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### Disease Complication in a Geriatric Pig-Tailed Macaque (*Macaca nemestrina*) reported from Wildlife Rescue Centre (WRC) Jogja – Case Study

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#### KEYWORDS

Conservation

Disease

Geriatric

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#### ABSTRACT

In the current study, a geriatric male pig-tailed macaque having a mass growing up to the left shoulder for the past five months has been reported from the Wildlife Rescue Centre (WRC) Jogja. It was an approximately 4x4x2 cm, firm, hairless focal non-encapsulated mass suspected as a skin-derivative tumor. A cytological test was performed on the mass and a skin biopsy was carried out to see the tissue content of the mass. Histopathological examination confirmed that the mass was identical to papilloma. In the next step of the study, the surgery was conducted and the mass was removed. However, after surgery, the health condition of the macaque gradually deteriorated and the performed hematological tests revealed a gradual increase in the number of leukocyte cells that indicated a developing chronic inflammatory response. Further, the erythrocyte level was in the normal range but showed a declining trend which suspecting progressing anemia. One month after the surgery general muscle stiffness was reported in the macaque which is a clinical sign of tetanus and the macaque died even after the ATT serum treatments. Necropsy findings confirmed a significant chronic bilateral diffuse pneumonia. This case study showed an unpredicted sequence of disease occurrence in geriatric macaque after undergoing the initial surgery of cutaneous mass extraction. Hence, the results of the study suggest that a routine regular health screening coupled with clinical laboratory examination may assist the early detection based on the subclinical signs of disease in geriatric animals in rehabilitation centers.

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## 1 Introduction

A male adult macaque was having more than 15 years of age was surrendered to the study center. During the routine monitoring, it was found that it often sounded ‘coughing’ and hiccup without any reason. In November 2017, a 4x4x2 cm, firm, hairless focal non-encapsulated mass grew up from its left shoulder, and results of this section biopsy revealed a proliferative tissue from epidermal derivative. After this abnormal growth, the health conditions of macaque was unexpectedly kept worsening during the next 6 months and the macaque was found dead after undergoing a series of spasmodic signs indicating tetanus. This study was conducted to evaluate the disease complication and sequential changes that occurred during the development of abnormal growth in a Geriatric Pig-Tailed Macaque.

## 2 Materials and Methods

The macaque having geriatric Pig-Tailed was sedated using a combination of ketamine-xylazine by following the common procedure applied at the research center. To rapidly assess the type of mass growing up, a chunk of mass tissue was incised and a biopsy was carried out by following the biopsy procedure proposed by Nischal et al. (2008). A series of peripheral blood collection and haematologic evaluations was also performed during the health monitoring period of this macaque. For this, 3-ml-blood was taken in each collection and analyzed by an automatic hematology analyzer under laboratory conditions.

The necropsy of the deceased macaque was performed by following the standard necropsy procedure. All suspected lesions found on the tissues during necropsy were preserved in 10% nonbuffered formalin for histopathologic examination. The tissues were processed through a common tissue processing

protocol for histopathology followed by haematoxylin-eosin staining.

## 3 Results

During this study, a series of blood tests were performed during March, April, and May 2018. A significant increase in haematocrit and thrombocyte was observed that indicating the increase in the number of cells and possibly caused acute vascular damage. Further, a slight rising in leukocytes and a decline in haemoglobin were reported which indicated symptoms of anemia. Differential leukocyte counts represent a sharp increase in neutrophil and lymphocyte number which revealed a prolonged infection pattern (Figure 1).

The gross inspection found abdominal fat atrophy indicated by thinning of fat deposits in the abdominal omentum and mesentery. The lungs seemed very congested, dark red on the right side with diffuse, poor demarcated, white discoloration and irregular surface on both sides. The transverse section of the lung revealed 2-5 mm in diameter, well-demarcated, multifocal, irregular yellow lesions (Figure 2).

Histopathologic examination of the mass revealed that there is an extensive proliferation of epidermal layers forming elevated papillary projection. The histological architecture shows clusters of epidermal cells in almost concentric fashion and fibrovascular tissue underlying the base of epidermal growth (Figure 3). The tissue growth is invasive and infiltrates the dermal layer. High numbers of pleomorphic cells were observed with moderate mitotic figure count and haemorrhages. The histopathology of the lungs showed thickening of alveolar walls and severe haemorrhages. The thickened alveolar walls were stuffed with cells consisting of polymorphonuclear cells and lymphocytes (Figure 4).

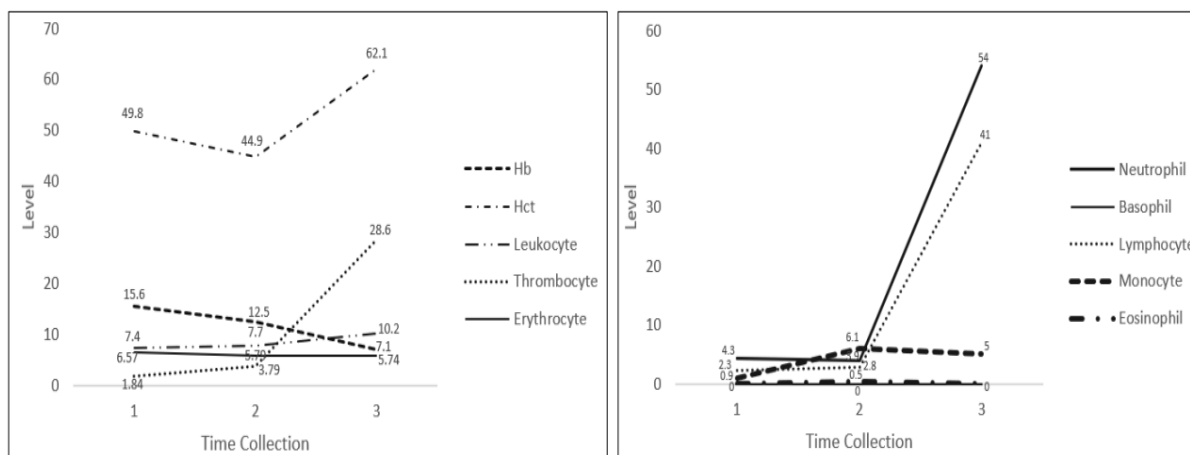


Figure 1 Line charts of macaque's haematological dynamics were compiled from three-month monitoring (left) and differential leukocyte count (right) was sharply increased to the end of the diseased event. The hypochromic anemia was observed in the second Hb check; however, the neutrophilic and lymphocytic inflammations were the predominant findings.

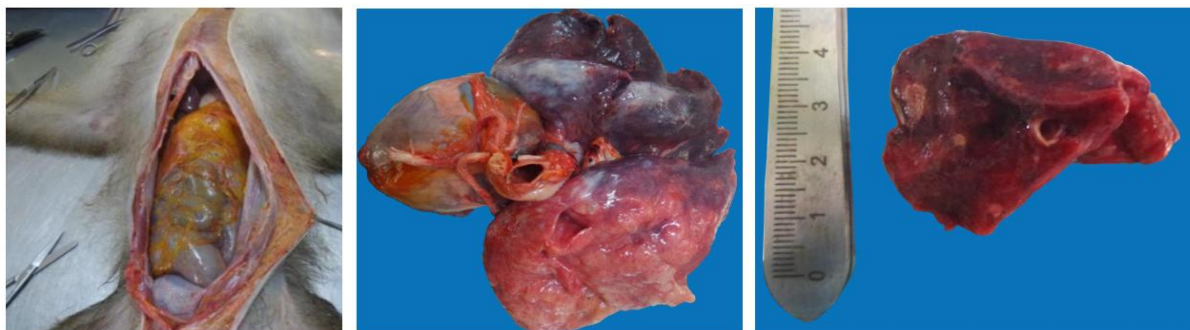


Figure 2 The gross finding showed a thin abdominal fat (left), asymmetrical enlargement of lung lobes, and white discoloration with darkening of almost 60% of the right lobe (middle). Transverse sections presented 2-5 mm in diameter multifocal lesions were observed in the parenchymal tissue of lungs (right).

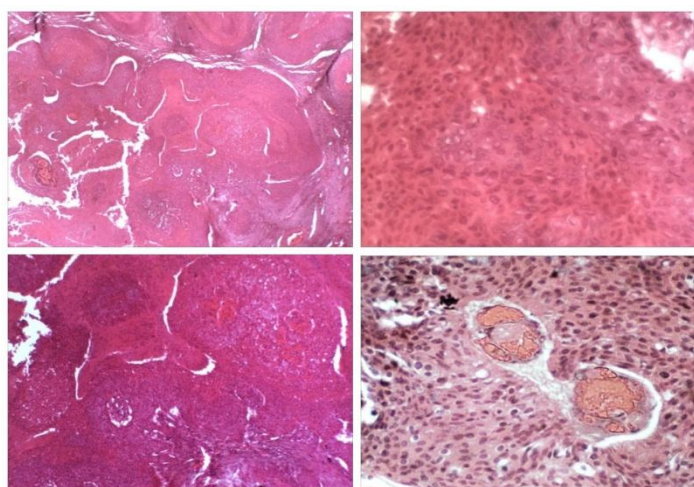


Figure 3 The histopathology of skin presents proliferative and invasive epidermal derivatives infiltrating the underneath tissue. The outward growth seems to form an irregular projection with no complete differentiation of the keratinized stratum. Anisokaryosis and haemorrhages (resembling keratin pearl) are observed (bottom right).

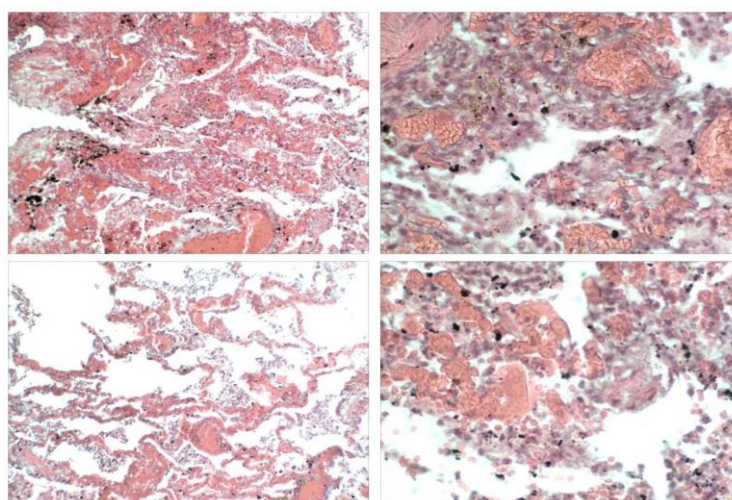


Figure 4 The histopathologic findings of diseased lungs showed thickening of alveolar walls (interstitial pneumonia), congestive capillaries, and haemorrhages. Presumptive alveolar edema might appear and induce coughing reflexes. Inflammatory cells predominantly neutrophilic and lymphocytic cells infiltrate the walls of alveoli.

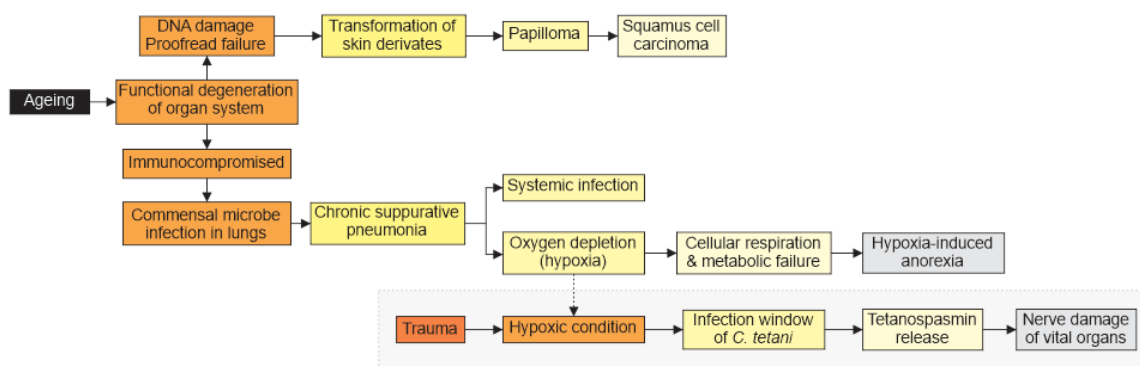


Figure 5 The deductive scheme of pathogenesis in this aging macaque. Results of this study presume that there were at least three complications that might play important role in disease development and need specific diagnosing approaches

#### 4 Discussions and Conclusion

Results of the study deduced that the presence of several unrelated lesions in this macaque was strongly associated with multiple infection events in a time. Aging might be the most plausible etiology of these prolonged diseased events (Figure 5). These results are also supported by the findings of Day (2010) those who reported that aging degenerates the organ systems which might affect the immune system and develop immunosuppressive conditions which make the animals more susceptible to commensal infections. Further, aging is also associated with the increased error of DNA replication and proofreading which contribute to the transformation of neoplastic tissue (Maynard et al. 2015).

According to this case study, coughing and poor body condition score may indicate a chronic and compensating respiratory syndrome; however, the prognostic decision might need ancillary tests. No report existed when the macaque started exhibiting the syndrome though our daily health supervision had recorded that the coughing remained persistent for about three years. Lung histopathology revealed a classic presentation of suppurative lobar pneumonia with congestive and haemorrhagic capillary vessels. The congestion leading to microhaemorrhages induced the increase of hydrostatic pressure and stretch of endothelial gaps, allowing the plasma to excessively infiltrate the nearby tissue interstitials (Ackermann 2017). The filling of alveolar lumens with plasma and blood cells induced the reflex to expel the fluidic alveolar contents through coughing (Polverino et al. 2012). Visual gross inspection of the lung lobes showed asymmetrical enlargement in the left lobe which might be associated with compensatory adaptation of prolonged low oxygen intake or merely pulmonary exudation. Similarly, Schols and Westerterp (2002) suggested that hypoxic conditions might induce the loss of body fat leading to hypoxia-induced anorexia. Moderate intermittent hypoxic conditions may also induce body weight loss due to the release of leptin and or liver leptin which inhibits fat deposition, food, and energy intake (Ling et al. 2008).

The series of haematologic tests observed a single event of hypochromic anaemia, however neutrophilic and lymphocytic inflammations might more significantly contribute to the severity. In general, all cellular indices of haematology increased through the progression of the disease, except haemoglobin level (Hb) which gradually declined to the end of the disease. Apparently, the sharp rise of neutrophil and lymphocyte levels contributed mostly to the haematocrit level (Hct). Neutrophil rise might be a classic presentation of a cellular phase of acute inflammation in response to bacterial infection (Ackermann 2017) which might be associated with the presence of suppurative pneumonia. Lymphocytes increase in the response to viral infection and poor physiologic condition and pain might induce stress leukogram (Latimer 2011). In the current study, prolonged pneumonia and pain might contribute to the haemodynamic of the macaque during disease progression.

The mass growing upon its shoulder was diagnosed as squamous cell carcinoma (SCC) according to its architecture and the presence of neoplastic figures. Several skin derivate tumors in macaques were located predominantly in the buccal cavity and it is showing resembling with the human cases (Kollias et al. 1975; Nakamura et al. 2000; Stockinger et al. 2014). Moreover, identification of SCC subtypes has been introduced and classified (Pereira et al., 2007). Either the biopsied and processed tissue from the mass in our case presented a proliferative and inwards invasive of epidermal cells. Outwards growth contained multiple layers of epidermal stratum with minimal thickness of keratinized stratum. Based on the buccal SCC subtype, it was identical to the moderate differentiation subtype which is recognized with no complete keratinized layer of stratum corneum and no presence of keratin pearl (Pereira et al. 2007). There were inflammatory infiltrates in the underneath of invasive projection to the dermal layer; however, the significance of this lesion to the deterioration of its health is apparently low. Several aetiologies have been reported inducing the SCC formation including herpesvirus and papillomavirus infection, UV exposure, some carcinogens, and aging (Molho-Pessach and Lotem 2007;

Tsatsou et al. 2012), however, the transformation causing of epidermal cells in the current study is still unknown. This superficial mass might be misdiagnosed as skin abscess but it can be easily discriminated by using basic cytological examination such as fine needle biopsy which can assess the cellular content (Kashi et al. 2011).

Tetanus came up as the final event of this disease complication. Although no ancillary test was performed in the current study to confirm the presence of *Clostridium tetani*, but the clinical symptoms suggested the tonic muscle spasm of the jaw and extremities (Hassel 2013). Springer et al. (2009) suggested that tetanus is very common in those nonhuman primates in which metal circumstance is suitable for the germination of clostridial spores.

In the current case study, it was believed that routine health examination and screening will be helpful in the early detection of visible animal diseases. According to our experience, health supervision in wild animals can be tricky considering their ability to mask the pain in the wild. The animals might look healthy with no sign of abnormality, however, there will be a concealed developing disease that visibly ends up as sudden severe disease. Thus, the results of the current study strongly recommend a regular periodic health examination and this will be beneficial in significantly reducing the morbidity and mortality of animals in rehabilitation centers.

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