



NOTE

Pathology

A bronchopulmonary artery fistula in a horse

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ABSTRACT. A 24-year-old, Thoroughbred gelding presented with difficulty breathing for a few days and intermittent nose bleeding before dying. At necropsy, the bronchoesophageal artery and the bronchial artery that flowed into the left anterior lobe were tortuous and dilated, and it was found that dilated tortuous branches of the bronchial artery ran over the dorsal and ventral surfaces of the left anterior lobe. Histopathologically, an anastomosis between a muscular artery and an elastic artery were demonstrated, which were identified as bronchial and pulmonary arteries, respectively. Based on the gross and histopathological findings, a bronchopulmonary artery fistula was diagnosed. To the best of our knowledge, this is the first case report of a pulmonary vascular anastomosis in a horse.

KEY WORDS: anastomosis, bronchial artery, horse, lung, pulmonary artery

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Two types of pulmonary vascular anastomosis are known to exist: arterial/arterial and arterial/venous anastomoses, depending on the types of blood vessels involved. In bronchopulmonary artery fistulas (BPAF), a bronchial artery from the systemic circulation and a pulmonary artery from the pulmonary circulation are in direct communication; i.e., they are connected by an anastomosis [5]. In humans, BPAF are characterized by meandering/dilation of the bronchial arteries and dilation of the pulmonary arteries, and they can sometimes cause hemorrhaging or dyspnea, which can be fatal [5, 11].

In horses, vascular anastomoses have been reported in several organs, including the skin [12], hoof [9], and testis [4]; however, no cases of vascular anastomoses in the lungs have been reported. In this paper, we describe the first case of a BPAF in a horse.

A 24-year-old, Thoroughbred gelding, was found dead in its stall. It had presented with breathing difficulties for a few days before its death, and intermittent nose bleeding had also been seen. It had developed osteoarthritis in both carpal joints and chronic laminitis in both forelimbs, and had been given treatment to ameliorate its symptoms and manage any pain. No other abnormalities were noted. For economic reasons, the horse had not been examined by a veterinarian since presenting with symptoms. Its whole body was submitted for a necropsy.

At necropsy, the gelding weighed 430 kg. Foam and hemoid fluid had accumulated in the bronchi, and the lungs were edematous. Pulmonary hemorrhages were observed in the anterior lobe and the anterior region of the posterior lobe of the left lung. The bronchoesophageal artery and the bronchial artery that flowed into the left anterior lobe were dilated and tortuous (Supplementary Fig. 1), and dilated tortuous bronchial artery branches ran over the dorsal and ventral surfaces of the left anterior lobe (Fig. 1a). The cut surface of the left anterior lobe revealed that the dilated bronchial artery had formed a multicystic and partially lobulated lesion (Fig. 1b). Hemorrhaging was also observed at the base of the skull and the base of the brain. No other similar lesions were seen in other organs, including other pulmonary lobes.

The tissues collected during the necropsy were fixed in 10% neutral-buffered formalin, processed routinely, embedded in paraffin wax, and cut into 4- μ m-thick sections. The sections were stained with hematoxylin and eosin (HE), elastica-van Gieson (EVG), Masson's trichrome (MT), and Berlin blue stain, before being subjected to light microscopic examinations.

Histologically, the multicystic lesion in the left anterior lobe was composed of two dilated and irregularly thickened vascular structures, which were confirmed to be a muscular artery and an elastic artery, respectively, by EVG staining (Fig. 2a and 2b), and a few bronchi. Since the cystic lesion was grossly contiguous with the bronchoesophageal artery, the muscular artery that formed the lesion was considered to be a bronchial artery, and the elastic artery was considered to be a pulmonary artery. The dilated bronchial artery had compressed the bronchial tissue, which had caused the bronchial tissue to deform and part of the dilated bronchial artery wall to protrude into the bronchial submucosa. The vascular walls of these arteries exhibited various degrees of thickening together with hyperplasia of the intima and tunica media. Staining of the thickened vascular walls revealed elastic fibers and fibromuscular hyperplasia in the intima, and increased fibrous density and smooth muscle hyperplasia in the tunica media,

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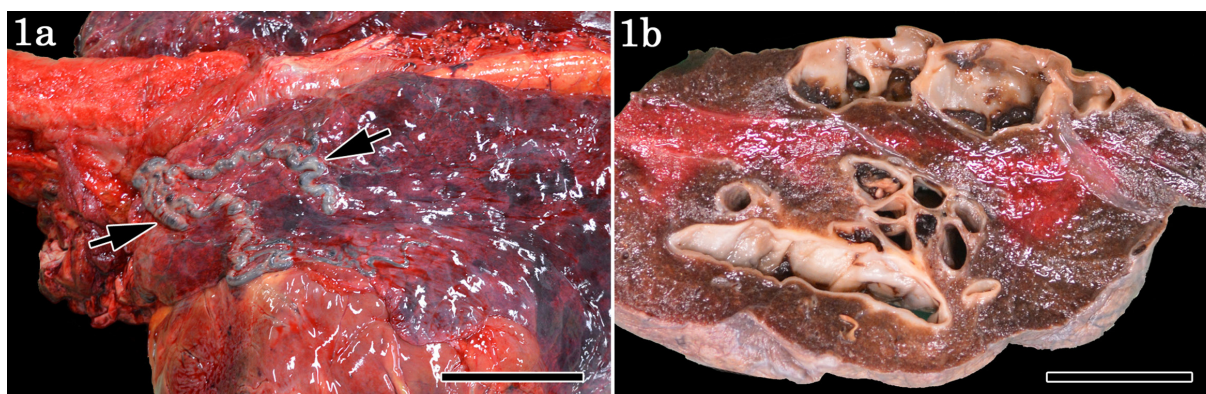


Fig. 1. Gross photographs of the lung of the gelding. **a.** The bronchial artery branches that ran across the ventral surface of the anterior lobe were dilated and tortuous (arrows). Bar=10 cm. **b.** The cut section of the anterior lobe showed a multicystic lesion and the partial retention of blood clots. Bar=2 cm.

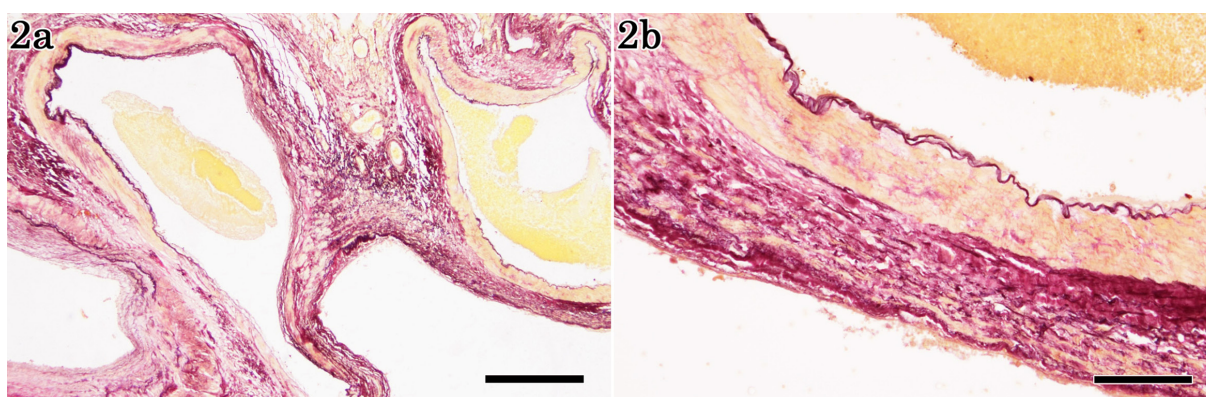


Fig. 2. Histopathological images of the multicystic lesion in the anterior lobe of the lung. **a.** The lesion was composed of markedly dilated and irregularly thickened vascular structures. Elastica-van Gieson (EVG). Bar=500 μ m. **b.** A higher magnification of the vascular walls depicted in 1a is shown. The dilated vascular walls displayed the characteristics of muscular or elastic arteries. EVG. Bar=100 μ m.

which were partly responsible for the observed variations in the degree of thickening (Supplementary Fig. 2a–f). In addition, the vascular walls of the dilated arteries had thinned in some regions due to the disappearance of medial structures. Serial sections of the multicystic lesion revealed that the walls of the thickened pulmonary artery exhibited marked fibrosis and elastin deposition, and the artery was anastomosed to the dilated and thickened bronchial artery wall (Fig. 3a–e). The vascular anastomotic lesions were detected only at this site through all histological examinations. The bronchial artery branches running across the left anterior lobe’s surface and the bronchoesophageal artery also exhibited varying degrees of thickening, together with hyperplasia of the intima and tunica media, as was seen in the bronchial artery. In the left anterior lobe, widespread alveolar hemorrhaging and a region of pulmonary edema accompanied by hemorrhaging and alveolar macrophage infiltration were observed, and Berlin blue stain revealed scattered hemosiderin deposits in the fibrotic stroma around the vascular lesion. Widespread pulmonary edema was also present in the other pulmonary lobes. Small arteries, veins, and capillaries that exhibited hyperemia and congestion were also widespread.

Based on its gross and histopathological findings, the lesion in the anterior lobe of the left lung was diagnosed as an anastomosis of bronchial and pulmonary arteries accompanied by aberrant dilation of the bronchoesophageal and bronchial arteries; i.e., a BPAF.

Pulmonary vascular anastomosis rarely occurs in animals, and only 3 cases have been reported. Spontaneous cases of pulmonary vascular anastomosis have been reported in a dog [8] and an alpaca [10], and the surgical creation of both a pulmonary arteriovenous anastomosis and a cavopulmonary anastomosis was described in a lamb [1]. In horses, vascular anastomoses have been reported in several organs, including the skin [12], hoof [9], and testis [4]; however, no cases of vascular anastomoses in the lungs have been reported. This is the first report about a pulmonary vascular anastomosis; i.e., a BPAF, in a horse.

In the present case, the bronchoesophageal artery and the bronchial artery that flowed into the left anterior lobe were found to take abnormal courses during a gross examination. In humans, it is known that abnormal bronchial artery courses can occur secondary to pulmonary vascular disorders, such as bronchial aneurysms and vascular anastomoses; pneumonia; and pulmonary tumors [11]. In the current case, an anastomosis between the bronchial and pulmonary arteries was noted during a histological examination, but no local lesions or other pulmonary diseases were observed. These findings indicated that the abnormal courses of the arteries had been caused by the anastomosis between the bronchial and pulmonary arteries. Generally, pulmonary vascular anastomoses are definitively diagnosed using angiography, CT, and/or MRI in human medicine [5]. In the current case, the

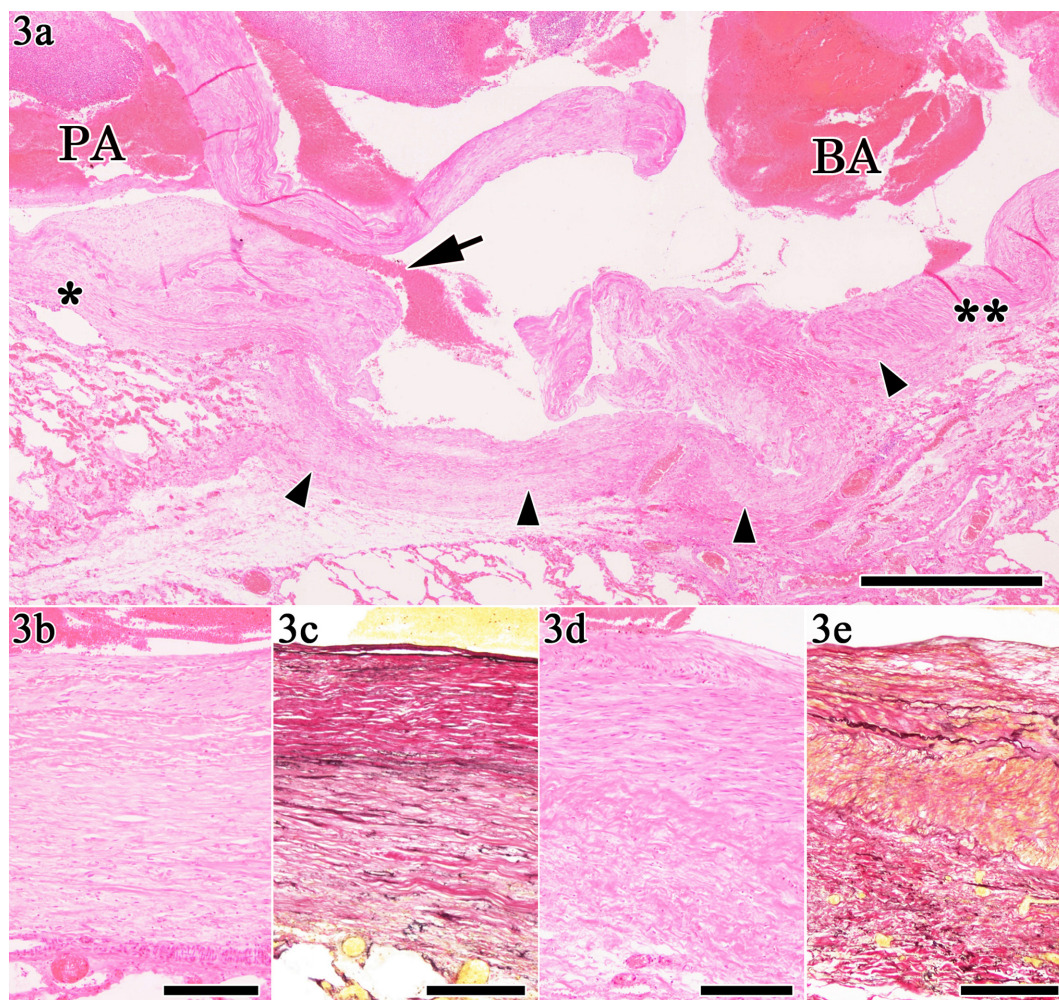


Fig. 3. Histopathological images of the site of the vascular anastomosis. **a.** The site of the anastomosis between a pulmonary artery (PA) and a bronchial artery (BA) is shown. A channel that allowed blood flow between the PA and BA formed (arrow). The wall on the pulmonary artery side (*) and bronchial artery side (**) are continuous as one blood vessel wall (arrowheads). Hematoxylin and eosin (HE). Bar=700 μ m. **b** and **c.** The vascular wall on the pulmonary artery side of the anastomosis was composed of an elastic artery, which had thickened markedly due to collagen fiber hyperplasia. **b:** HE. Bar=200 μ m. **c:** elastica-van Gieson (EVG). Bar=200 μ m. **d** and **e.** The vascular wall on the bronchial artery side of the anastomosis displayed elastic fibers and fibromuscular hyperplasia in the intima, a multilayered inner elastic membrane, and increased fibrous density and smooth muscle hyperplasia in the tunica media. **d:** HE. Bar=200 μ m. **e:** EVG. Bar=200 μ m.

bronchoesophageal artery and a bronchial artery exhibited abnormal courses during gross examinations, and an anastomosis between the bronchial artery and a pulmonary artery was found during a histological examination. In horses, the BPAF could be difficult to detect clinically at present. The present case suggested that it is necessary to carefully search of the tissues for detection of the vascular anastomosis site, when the characteristic vascular abnormalities are grossly observed.

Histopathologically, the lesion in the left anterior lobe was composed of two different types of blood vessels, and the walls of the blood vessels varied in thickness, due to the presence of elastic fibers and fibromuscular hyperplasia in the intima and increased fibrous density and smooth muscle hyperplasia in the tunica media. These histological findings were considered to reflect changes in the bloodstream and blood pressure [3, 10]. Furthermore, the presence of hyperplastic changes in the vascular walls of two different types of blood vessel was suggestive of an anastomosis between the blood vessels. It was considered that the vascular wall thickening and dilation seen in the present case were produced by blood flow from the high-pressure bronchial artery into the low-pressure pulmonary artery. The severe fibrosis observed in the pulmonary artery walls in the anastomotic region indicated that the lesion had existed for a long time.

In humans, BPAF are classified into congenital and acquired types, according to their causes [6, 7]. Congenital BPAF are caused by developmental vascular anomalies that arise during the fetal period [14]. Acquired BPAF occur secondary to pulmonary conditions, such as inflammation or tumors, and are caused by pulmonary artery stenosis or occlusion [6, 7]. In addition, it has been reported that the congenital types of BPAF was diagnosed not only in young patients but also in elderly patients with BPAF based on the absence of primary pulmonary disease [6]. In the current case, no pulmonary disease was found during gross or histological examinations, and thus, it was presumed that the horse might have had congenital pulmonary vascular disease.

However, it was difficult to definitively determine the type of the lesion because a detailed anamnesis was not available.

In the present case, except for the vascular lesion in the left anterior lobe, no lesions that could have caused the respiratory problems or nose bleeding observed before the horse's death were found during the autopsy; therefore, it was concluded that these symptoms were caused by the pulmonary vascular lesion. In addition, it was considered that the presence of old and widespread hemorrhaging around the vascular lesion and in the pulmonary parenchyma and the bronchial compression caused by the vascular lesion confirmed the involvement of the vascular lesion in these symptoms.

In human BPAF, severe bleeding related to vascular anastomoses can be fatal [5, 11]. Depending on the degree of blood vessel anastomosis, hypoxemia and heart failure can also arise [5]. Regarding the pulmonary bleeding seen in the current case, it was considered that the amount of bleeding was not directly related to the cause of death, and no obvious ruptured blood vessels were found during gross or histological examinations. Therefore, the pulmonary bleeding was considered to have been due to a vascular leak caused by an increase in vascular pressure associated with the anastomosis, and the pulmonary edema was also considered to be related to the vascular anastomosis (which might have caused pulmonary congestion). Although the definitive cause of death could not be determined in the present case, as the anastomosis involved bronchial and pulmonary arteries it would have resulted in the mixing of arterial and venous blood, leading to conditions such as insufficient oxygenation of the blood, congestion, blood leakage, and/or pulmonary edema, and it was presumed that these conditions led to a vicious cycle that resulted in dyspnea and/or heart failure. The hemorrhage seen at the base of the cerebrum and the right skull was relatively new, suggesting that it had occurred just before death, and it was suspected that it might have been caused by a trauma, such as a fall due to loss of consciousness or limb disease. The intracranial hemorrhage might have exacerbated the pulmonary edema.

In horses, various pulmonary diseases that cause nose bleeding and respiratory abnormalities have been reported [13], and exercise-induced pulmonary hemorrhaging (EIPH) is a relatively common vascular lesion-induced disease [2]. The characteristic lesion of EIPH, which is composed of venous fibrosis, particularly affects the adventitia of small veins and is usually observed in the posterior lobe of the lung. In some veins, fibrosis also affects the intima and can narrow the vein lumen [2]. The vascular lesion in the current case was macroscopically located in the blood vessels that supplied blood to the anterior lobe of the left lung. Furthermore, the anastomosis was composed of two different histological types of thick blood vessels; i.e., a pulmonary artery (an elastic artery) and a bronchial artery (a muscular artery). These gross and histological features of the vascular lesion indicated that the horse's pathological condition was distinct from EIPH.

This paper reported the occurrence of a BPAF in an aged horse, which died with clinical signs of epistaxis and respiratory abnormalities. Equine pulmonary vascular disease causes epistaxis and respiratory abnormalities in horses. Vascular anastomoses; i.e., BPAF, can also cause these symptoms, and BPAF should be added to the list of differential diagnoses for horses that present with such symptoms.

DECLARATION OF CONFLICT INTERESTS. The authors declare that there are no potential conflicts of interest with this manuscript.

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