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Lung Metastatic Ameloblastoma: A Hidden Cause of Pulmonary Nodules

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Ameloblastoma is a locally aggressive odontogenic tumor that appears benign microscopically but can metastasize to distant organs long after initial treatment. Metastasis occurs in fewer than 2% of cases, most commonly affecting the lungs, with a mean latency of 15-18 years.[1] We report the case of a 57-year-old man who had an impacted left mandibular third molar extracted 35 years earlier. In 2020, he developed a painful swelling at the extraction site that was diagnosed as a dental abscess, and the residual tissue was curetted. Histological examination, not disclosed to the patient at that time, revealed ameloblastoma. He remained asymptomatic until 2023, when a preoperative chest X-ray for an unrelated procedure revealed multiple bilateral lung nodules. High-resolution computed tomography (CT) demonstrated well-defined lesions up to 12 mm in size, while positron emission tomography (PET)/CT showed no uptake beyond the pulmonary nodules (Figure 1). A CT-guided core biopsy of a right lower lobe nodule demonstrated nests of odontogenic epithelium with peripheral palisading and stellate reticulum-like areas, consistent with the archived 2020 mandibular specimen. Immunohistochemistry revealed strong expression of CK5/CK6, CK19, and CD56, focal positivity for p40 in areas of peripheral after palisading, enter (Figure 2) and negative staining for S 100, SMA, TTF 1 and p53. β catenin showed cytoplasmic and membranous staining, the Kİ-67 index was < 1%, and both BRAF immunohistochemistry and real time polymerase chain reaction confirmed a *V600E* mutation in exon 15 of the *BRAF* gene.

A diagnosis of metastatic ameloblastoma harboring a BRAF *V600E* mutation was established. A multidisciplinary tumor board determined that the presence of an actionable mutation warranted systemic targeted therapy with local control measures. The patient subsequently underwent thoracoscopic wedge resection of the largest nodule for debulking and molecular confirmation, followed by initiation of first-line BRAF inhibitor therapy with vemurafenib

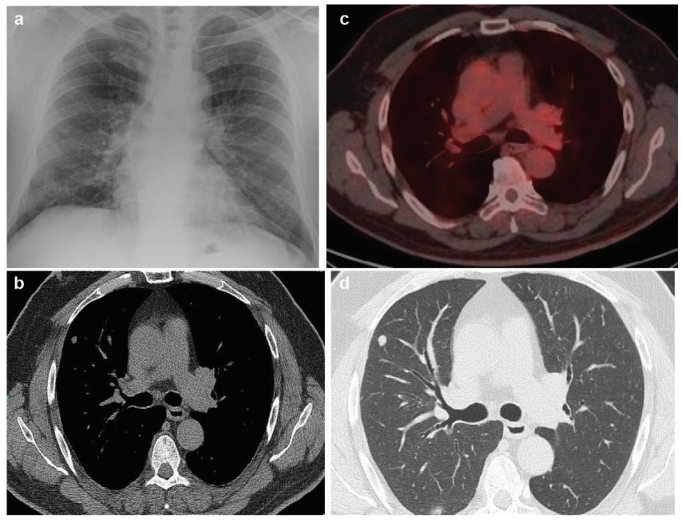

FIG. 1. (a) Posteroanterior chest radiograph showing bilateral reticulonodular opacities. (b) Axial chest CT demonstrates a 12 mm well circumscribed nodule in the right lower lobe. (c) Fused ^{18}F FDG PET/CT shows mild hypermetabolic uptake in the same lesion (SUV_{max} 4.8). (d) High-resolution CT confirms a solid subpleural nodule with sharp margins.

^{18}F FDG PET/CT, fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography; SUV_{max}, maximum standardized uptake value.

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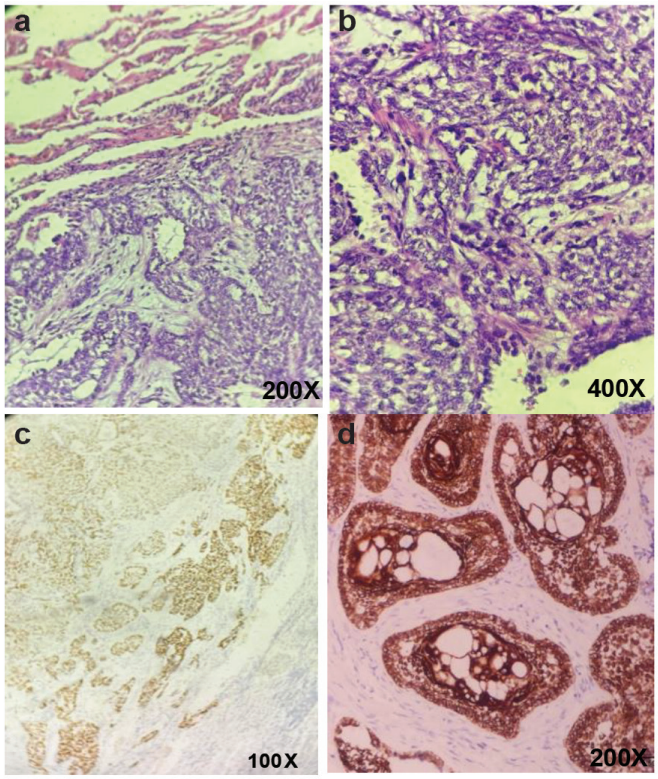

FIG. 2. (a, b) Hematoxylin-eosin sections of the wedge resection specimen at 200×, and 400× magnification reveal nests of odontogenic epithelium with peripheral palisading and stellate reticulum–like areas, consistent with metastatic ameloblastoma. (c) p63 immunohistochemistry (100×) shows diffuse nuclear positivity in tumor islands, supporting odontogenic origin. (d) Cytokeratin-19 immunohistochemistry (200×) shows diffuse cytoplasmic positivity in the tumor islands, consistent with odontogenic epithelial differentiation.

(960 mg twice daily), the current standard of care for BRAF-mutated ameloblastoma. Baseline dermatologic and cardiac assessments were unremarkable.

Metastasizing ameloblastoma exhibits deceptively benign histological features, often leading to long latency periods and delayed detection. The lungs are affected in up to 88% of metastatic cases, with proposed mechanisms including hematogenous spread, lymphatic dissemination, and, rarely, endobronchial implantation.[2] Although platinum-based chemotherapy and radiotherapy yield variable outcomes, current evidence indicates that tumors harboring the BRAF *V600E* mutation (present in approximately 50% of mandibular ameloblastomas) may respond favorably to targeted BRAF inhibitors.[3,4] Broudic-Guibert et al.[5] reported a sustained complete response beyond 2 years, with other small series showing comparable results.[6] Our case supports these findings and, to our knowledge, represents the first report in which fluorine-18-fluorodeoxyglucose PET-CT identified metabolically active pulmonary nodules of ameloblastoma that were subsequently confirmed by histology and BRAF mutation analysis, with the patient now receiving targeted therapy.

This case underscores the importance of transparent communication of pathology results. Patients with a history of ameloblastoma require lifelong surveillance, ideally with low-dose CT or PET-CT, and molecular profiling should be pursued in cases of recurrence or metastasis. This report documents a rare instance of pulmonary metastasizing ameloblastoma harboring a BRAF mutation. Functional imaging-guided biopsy and histological examination confirmed its odontogenic origin, while molecular testing identified a targetable driver mutation, enabling personalized therapy. Careful reporting of such cases is essential to refine surveillance strategies and improve patient outcomes.

Informed Consent: Written informed consent was obtained from the patient.

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