T interval in humans[15]. A variety of possible causes can be considered for electolyte imbalance, but one that should be considered in birds is water quality. In humans, hard water is protective and soft water is apparently associated with cardiac problems. It is possible that birds whose water supply consists of artificially softened or ionized water could develop an electrolyte imbalance.

Physical stress may be suspected if the owner is a good observer, but the possibility of mental stress is difficult to affirm in birds. If environmental conditions include overcrowding, noise, and species/size mixture, however, stress is certainly possible. Since many cases of avian “sudden” death occur during routine handling procedures, it may be possible to construct a profile of birds that have potential markers suggestive of cardiac risk, and if so, it may be possible to prevent some of these unfortunate occurrences. Obvious criteria would include detectable cardiac problems such as hypertrophic/dilated cardiomyopathy, obesity and possible atherosclerosis, or electrocardiographic abnormalities. Other criteria to consider would be species, temperament and environment. Humans that have acute myocaridal infarction may have impaired coping during subsequent ischemic events due to posttraumatic stress disorder.[16]

There may be a connection between the adrenal gland and heart that leads to sudden death. With stress, there is an increase in cortical (interrenal) hormone production which increases target organ sensitivity to the b adrenegic effects of epinephrine leading to cardiotoxicity[13].

Some drugs (b receptor agonists) can be sensitizing agents, but chronic stress is also a cause. In birds the source of the stress may not be obvious (environmental-emotional), and these birds will show no clinical signs prior to death, as well as no lesion at necropsy.

Adrenal lesions can affect the cortex (interrenal cells) or medulla (chromaffin cells). The cortex is a mesodermal derivative while the medulla arises from neuroectoderm[9]. Problems leading to sudden death are often associated with hypofunction of the cortex[10] (Addison’s Disease), with sudden weakness, vomiting, tachycardia collapse and death. The primary problem is usually a mineralocorticoid deficiency In humans, Addison’s Disease has a familial tendency, is often seen in females, and is associated with organ specific antibodies[11] Autoimmune disease of the adrenal glands may be associated with autoimmune thyroiditis, and clinical hypothyroidism. Lymphocytic infiltration and atrophy of the adrenal cortex are noted histologically.[11,12]. In birds, there is essentially no information on age, sex, or possible genetic links to adrenal disease, and clinical Addison’s disease has not been described. Another potential cause of adrenal insufficiency is a pituitary tumor producing excessive melanocyte stimulating hormone. There may be associated pigment changes. Primary

adrenocortical atrophy is rarely described in humans[14], and has not been reported in pet birds. Psittacine birds with proventricular dilatation syndrome often have a lymphocytic adrenalitis involving the chromaffin cells which are embrologically related to nerve tissue. Occasionally birds are examined that have adrenalitis with no other change seen. The possibility of either direct action of the virus, or an immune-mediated, or auto-immune disease is considered in these cases.

Adrenal cortical hyperfunction has also been a cause of sudden death in humans. Primary aldosteronism associated with a cortical adenoma lead to ventricular fibrillation. Hypokalemia and hypertension were also present.[17] Detecting proliferative lesions of the avian adrenal is difficult, but in cases of sudden death, complete gross and histologic examination of the adrenals is necessary.

In African grey parrots however, two apparent entities are occasionally associated with acute death. One is a lymphocytic thyroiditis, which morphologically resembles that seen in humans and chickens, and the other is diffuse vacuolation of the interrenal cells seen in birds that die acutely with no signs. Some of these birds are found dead, but others are being handled for routine examination or beak and nail trimming. The possibility of adrenal hypofunction is a consideration based on the appearance of the gland in these cases.

Although infrequently seen, thyroiditis occurs in psittacine birds, particularly the african grey parrot, and histologic examination of the thyroid is necessary to rule out disease. Sudden death associated with thyroiditis has been reported in humans[18]. Lesions suggesting possible autoimmune thyroiditis were present.

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