Radiology Case Reports 19 (2024) 5507–5512

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journal homepage: www.elsevier.com/locate/radcr

Case Report

Catheter embolization for pulmonary arteriovenous malformations during chemotherapy for appendiceal adenocarcinoma: A case report of associated brain abscess ☆

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ARTICLE INFO

Article history:
Received 14 June 2024
Revised 11 August 2024
Accepted 12 August 2024

Keywords:
Catheter embolization
Arteriovenous malformation
Brain abscess
Chemotherapy
Appendiceal adenocarcinoma

ABSTRACT

Pulmonary arteriovenous malformations are rare, abnormal, low-resistance vascular structures that connect a pulmonary artery to a vein. They are common in patients with hereditary hemorrhagic telangiectasia; however, acquired malformations can occur in patients with underlying diseases such as chest trauma, hepatic cirrhosis, and mitral stenosis. Pulmonary arteriovenous malformations bypass the normal pulmonary capillary bed and result in intrapulmonary right-to-left shunts, which may cause central nervous system complications such as brain abscesses or ischemic stroke. Brain abscesses related to pulmonary arteriovenous malformations are not uncommon; however, reports of their occurrence during chemotherapy are limited. Here, we report the case of a 68-year-old woman with bilateral pulmonary arteriovenous malformations and appendiceal adenocarcinoma who developed a bacterial brain abscess during chemotherapy. The infection was treated using abscess drainage and antibiotic therapy. After the brain abscess healed, catheter embolization was performed on the pulmonary arteriovenous malformations and chemotherapy was resumed. The present case suggests that if a patient with a malignancy has a pulmonary arteriovenous malformation, clinicians should pay special attention to complications such as brain abscesses during chemotherapy. For patients who do not urgently need chemother-

☆ Competing Interests: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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https://doi.org/10.1016/j.radcr.2024.08.066

apy, embolization of the pulmonary arteriovenous malformation before chemotherapy may be a better treatment option.

Introduction

Brain abscess is a rare, life-threatening intracerebral infection. It begins as a localized lesion of cerebritis and develops into an encapsulated collection of pus. A brain abscess can be caused by bacteria, fungi, parasites, mycobacteria, and other microorganisms. It is encountered at a frequency of approximately 0.4 to 0.9 cases per 100,000 people per year [1,2]. Increased rates are observed in immunocompromised patients, such as solid organ transplant recipients [3]. Many patients with brain abscesses have predisposing diseases such as otitis media, mastoiditis, dental infection, respiratory infection, bacterial endocarditis, congenital heart disease, and immunocompromise (neutropenia, post-transplantation period, or human immunodeficiency virus infection) [1]. Moreover, hereditary hemorrhagic telangiectasia (HHT) and pulmonary arteriovenous malformation (PAVM) are considered risk factors for brain abscess development [4]. Here, we present a patient with appendiceal cancer and bilateral PAVMs who developed a bacterial brain abscess during chemotherapy.

Case report

A 68-year-old woman with appendiceal adenocarcinoma was referred to our hospital for further treatment. On the first visit to our hospital, the patient had no symptoms or notable medical history. Laboratory test results were mostly within normal limits, except for slightly increased levels of total cholesterol (254 mg/dL; normal range [NR]: 142–248 mg/dL), C-reactive protein (0.24 mg/dL; NR: <0.14 mg/dL), fibrinogen (453 mg/dL; NR: 200–400 mg/dL), and D-dimer (1.2 μg/mL; NR: 0–0.9 μg/mL). The patient's appendiceal cancer was diagnosed as inoperative because computed tomography (CT) revealed multiple metastases to the bilateral supraclavicular, mediastinal, and abdominal para-aortic lymph nodes. Additionally, bilateral PAVMs were identified on CT images (Figs. 1A and B). A 3-weekly capecitabine and oxaliplatin regimen (XELOX) + bevacizumab was initiated. Oxaliplatin was removed from the regimen after 8 courses of XELOX + bevacizumab to prevent further peripheral sensory neuropathy, while the other drugs were continued.

Nine months after the start of chemotherapy, the patient complained of poor appetite, dizziness, and right occipital pain and was admitted to the clinical oncology department. On admission, the patient had a normal level of consciousness, and manual muscle testing showed left hemiparesis with 4/5 and 3/5 strength in the upper and lower extremities, respectively. The patient's body temperature was 39.4°C. The laboratory test results are listed in Table 1. The patient had an elevated white blood cell count and high levels of fibrinogen and D-dimer. Head CT without contrast revealed a low-density area with greatest diameter of 33 mm with surrounding edema lateral to the right lentiform nucleus (Fig. 2A). This area showed a very high-intensity signal on diffusion-weighted magnetic resonance imaging (MRI) (Fig. 2B) and hypointensity on the corresponding apparent diffusion coefficient (ADC) map (Fig. 2C). The mean ADC value was 0.916×10^{-3} mm^2/s). On gadolinium-enhanced T1-weighted MRI, this lesion was accompanied by a smooth, ring-shaped enhancement (Fig. 2D). A metastatic brain tumor was suspected based on the CT image; however, the diagnosis was changed to brain abscess based on the high fever and MR images. Emergent drainage of the brain abscess was performed the day after the MRI. *Streptococcus anginosus* group, *Parvimonas micra*, and *Fusobacterium* spp. were detected in a bacterial culture of the pus. Ceftriaxone sodium hydrate (2 g IV infusion, twice daily) and metronidazole (500 mg IV infusion, 4 times daily) were administered for 6 weeks postoperatively. The patient recovered from the brain abscess with incomplete left hemiparesis.

Catheter embolization using detachable coils was performed on the left PAVM (A9) and right PAVM (A10) 85 days after drainage to prevent recurrence of the brain abscess (Figs. 3A and B). Treatment with capecitabine was resumed 28 days after embolization. The patient was diagnosed with right cerebellar metastasis of the appendiceal adenocarcinoma 3 months after embolization and right occipital metastasis 5 months after embolization. Biopsy was not performed in either region, and the metastases were successfully treated using stereotactic radiotherapy. Except for the central nervous system (CNS) metastases, the patient's appendiceal adenocarcinoma has remained stable, and, at the time of writing, the patient was at the 13th month of resumed capecitabine treatment.

Discussion

PAVMs are rare, abnormal, low-resistance vascular structures that connect a pulmonary artery to a pulmonary vein. PAVMs bypass the normal pulmonary capillary bed, resulting in intrapulmonary right-to-left shunts [5]. PAVMs are common in patients with HHT. However, acquired PAVM can be complicated in patients with chest trauma, thoracic surgery, hepatic cirrhosis, mitral stenosis, actinomycosis, schistosomiasis, systemic amyloidosis, and metastatic cancer [6]. Although patients with PAVMs can be asymptomatic, they become symptomatic with an increasing degree of mixing of deoxygenated blood through PAVMs. Patients may complain of fatigue, dyspnea, and cyanosis due to hypoxemia. Commonly reported complications are associated with the CNS. In 1 study, the incidences of brain abscess and ischemic stroke in patients with PAVMs were 12.8% and 13.7%, respectively [7].

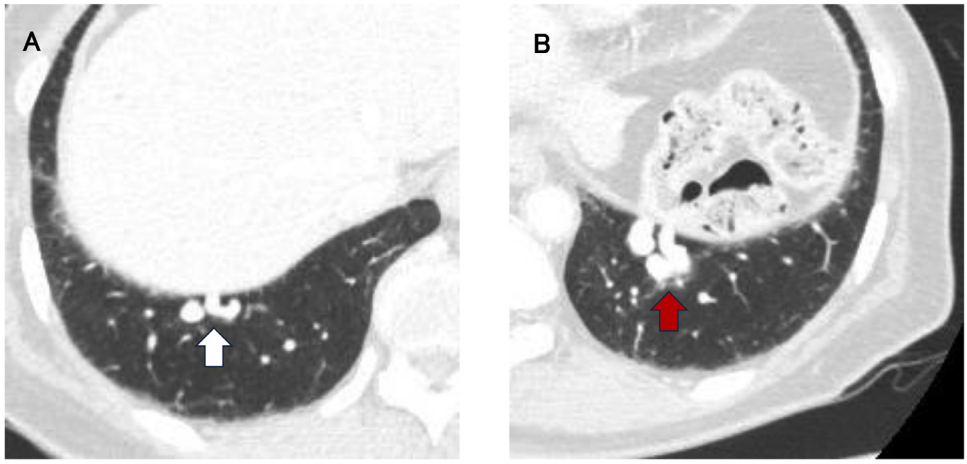

Fig. 1 – Axial computed tomography images of the chest at the first visit. (A) Abnormally dilated vessels are shown in the right lower lobe (white arrow). (B) Similar abnormal vessels are shown in the left lower lobe (red arrow).

Table 1 – Summary of the laboratory data.

		Normal range	admission day
Complete blood count			
White blood cells	× 10 [9]/L	3.3-8.6	12.32
Neutrophils	%	30.0-70.0	90.3
Lymphocytes	%	18.0-55.0	4.5
Monocytes	%	≤12.0	4.4
Eosinophils	%	≤8.0	0.1
Basophils	%	≤2.0	0.2
Large unstained cells	%	1.0-4.0	0.4
Hemoglobin	g/dL	11.6-14.8	13.8
Platelets	× 10 [9]/lL	158-348	174
Biochemistry			
Aspartate aminotransferase	U/L	13-30	22
Alanine aminotransferase	U/L	7-23	12
Lactate dehydrogenase	U/L	124-222	212
Total bilirubin	mg/dL	0.4-1.5	1.2
Blood urea nitrogen	mg/dL	8.0-20.0	12
Creatinine	mg/dL	0.47-0.79	0.63
Total protein	g/dL	6.6-8.1	7.7
C-reactive protein	mg/dL	<0.14	0.11
Coagulation			
PT-INR		0.85-1.20	1.1
APTT	sec	24.0-39.0	25.9
Fibrinogen	mg/dL	200-400	434
D-dimer	μg/mL	<1.0	3.3

APTT, activated partial thromboplastin time; PT-INR, prothrombin time-international normalized ratio.

HHT, also known as Rendu–Osler–Weber syndrome, is a rare autosomal dominant disease characterized by systemic vascular dysplasia [8]. Most HHTs are caused by pathogenic variants of *ENG, ACVRL1*, or *SMAD4* [9]. The Curaçao criteria are used for the clinical diagnosis of HHT. Briefly, 4 parameters are included: i) spontaneous and recurrent epistaxis, ii) mucocutaneous telangiectasias, iii) arteriovenous visceral lesions in internal organs, and iv) familial aggregation. At least 2 parameters are needed for a "probable" diagnosis, and at least 3 parameters must be present for a "definitive" diagnosis [10]. The prevalence of PAVM in HHT was reported to be 15%-50% [8].

To our knowledge, a few case reports have described brain abscesses related to PAVMs during chemotherapy. Bruzzi et al. [11] reported 2 cases of acquired PAVMs within pulmonary metastases of extrathoracic malignancies. Our patient had no lung metastasis and exhibited no size change in PAVMs during chemotherapy. Therefore, PAVMs in this case were considered to have no relationship with the appendiceal cancer. No treatment for PAVMs was administered before chemotherapy initiation. HHT was suspected after the development of the brain abscess. Our patient had bilateral PAVMs; however, no family member presented with HHT, and no symptoms of recurrent epistaxis or mucocutaneous telangiectasias were noted.

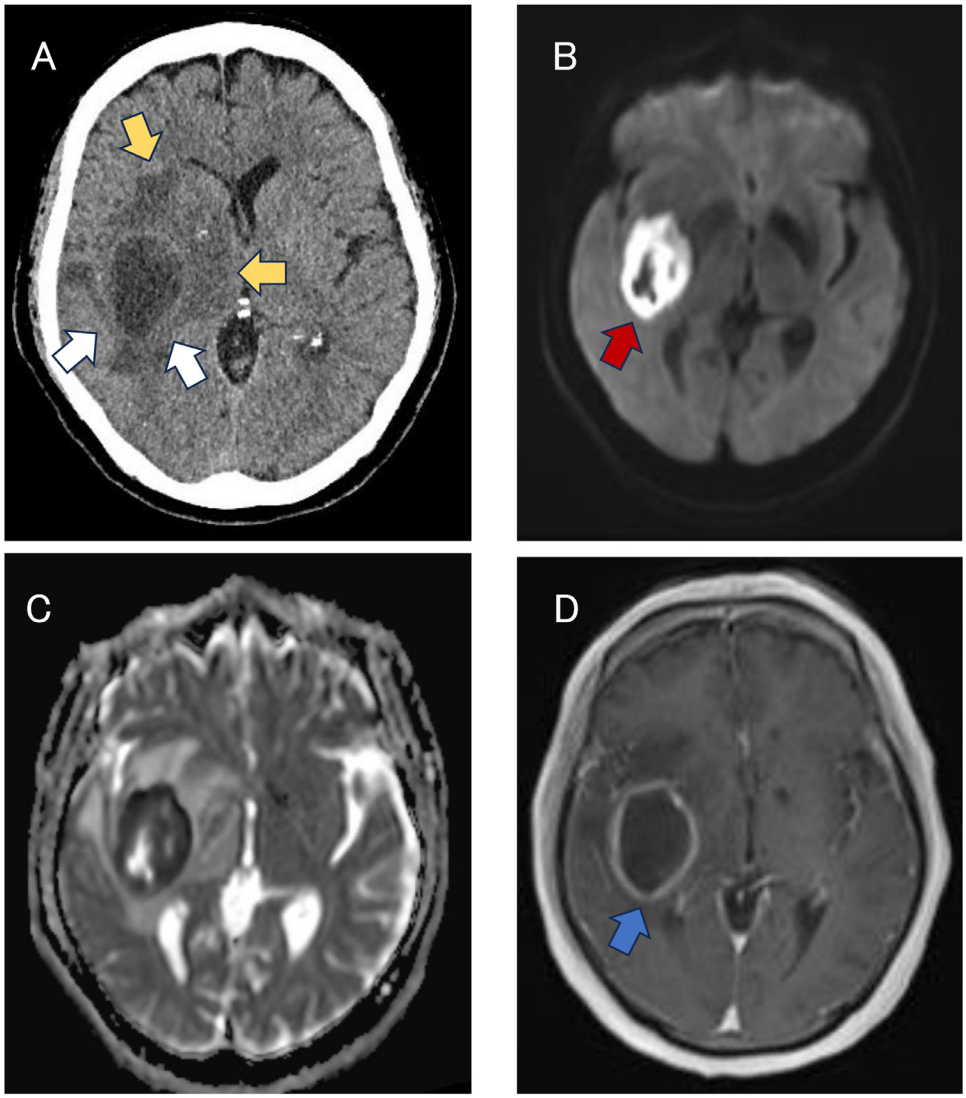

Fig. 2 – Images at the brain abscess onset. (A) Axial noncontrasted head computed tomography images show a low-density region (white arrows) with surrounding edema (yellow arrows) on the lateral side of the right lentiform nucleus. (B) Axial diffusion-weighted magnetic resonance images show very high signal intensity in this region (red arrow). (C) The corresponding apparent diffusion coefficient map. (D) Axial gadolinium-enhanced T1-weighted magnetic resonance images show ring-shaped enhancement in this area (blue arrow).

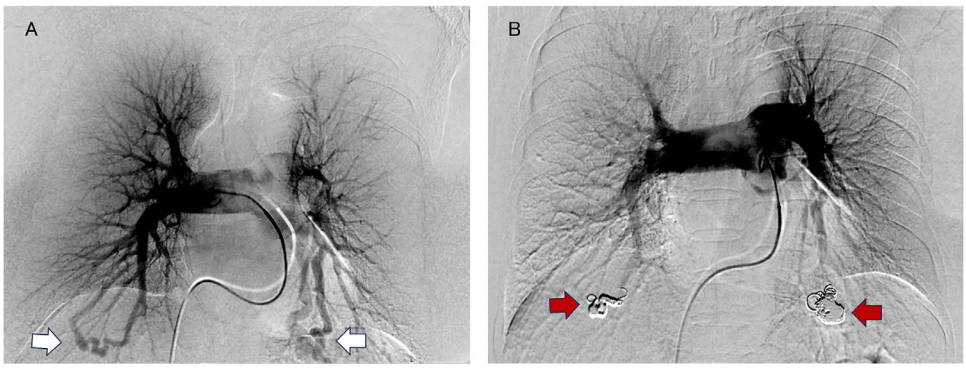

Fig. 3 – Pulmonary artery angiography. (A) Pulmonary arteriovenous malformations are observed before catheter embolization (white arrows). (B) The image after catheter embolization (red arrows).

Therefore, HHT was not diagnosed, and the PAVMs may have been acquired. Na et al. retrospectively analyzed the risk factors for cerebral complications in patients with PAVM in Korea and reported that age >65 years was a risk factor for cerebral complications. In their report, only 1 (1.8%) of 55 patients was diagnosed with HHT [12]. In our case, we cannot completely rule out HHT because genetic tests could not be performed. We acknowledge that this comprises a substantial limitation of this case report.

Regardless of the baseline presence of PAVM, the immunosuppressive state caused by chemotherapy may have triggered the occurrence of a brain abscess. Oncologists generally suspect cerebral metastasis in patients with neurological symptoms during chemotherapy. Our patient was initially diagnosed with a metastatic cerebral tumor based on the CT images. However, the diagnosis changed to brain abscess because of the high fever and MRI findings, and emergent drainage of the abscess was performed. This case suggests that clinicians should always consider serious complications such as brain abscesses during chemotherapy in patients with PAVM.

In the guidelines for the diagnosis and management of HHT, the expert panel recommends that clinicians treat PAVMs with transcatheter embolotherapy [13]. In our case, catheter embolization of the PAVMs was performed after antibiotic therapy to prevent the recurrence of CNS complications. To our knowledge, a few case reports have described PAVM embolization after the occurrence of brain abscesses. Li et al reported a case of PAVM in a patient who underwent craniotomy for decompression of a brain abscess. This patient underwent PAVM embolization to prevent recurrence of the brain abscess 1 month after craniotomy [14]. However, the effectiveness of PAVM embolization after the occurrence of a brain abscess is not clear because of the small number of reported cases. Considering the safety of the current embolization technique for PAVM [15], we considered that, even after the treatment of the brain abscess, the choice to perform embolization and reduce the risk of developing a further brain abscess was reasonable. At the time of submission of this paper, i.e., 13 months since the resumption of chemotherapy, no recurrence of the brain abscess had been observed.

In our patient, chemotherapy with capecitabine was resumed 28 days after embolization and, as a result, the development of the brain abscess interrupted chemotherapy for 4 months. Moreover, minor brain metastases of the appendiceal adenocarcinoma occurred after catheter embolization. We speculate that early catheter embolization might have prevented the development of both the brain abscess and brain metastases. For patients who do not urgently need chemotherapy, embolization before chemotherapy may be a better option.

In summary, we have presented a patient with appendiceal cancer and bilateral PAVMs who developed a bacterial brain abscess during chemotherapy. Our case suggests that if a patient with a malignancy presents with PAVM, clinicians should pay special attention to potential complications such as brain abscess development during chemotherapy. For patients who do not require urgent chemotherapy, embolization before chemotherapy may be a better treatment option.

Data availability

The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

Ethical approval

The authors obtained the informed consent of this patient and approval of submission, according to the protocol approved by Osaka International Cancer Institute (Osaka, Japan).

Patient consent

Written informed consent was obtained from the patient for the publication of patient data and associated images.

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