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Case report

Occult lung metastases of papillary thyroid cancer detected in a resected pulmonary arteriovenous malformation specimen

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A B S T R A C T

A 41-year-old man with exertional dyspnea was referred to our hospital. Chest computed tomography (CT) showed a pulmonary arteriovenous malformation (PAVM) in the left lingular lobe, and magnetic resonance imaging showed a brain abscess. After antimicrobial therapy, the patient underwent thoracoscopic lingulectomy of the PAVM. Pathological examination revealed lung metastases of papillary thyroid cancer (PTC) that were undetectable by CT. The patient underwent total thyroidectomy and D2b lymphadenectomy for the PTC (the pathological stage was T1bN2M1, Stage II). After surgery, the patient received 100 mCi of ¹³¹Iodine; post-treatment scans revealed only neck (remnant) uptake and the patient continued with thyroid hormone replacement therapy. To the best of our knowledge, this is the first report of a case of combined PAVM and occult lung metastases of PTC. Clinicians should remember that they may detect micro lung metastases of any cancer when investigating resected lung specimens.

1. Introduction

Pulmonary arteriovenous malformations (PAVMs) are abnormal communications between the pulmonary arteries and veins that lack a normal capillary system, resulting in anatomic right-to-left shunting. PAVMs are associated with significant morbidity and mortality rates. Embolotherapy is recommended even for asymptomatic patients, if technically feasible. PAVM treatment reduces risks of paradoxical emboli and improves oxygenation and alleviates symptoms associated with right-to-left shunting or haemorrhage [1].

Papillary thyroid cancer (PTC), a well-differentiated type of thyroid cancer, generally has a favorable prognosis. However, patients with distant metastases experience disease progression with higher mortality rates [2] and require multidisciplinary treatment (total thyroidectomy with lymphadenectomy, radionuclide therapy, and thyroid hormone replacement therapy). Three percent of patients with PTC have metastases at the time of diagnosis, with the lungs being the most common site of distant metastasis [3].

Herein, we report a rare case of occult lung metastases of PTC, undetectable by computed tomography (CT), which was incidentally discovered in a lung specimen resected during PAVM treatment.

2. Case report

A 41-year-old man with exertional dyspnea and mild headache was referred to our hospital. He was a former smoker (Brinkman index, 440) with bronchial asthma and a severe iodine allergy, but no relevant medical family history. A physical examination revealed

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normal heart and chest sounds. Pulse oximeter readings indicated oxygen saturations, in room air, of 94% at rest and 90% after exertion. His complete blood count results were normal; his serum C-reactive protein level was slightly elevated (0.24 mg/dL) and an arterial blood gas analysis showed an elevated alveolar-arterial oxygen difference (A-aDO₂) (31.0 Torr). CT showed a nodule in the right lobe of the thyroid (Fig. 1A) and thin-sliced CT showed a 20-mm diameter nodule with 5-mm diameter feeding and draining vessels in the left lingular lobe, which is typical for a PAVM (Fig. 1B). Brain magnetic resonance imaging (MRI) revealed multiple ring-enhanced nodules in the bilateral hemispheres. A craniotomy biopsy led to the brain abscesses being diagnosed as caused by *Streptococcus intermedius* and *S. milleri*. No malignant findings were found in the brain abscess biopsy specimen. After 10 weeks of antimicrobial treatment, the patient underwent a thoracoscopic lingulectomy for the PAVM. After surgery, the patient's arterial blood gas analysis showed a normalized A-aDO₂ (10.8 Torr). Specimen pathology revealed that numerous tumor cells (mostly, 0.3–0.4 mm in diameter; maximum diameter, 1.4 mm) with a papillary structure were present in the lung alveolar wall around the PAVM (Fig. 2A–D). Tumor cells were positive for thyroid transcription factor-1 and thyroglobulin, leading to a diagnosis of metastatic PTC. His serum thyroglobulin level was not elevated (0.13 ng/mL), but his anti-thyroglobulin antibody titer was high (4,000 IU/mL). Ultrasonography showed a 20-mm nodule in the right lobe of the thyroid and right neck lymphadenopathies; fine-needle aspiration cytology revealed PTC. Fluorodeoxyglucose (FDG)-positron emission tomography/CT showed FDG uptake in the nodule of the right thyroid lobe and right neck lymphadenopathies, but no FDG uptake in the lung. The patient underwent total thyroidectomy and D2b lymphadenectomy. The specimen pathology indicated pT2N1bM1, Stage II, according to the 8th edition of the American Joint Committee on Cancer staging system for thyroid cancer. After surgery, the patient underwent treatment with 100 mCi of ¹³¹Iodine; post-treatment scans revealed only neck (remnant) uptake and the patient continued with thyroid hormone replacement therapy. Presently, the patient is alive and well 17 months post-surgery.

3. Discussion

This case followed a unique clinical course involving occult metastatic PTC in the lung that was undetectable by thin-sliced CT but was incidentally discovered in a lung specimen resected during the treatment of a PAVM. To the best of our knowledge, this is the first report of a case of combined PAVM and occult lung metastases of PTC. Notably, clinicians should bear in mind the possible detection of micro lung metastases of all cancers when examining resected lung specimens. In this case, the recognition of a distant metastasis led to the appropriate multidisciplinary treatment of a high-risk PTC.

This PAVM case was indicated for treatment due to a feeding artery diameter of 5 mm, accompanied by symptomatic hypoxemia and brain abscesses. In several studies, the incidence of central nervous system complications, such as stroke and brain abscesses, has been reported to be 9–41%, and mortality has been reported to be 11% after 6 years of treatment-free follow-up after a diagnosis [4]. Although embolotherapy is the mainstay of treatment for most PAVMs, surgical resection is an option for PAVMs that are deemed unsuitable for embolotherapy. In this case, surgery was chosen due to the patient's untreatable contrast allergy and anatomically limited disease; the symptomatic hypoxemia caused by the PAVM improved promptly after resection of the solitary PAVM.

Lung metastases of PTC are typically indolent and frequently present with spotty lung distribution, various tumor sizes, and tumor nodules with homogenous densities. Occult lung metastases of PTC undetectable by CT are sometimes detected by radioiodine imaging [5]. However, if the metastatic PTC does not have iodine accumulation capacity, it is extremely difficult to detect. Although several case reports of occult lung metastases of PTC have been reported in resected lung specimens from patients with primary lung cancer [6], we have not found any reports of occult metastatic PTC in the lungs of patients with concomitant PAVMs.

In general, high-flow shunting of an arteriovenous malformation (AVM) is believed to drastically reduce the chances of successful implantation of metastatic cells within or around the AVM [7]. Hematogenous metastatic cells require a normal capillary system and venules for successful adhesion to the endothelium and subsequent proliferation [8]. In this case, tumor cells were not observed in the intravascular lumina of the AVM but in the lung around the AVM. Therefore, it is unlikely that the haemodynamic changes brought about by the PAVM affected the lung metastases. Hence, we believe that the lung metastases of PTC were an incidental complication. However, hematogenous metastases might have occurred outside the lung through the PAVM shunt, suggesting the need for careful

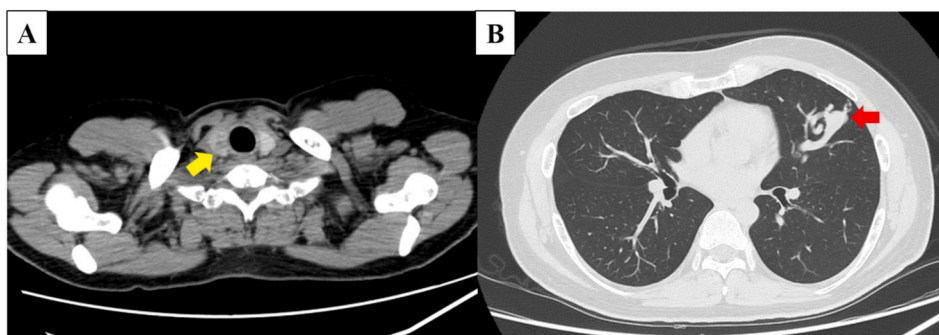


Fig. 1. (A) Computed tomography (CT) showing a nodule in the right lobe of the thyroid (yellow arrow). (B) Thin-sliced CT showing a 20-mm diameter nodule (red arrow) with 5-mm diameter feeding and draining vessels in the left lingular lobe of the lung. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

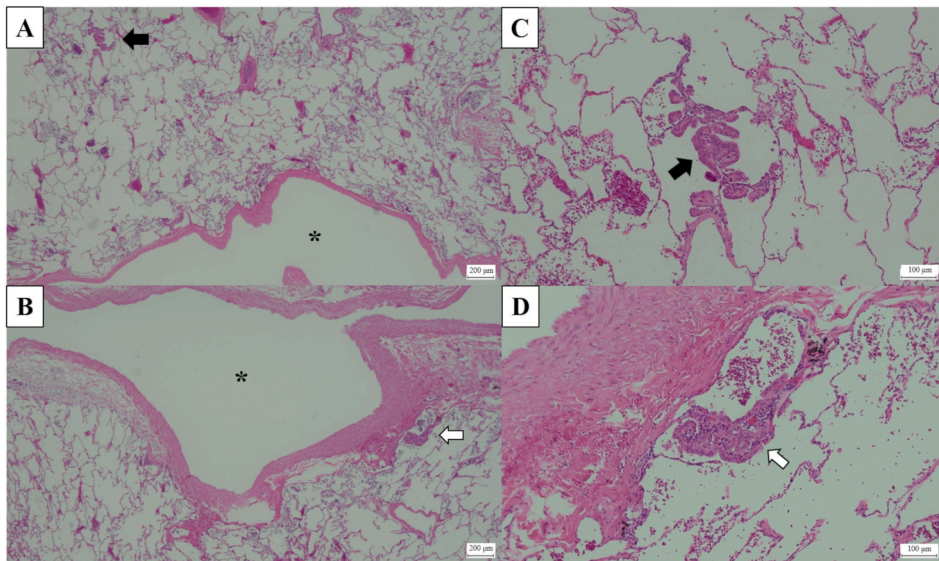


Fig. 2. (A, B) Hematoxylin-eosin staining showing tumor cells in the background of the lung specimens (black and open arrows) around a pulmonary arteriovenous malformation (asterisk). (C, D) Higher power image showing the tumor cells with a papillary structure present in the lung alveolar wall (black and open arrows).

systemic follow-up in this case. The relationship between an AVM and cancer metastasis remains unclear, and further case accumulation and pathological studies are expected.

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Declarations of competing interest

None.

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