

[CASE REPORT]

Hemorrhaging from an Intramedullary Cavernous Malformation Diagnosed Due to Recurrent Pneumonia and Diffuse Aspiration Bronchiolitis

Yuki Yoshimatsu^{1,2}, Kazunori Tobino^{1,3}, Takafumi Kawabata¹, Naoki Noguchi⁴,
Ryo Sato⁵, Daisuke Motomura⁶, Takuto Sueyasu¹, Kohei Yoshimine¹,
Saori Nishizawa¹ and Yoshihiro Natori⁴

Abstract:

While aspiration pneumonia constitutes the majority of pneumonia cases in the elderly, it remains highly underdiagnosed. We experienced a case of recurrent pneumonia and chronic cough that was later diagnosed as aspiration pneumonia and diffuse aspiration bronchiolitis (DAB) due to recurrent hemorrhaging from an intramedullary cavernous malformation. The patient was finally diagnosed when life-threatening respiratory depression caused emergency attention. This is the first report of hemorrhaging from an intramedullary cavernous malformation diagnosed due to aspiration pneumonia and DAB. These findings highlight the importance of considering aspiration in cases with recurrent pneumonia or chronic cough. The underlying cause may be a life-threatening condition.

Key words: aspiration pneumonia, diffuse aspiration bronchiolitis, dysphagia, stroke, intramedullary cavernous malformation

(Intern Med 60: 1451-1456, 2021)
(DOI: 10.2169/internalmedicine.5752-20)

Introduction

The majority of elderly patients hospitalized for pneumonia have been found to have aspiration pneumonia. In one study, 80.1% of patients ≥ 70 years old who were admitted for pneumonia had aspiration pneumonia (1). However, it can be difficult to distinguish whether pneumonia is due to aspiration or not, and the entity remains highly underdiagnosed despite its high morbidity and mortality. Even when aspiration is suspected, the cause remains undiagnosed or uninvestigated in many cases. In our previous study, 30.7% of those suspected of having aspiration pneumonia were later diagnosed with a causative condition of aspiration that was initially left unrecognized (2).

We herein report a patient who suffered recurrent pneu-

monia and chronic cough that turned out to be aspiration pneumonia and diffuse aspiration bronchiolitis (DAB), owing to a swallowing disorder due to hemorrhaging of an intramedullary cavernous malformation. She was finally diagnosed when life-threatening respiratory depression caused emergency attention. The cavernous malformation was managed conservatively, while the dysphagia assessment and treatment required substantial time and effort. Evidence concerning the conservative management of cavernous malformation and swallowing disorders due to this condition is insufficient at present. To our knowledge, this is the first case report of hemorrhaging from an intramedullary cavernous malformation that was diagnosed due to aspiration pneumonia and DAB.

¹Department of Respiratory Medicine, Iizuka Hospital, Japan, ²Department of Physiology, Hyogo College of Medicine, Japan, ³Department of Respiratory Medicine, Juntendo University Graduate School of Medicine, Japan, ⁴Department of Neurosurgery, Iizuka Hospital, Japan, ⁵Department of Gastroenterology, Iizuka Hospital, Japan and ⁶Department of Rehabilitation, Iizuka Hospital, Japan
Received: July 1, 2020; Accepted: October 7, 2020; Advance Publication by J-STAGE: December 7, 2020
Correspondence to Dr. Yuki Yoshimatsu, yukitsukihana0105@gmail.com

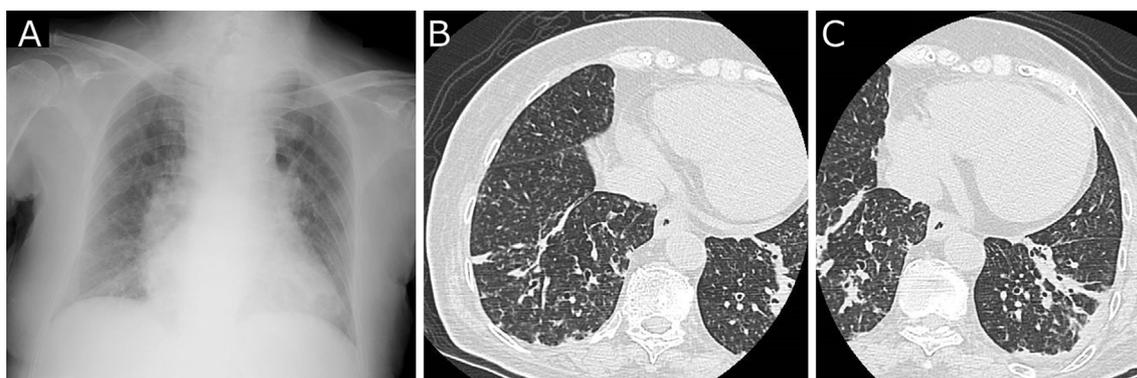


Figure 1. Chest images on admission. (A) Chest X-ray shows bilateral micronodular changes in the lower lung fields. (B) (C) Chest computed tomography shows diffuse micronodules, branching areas of increased attenuation (tree-in-bud opacities), bronchiectasis, band-like opacities, and partial atelectasis, all of which were more predominant in the lower lobes and posterior regions than in other areas.

Case Report

A 74-year-old woman hospitalized for pneumonia in an acute care hospital was transferred to our hospital for respiratory depression. She had also been hospitalized for pneumonia five months ago, after which a low-grade fever and productive cough had continued until the second admission. This time, she was hospitalized for pneumonia and was recovering with antibiotic treatment. However, after five days, she suddenly fell unconscious and was found to be in respiratory depression (hypopnea). Manual ventilation was immediately initiated while she was being transferred to our hospital.

She had a history of an intramedullary cavernous malformation, which had first been diagnosed two years ago during the investigation of hypoalgesia on the left side of her body (including the arm, torso, and leg) and had since been observed regularly. The cavernous malformation had originally been 10 mm in diameter but had enlarged to 13 mm at the most recent magnetic resonance imaging (MRI) session, performed 2 months prior to admission. In addition, she had a history of a thyroid tumor that was also being observed regularly, breast cancer that had been treated surgically four months previously, type 2 diabetes mellitus, hypertension, and hyperlipidemia. Her regular medication included linagliptin, amlodipine, telmisartan, atorvastatin, pregabalin, methylcobalamin, anastrozole, and levothyroxine. She had never smoked and did not drink alcohol. She had no family history of cerebrovascular or respiratory disease.

On arrival, she had regained full consciousness, and her breathing had also stabilized. Oxygen saturation was 98% on 2 L of oxygen per minute, and the respiratory rate was 18 per minute. Blood pressure was 145/70 mmHg, heart rate was 95 per minute, and body temperature was 36.8°C. Slight coarse crackles were heard bilaterally in the lower lung fields on inspiration, and the heart sounds were normal. A neurological examination revealed hypoalgesia on the left

side of her body (the torso and upper and lower extremities) and decreased superficial sensation and partial paralysis on the right (excluding the face), all of which she reported to be chronic symptoms. Laboratory data were unremarkable, except for elevated inflammatory marker and glucose levels (white blood cell count 18,170/mm³, C-reactive protein 7.39 mg/dL, blood glucose level 258 mg/dL). Chest X-ray showed bilateral micronodular changes in the lower lung fields. Chest computed tomography (CT) showed diffuse micronodules, branching areas of increased attenuation, bronchiectasis, band-like opacities, and partial atelectasis, all of which were predominant in the lower lobes and posterior regions (Fig. 1). Head CT revealed a 25-mm high-density tumor-like lesion in the medulla compressing the cerebellar vermis and tonsils, suggesting hemorrhaging from the intramedullary cavernous malformation (Fig. 2).

The hemorrhaging from the cavernous malformation was managed conservatively with strict control of blood pressure, intravenous tranexamic acid infusion, and bed rest. Confirming that there was no further hemorrhaging or enlargement of the hemangioma with regular CT follow-up, the patient was mobilized gradually under careful blood pressure monitoring. MRI performed on day 12 after admission showed a 20-mm hypointense lesion in the medulla with peripheral hyperintensity on T1-weighted imaging and a hyperintense lesion with peripheral hypointensity on T2-weighted imaging (Fig. 2). These MRI findings confirmed the diagnosis of subacute hemorrhaging from the known intramedullary cavernous malformation.

Treatment for the pneumonia was continued with intravenous antibiotics and pulmonary rehabilitation, but the pneumonia continued to worsen. Sputum and blood cultures taken on admission and on each day after admission were unremarkable, including no indication of mycobacterium species. Empiric antibiotic treatment with piperacillin tazobactam and meropenem was ineffective. She developed hypercapnia and respiratory failure. An arterial blood gas analysis revealed a pH of 7.307, partial pressure of oxygen

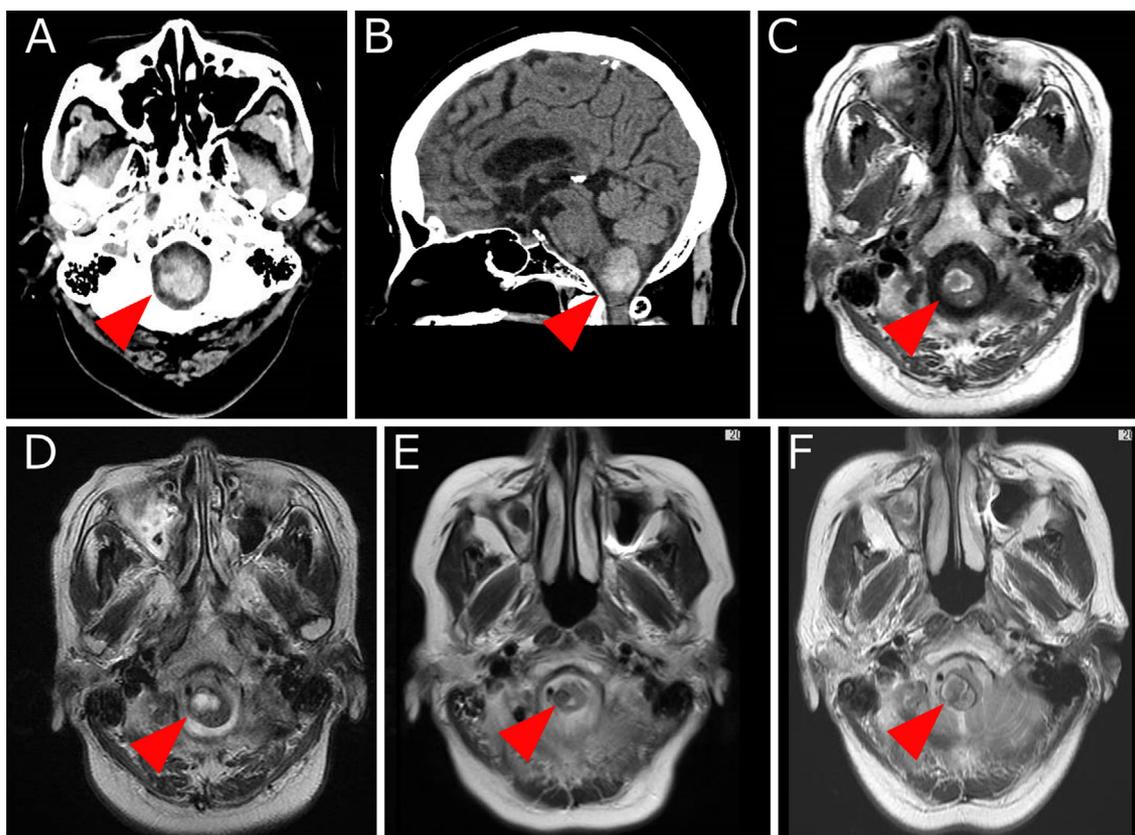


Figure 2. Images of the head. Head CT (A, B) taken on admission shows a 25-mm high-density tumor-like lesion in the medulla compressing the cerebellar vermis and tonsils. Magnetic resonance imaging performed on day 12 shows a 20-mm hypointense lesion in the medulla with peripheral hyperintensity on T1-weighted imaging (C) and a hyperintense lesion with peripheral hypointensity on T2-weighted imaging (D). T2-weighted images taken one year (E) and two months (F) prior to presentation are shown for reference. The cavernous malformation is shown with red arrowheads.

104.3 mmHg, and partial pressure of carbon dioxide 65.9 on oxygen (10 L/min by mask). Therefore, she required respiratory support with noninvasive positive-pressure ventilation.

Bedside screening tests for dysphagia (modified water swallowing test and food test) were unremarkable; however, silent aspiration was suspected due to an episode of respiratory distress after taking sips of water. On a videoendoscopic evaluation of swallowing (VE), the right vocal cord was paralyzed, and the left vocal cord showed extensive adduction. Laryngeal sensation and cough reflex was diminished. Silent aspiration of thickened liquid could be identified (Fig. 3A). This was confirmed on a videofluoroscopic swallow examination (VFSE). She was diagnosed with swallowing disorder of the pharyngeal phase. Swallowing compensation techniques (such as head rotation to the right, or body tilting to the left with or without head rotation to the right) did not enable safer swallowing (Fig. 3B). Therefore, it was decided that continuing to eat or drink would cause a high risk of aspiration. All oral intake was stopped, and nutrition was administered through an 8-Fr nasogastric feeding tube. Specialized oral care was performed by dental hygienists to limit the risk of aspiration pneumonia.

The patient's pneumonia and respiratory condition improved after stopping all oral intake and introducing regular

oral care by dental hygienists. However, daily swallowing training by a speech therapist had little effect on the swallowing function. Surgical resection of the cavernous malformation was considered. However, after carefully weighing the potentially life-threatening risks related to the procedure and the likelihood that it might not completely cure the dysphagia, the patient chose not to undergo surgery.

Through multidisciplinary team discussions, it was decided that long-term training was necessary, and that safe nutritional management during that period was vital. The nasogastric feeding tube that was meant to help maintain an adequate nutritional status was disrupting the pharyngeal movement and possibly worsening the risk of silent aspiration. Therefore, gastrostomy was performed on day 35 of admission. After gastrostomy (and subsequent removal of the nasogastric tube), the symptoms and findings of DAB resolved (Fig. 4), and the chest sounds were normal. Adequate nutrition was able to be provided without discomfort or increased salivation, and swallowing training showed more prominent effects. VFSE on day 51 showed an improved swallowing function and no aspiration with small amounts of thickened liquids, so it was decided that direct training with liquids and pureed diets could be initiated. The patient was transferred to a rehabilitation hospital on day 63

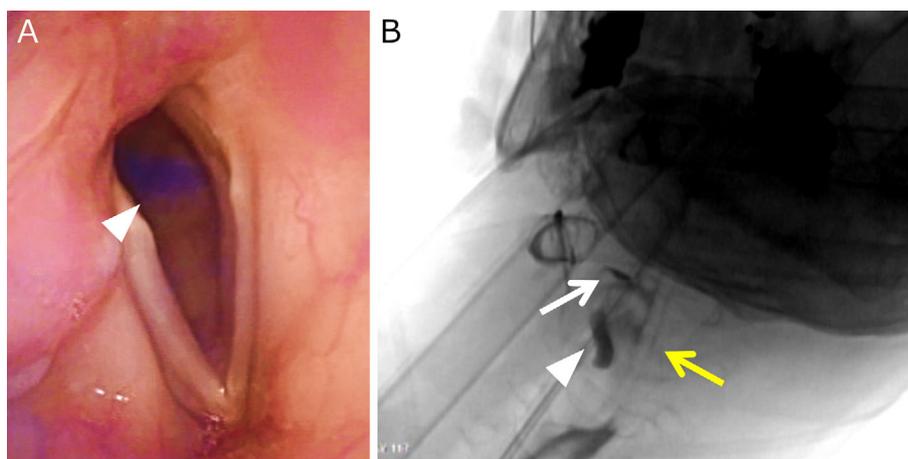


Figure 3. A swallowing assessment. (A) A videoendoscopic swallow examination using purple-dyed thickened liquid showed silent aspiration (arrowhead). The right vocal cord was paralyzed, and the left vocal cord showed extensive adduction. (B) On a videofluoroscopic swallow examination, silent aspiration was seen despite swallowing compensation techniques (tilting the body to the left with head rotation to the right). The aspirated material is indicated with an arrowhead. The vocal cords are shown with a white arrow, and the nasogastric tube (and esophagus) is shown with a yellow arrow.

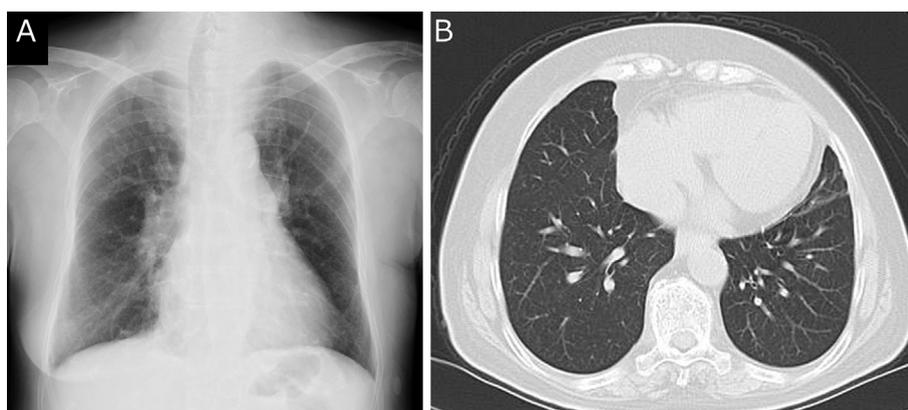


Figure 4. Chest images two months after the onset. (A) Chest X-ray shows improved opacity in all lung fields. (B) Chest computed tomography shows that the diffuse micronodules and tree-in-bud opacities have resolved.

for further training and discharged home on day 98. At that point, she was eating normal foods and liquids. There were no sequelae in the extremities attributed to this hemorrhagic episode, apart from the chronic symptoms she had already had before this hospitalization.

Follow-up MRI showed that the hemorrhaging had receded, and there was no enlargement or further hemorrhaging from the intramedullary cavernous malformation; in addition, follow-up chest CT also showed no recurrence of DAB. For two years since the first episode, there has been no recurrence of hemorrhaging, pneumonia, or DAB.

Discussion

We experienced a case of life-threatening hemorrhaging from an intramedullary cavernous malformation that caused respiratory depression and unresolving pneumonia. The cav-

ernous malformation and symptoms of pneumonia and DAB were both being followed up in different clinics. However, the underlying swallowing disorder and the causal relationship between them were unclear. It is important for physicians to be aware of the different entities causing pneumonia and to be able to investigate the causes efficiently (2).

Cavernous malformations (or cavernomas, cavernous angiomas, or cavernous hemangiomas) are cerebral vascular abnormalities composed of clusters of malformed, hyalinized capillaries surrounded by hemosiderin deposits and a gliotic margin (3). Its incidence is reported to be 0.4% to 0.8% and is seen in various parts of the brain, with up to 80% of cases being supratentorial (3, 4). Primary symptoms range from new-onset seizures or headaches in supratentorial cavernous malformations to progressive neurological deficits in infratentorial lesions (5). The risk of primary hemorrhaging is said to be 0.7-1.1% annually, rising to 4.5% after a previ-

ous instance of hemorrhaging (6). This risk increases in cases with an infratentorial location, larger and more deeply located lesions, and female gender (6).

Treatments of cavernous malformations generally consist of either conservative management (control of blood pressure and yearly MRI), surgical resection, or stereotactic radiosurgery. Since there is a risk associated with invasive intervention, conservative management is recommended in cases with no clinical symptoms or patients with a single episode of severe hemorrhaging in an eloquent cortex (which directly control physical functions). Intervention is recommended when there are symptoms, such as seizure, progressive neurological deterioration, or hemorrhaging, in a non-eloquent cortex (where symptoms are less severe) or two instances of hemorrhaging in an eloquent cortex (where symptoms can be more severe) (7). The risks of complications associated with surgery vary depending on the location of the lesion.

Brainstem cavernous malformations make up approximately 20-35% of all cavernous malformations, and the annual hemorrhaging rate is higher than those in other areas of the brain (0.25-6.5% per patient-year, and as high as 3.8-60% after previous incident of hemorrhaging) (8). Hemorrhaging in the brainstem causes neurological deficits in 60% of patients, which decreases with time as the hemorrhaging improves or the blood is absorbed (6). Because of this characteristic attenuation in symptoms and the relatively high risk of intervention, surgical resection is limited to cases with a severe clinical presentation.

In the present case, the symptoms were severe, including loss of consciousness, respiratory depression, and swallowing disorder of the pharyngeal phase (silent aspiration). It was suspected that there had already been multiple instances of hemorrhaging, as the hemangioma was growing yearly with a characteristic “popcorn” appearance on MRI and fluctuating neurologic symptoms. However, after weighing the risks associated with surgery and the likelihood that the whole lesion could not be resected (as the size was too large and intervention was considered likely to interfere with innervation of the heart), the patient opted for conservative management. Decisions like this are extremely difficult to manage. We held multiple multidisciplinary team discussions with physicians from the neurosurgery, pulmonology, rehabilitation, and otolaryngology departments as well as speech therapists, nurses, and a dietician, along with the patient and her family. This enabled the patient to make decisions based on her beliefs and values, as well as the medical expertise offered.

Conservative management in our patient included antihypertensive drugs and dietary restrictions to keep the systolic blood pressure below 120/80 mmHg and close follow-up with MRI every 6 months. This was effective, and her neurological symptoms continued to improve, while imaging findings also showed improvement. Had the treatment been initiated earlier, this lethal hemorrhagic episode may have been prevented. It is important to manage blood pressure

strictly in cases with cavernous malformations, especially when located in the brainstem. However, there is still no consensus regarding the optimal blood pressure for preventing hemorrhaging from a cavernous malformation. Guidelines for intracranial hemorrhaging recommend maintaining the systolic blood pressure below 140 mmHg (9). In the clinical setting, this is often considered in the conservative management of hemorrhaging from cavernous malformations. Measures such as a blood pressure diary or a wearable continuous blood pressure monitor may be effective for monitoring the blood pressure throughout the day.

The chronic low-grade fever, cough, and tree-in-bud opacities on chest CT were suggestive of tuberculosis or diffuse panbronchiolitis (DPB). However, these differential diagnoses did not explain the abrupt onset five months ago or the improvement with antibiotics. A careful history collection, physical examination, and clinical reasoning concerning the intramedullary cavernous malformation hemorrhaging led to a suspected diagnosis of DAB. This was confirmed with silent aspirations seen on the swallowing assessment. The symptoms and image findings receded by stopping all oral intake and performing specialized oral care, which also supported the diagnosis. When physicians encounter recurrent pneumonia or an unresolving low-grade fever and chronic cough, the possibility of aspiration must always be kept in mind. Intramedullary lesions, such as cavernous malformations or Wallenberg’s syndrome, can often present with mere globular palsy (i.e., symptoms concerning swallowing or articulation) and no other apparent symptom. However, these less-symptomatic conditions are nonetheless life-threatening when left unnoticed. In our previous study, 30.7% of cases suspected of having aspiration pneumonia were later diagnosed with a causative condition of aspiration that was initially unrecognized, 9.6% of which were acute stroke (2). This highlights the importance of considering brainstem lesions in patients with suspected dysphagia, regardless of the patient’s general condition.

DAB can occur with only mild symptoms and is often unrecognized. Common symptoms include cough, sputum, fever, and dyspnea, and the diagnosis can be confirmed with characteristic tree-in-bud micronodules on chest CT and an underlying swallowing disorder (10). The most important treatment of DAB is, understandably, the treatment of the condition causing the aspiration. There is also a report on the possible effect of treatment with macrolides (11) and a case report on the successful prevention of aspiration with cricopharyngeal myotomy (12). Only when the correct diagnosis of DAB is made can the patient be administered available treatment.

Conclusion

We experienced a severe case of hemorrhaging from an intramedullary cavernous malformation that presented with respiratory depression and unresolving pneumonia. The hemorrhaging was successfully treated with conservative management, and pneumonia was manageable with adequate

nutrition management and rehabilitation. This case highlights the importance of considering silent aspiration and DAB in cases with recurrent pneumonia or a chronic cough and fever. Investigating the cause of aspiration is essential, as the underlying condition may be potentially life-threatening, as was seen in this case.

Informed consent was obtained from the patient and her family discussed in the report.

The authors state that they have no Conflict of Interest (COI).

Acknowledgement

The authors express their sincere gratitude to Takeichiro Aso and Tomohiro Yamashita for their input in swallowing assessment and training.

References

1. Teramoto S, Fukuchi Y, Sasaki H, Sato K, Sekizawa K, Matsuse T. High incidence of aspiration pneumonia in community- and hospital-acquired pneumonia in hospitalized patients: a multicenter, prospective study in Japan. *J Am Geriatr Soc* **56**: 577-579, 2008.
2. Yoshimatsu Y, Tobino K, Ko Y, et al. Careful history taking detects initially unknown underlying causes of aspiration pneumonia. *Geriatr Gerontol Int*. Forthcoming.
3. Dalyai RT, Ghobrial G, Awad I, et al. Management of incidental cavernous malformations: a review. *Neurosurg Focus* **31**: E5, 2011.
4. D'Angelo VA, De Bonis C, Amoroso R, et al. Supratentorial cerebral cavernous malformations: clinical, surgical, and genetic involvement. *Neurosurg Focus* **21**: 7, 2006.
5. Hauck EF, Barnett SL, White JA, Samson D. Symptomatic brainstem cavernomas. *Neurosurgery* **64**: 61-71, 2009.
6. Mouchtouris N, Chalouhi N, Chitale A, et al. Management of cerebral cavernous malformations: from diagnosis to treatment. *Sci World J* 808314, 2015.
7. Steinberg GK, Chang SD, Gewirtz RJ, Lopez JR. Microsurgical resection of brainstem, thalamic, and basal ganglia angiographically occult vascular malformations. *Neurosurgery* **46**: 260-271, 2000.
8. Garrett M, Spetzler RF. Surgical treatment of brainstem cavernous malformations. *Surg Neurol* **72**: S3-S10, 2009.
9. Hemphill JC 3rd, Greenberg M, Anderson C, et al. Guidelines for the management of spontaneous intracerebral hemorrhage: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* **46**: 2032-2060, 2015.
10. Hu X, Yi ES, Ryu JH. Diffuse aspiration bronchiolitis: analysis of 20 consecutive patients. *J Bras Pneumol* **41**: 161-166, 2015.
11. Miyashita N, Kawai Y, Kato T, et al. Macrolide therapy for prevention of exacerbation in individuals with diffuse aspiration bronchiolitis. *J Am Geriatr Soc* **64**: 665-666, 2016.
12. Inoue T, Oida K, Kohri Y, et al. Successful treatment of diffuse aspiration bronchiolitis by cricopharyngeal myotomy. *Nihon Kyobu Shikkan Gakkai Zasshi* **34**: 926-930, 1996 (in Japanese, Abstract in English).

The Internal Medicine is an Open Access journal distributed under the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License. To view the details of this license, please visit (<https://creativecommons.org/licenses/by-nc-nd/4.0/>).