## MINIREVIEWS

128  Prosthetic reconstruction of the trachea: A historical perspective  
Virk J, Zhang H, Nouraei R, Sandhu G

## ORIGINAL ARTICLE

### Retrospective Study

134  Esophageal squamous papilloma lacks clear clinicopathological associations  
Jideh B, Weltman M, Wu Y, Chan CHY

140  Efficacy of intragastric balloon on weight reduction: Saudi perspective  
Almeghaiseeb ES, Ashraf MF, Alanro RA, Almasoud AO, Alrobayan AA

## CASE REPORT

148  Incidental echocardiographic finding: Fractured inferior vena cava filter  
Sivasambu B, Kabirdas D, Movahed A

153  Ominous lung cavity “Tambourine sign”  
Editorial Board Member of World Journal of Clinical Cases, Dr. Ridvan Hamid Alimehmeti, MD, PhD, Associate Professor, Lecturer, Surgeon, Department of Neurology, Neurosurgery and Psychiatry, University of Medicine, Tirana 1000, Albania

World Journal of Clinical Cases (World J Clin Cases, WJCC, online ISSN 2307-8960, DOI: 10.12998) is a peer-reviewed open access academic journal that aims to guide clinical practice and improve diagnostic and therapeutic skills of clinicians.

The primary task of WJCC is to rapidly publish high-quality Autobiography, Case Report, Clinical Case Conference (Clinicopathological Conference), Clinical Management, Diagnostic Advances, Editorial, Field of Vision, Frontier, Medical Ethics, Original Articles, Clinical Practice, Meta-Analysis, Minireviews, Review, Therapeutics Advances, and Topic Highlight, in the fields of allergy, anesthesiology, cardiology, clinical genetics, clinical neurology, critical care, dentistry, dermatology, emergency medicine, endocrinology, family medicine, gastroenterology and hepatology, geriatrics and gerontology, hematology, immunology, infectious diseases, internal medicine, obstetrics and gynecology, oncology, ophthalmology, orthopedics, otolaryngology, pathology, pediatrics, peripheral vascular disease, psychiatry, radiology, rehabilitation, respiratory medicine, rheumatology, surgery, toxicology, transplantation, and urology and nephrology.

World Journal of Clinical Cases is now indexed in PubMed, PubMed Central.

NAME OF JOURNAL
World Journal of Clinical Cases
ISSN
ISSN 2307-8960 (online)
LAUNCH DATE
April 16, 2013
FREQUENCY
Monthly
EDITORS-IN-CHIEF
Giuseppe Di Lorenzo, MD, PhD, Professor, Genitourinary Cancer Section and Rare-Cancer Center, University Federico II of Napoli, Via Sergio Pansini, 5 Ed. 1, 80131, Naples, Italy
Jan Jacques Michiels, MD, PhD, Professor, Primary Care, Medical Diagnostic Center Rijnmond Rotterdam, Bloodcoagulation, Internal and Vascular Medicine, Erasmus University Medical Center, Rotterdam, Goodheart Institute and Foundation, Erasmus Tower, Veenmolen 13, 3069 AT, Erasmus City, Rotterdam, The Netherlands
Sandro Vento, MD, Department of Internal Medicine, University of Botswana, Private Bag 00713, Gaborone, Botswana
Shuhei Yoshida, MD, PhD, Division of Gastroenterology, Beth Israel Deaconess Medical Center, Dana 509, Harvard Medical School, 330 Brookline Ave, Boston, MA 02215, United States

EDITORS FOR THIS ISSUE
Responsible Assistant Editor: Xiang Li
Responsible Electronic Editor: Dan Li
Proofing Editor-in-Chief: Lian-Sheng Ma
Responsible Science Editor: Fang-Fang Ji
Proofing Editorial Office Director: Xiu-Xia Song
Help Desk: http://www.f6publishing.com/helpdesk
http://www.wjgnet.com

PUBLISHER
Baishideng Publishing Group Inc
8226 Regency Drive, Pleasanton, CA 94588, USA
Telephone: +1-925-2238242
Fax: +1-925-2238243
E-mail: bpgoffice@wjgnet.com

COPYRIGHT
© 2017 Baishideng Publishing Group Inc. Articles published in journals owned by the Baishideng Publishing Group (BPG) represent the views and opinions of their authors, and not the views, opinions or policies of the BPG, except where otherwise explicitly indicated.

INSTRUCTIONS TO AUTHORS
http://www.wjgnet.com/bpg/gerinfo/204

ONLINE SUBMISSION
http://www.f6publishing.com
Ominous lung cavity “Tambourine sign”

Ritu Verma, Ashu Seith Bhalla, Ankur Goyal, Deepali Jain, N Loganathan, Randeep Guleria

Abstract

Mucinous adenocarcinoma represents a rare subtype of adenocarcinoma of the lung, which is frequently invasive and has a poorer prognosis. Of its wide range of imaging appearances, air-space consolidation is the most frequent pattern while cavitary form has only rarely been reported. Despite imaging advancements, the differentiation of benign and malignant cavitary lung lesions sometimes remains imperfect. We propose “Tambourine” sign on computed tomography to raise the suspicion of mucinous adenocarcinoma in a lung cavity, under appropriate clinical settings. The sign indicates an irregular cavity with undistorted prominent thick walled bronchioles within the wall and draping along thereby resembling the musical instrument “tambourine”. Adjacent ground glass and internal septations may also be seen.

Key words: Lung cavity; Tambourine; Adenocarcinoma mucinous; Tomography; X-ray
more sinister lesion as in our case and in similar cases reported in literature. Hence in appropriate clinical and imaging background this sign should be carefully looked at and appropriate workup should be done for timely diagnosis.

INTRODUCTION
Lung cancer is the most common cause of malignancy-related mortality in both sexes[1]. In the recent decades, there has been a substantial increase in the proportion of adenocarcinomas, making it the most common type. The spectrum of lung adenocarcinoma ranges from atypical adenomatous hyperplasia to frankly invasive lesion[2]. Invasive mucinous adenocarcinoma (IMAC) is a special subtype of adenocarcinoma lung that was earlier termed as mucinous broncho-alveolar carcinoma (BAC) and is known to be more aggressive than conventional adenocarcinoma[3]. IMAC may have a wide range of imaging appearances, of which air-space consolidation is the most common[2] pattern. We present a case of 37-year female who presented with a thin-walled left lower lobe (LLL) lung cavity six years ago, but remained undiagnosed despite adequate workup, till a final diagnosis of IMAC was made. Review of literature focusing on radiological findings of this unusual cavitary appearance of IMAC is discussed.

CASE REPORT
A 37-year non-smoker female presented to our institute with history of cough, sputum, shortness of breath, loss of weight and episodic hemoptysis in November 2014. Her problem began in 2008 with an episode of cough, streaky hemoptysis and copious sputum production, which was treated with antibiotics as respiratory tract infection. Multiple subsequent hospital admissions and extensive clinical/radiological workup was done (Figure 1) for similar complaints but was inconclusive (Figures 2 and 3).

The laboratory investigations in the current admission were again non-contributory (Figure 1). Contrast-enhanced computed tomography (CECT) was done and it revealed multiple cavitary lesions in bilateral lungs with the largest in LLL showing large enhancing solid component. Many of the cavitary lesions in current CT showed a peculiar imaging appearance: Irregular inner and outer walls with thick walled bronchioles seen near the edge and within the walls of the cavities. No surrounding ground glass opacity (GGO) was seen in the current CT. There was no pleural effusion or mediastinal adenopathy. The included sections of upper abdomen were unremarkable.

Review of the prior imaging (Figures 2 and 3) demonstrated progression over the last six years. The lesion began (in 2008) as a thin-walled (4 mm) well-defined cavity in superior segment of LLL (Figure 2A-C). Both the inner and outer margins of the wall showed irregularity. Adjacent thick walled prominent undistorted bronchioles (dotted arrows) were seen near the edge and within the wall of cavity. Mild surrounding GGO was also seen. There was an additional smaller cavitating nodule in right upper lobe (RUL) with subtle surrounding GGO (not shown). Combining clinical and laboratory data, patient was presumed to have respiratory infection and treated for the same. Subsequent imaging in 2010 (Figure 2D-F) showed increase in size and wall thickness of the LLL cavity. Imaging done in 2012 depicted multiple new cavitating nodules in RUL (Figure 3A and B) and increase in size of LLL cavity, along with development of internal septations. No GGO or consolidation was seen and there was no solid component in any of these cavities.

Current CECT images showed further increase in the size of the lesions and development of significant soft tissue component in LLL cavity (Figure 3C-E). Many of the cavitary lesions in the current CT showed multiple internal septations. Considering disease progression and development of solid component, malignancy was kept as the first differential. Other possibilities included atypical infections (fungal, atypical mycobacterial, nocardia, etc.) and vasculitis. However, long disease course (approximately 6 years) was unusual for both infection and malignancy.

USG-guided biopsy was done from the LLL mass (solid component) that showed atypical glands in the background of abundant mucin with areas of frank invasion suggestive of well-differentiated IMAC (Figure 4A and B). Analysis for ALK and EGFR mutation was negative. 18F-FDG PET-CT was done to rule out lung metastasis from extrathoracic primary which did not reveal any other primary site and the lung lesions showed patchy foci of mild FDG uptake (Figure 4C). The patient was started on chemotherapy (Pemetrexed and Carboplatin) but she continued to progress and developed bone metastases and soon became bedridden.

DISCUSSION
Lung cavities are commonly encountered in routine radiology practice. While in most cases the distinction between benign and malignant cavities is straightforward, some of the lesions may pose a diagnostic challenge. Differential diagnosis of acquired cavitary lung lesions include pyogenic infections such as lung abscess, necrotising pneumonia, septic emboli; granulomatous infections like tuberculosis, fungal; vasculitis including granulomatosis with polyangitis (Wegener’s) and Churg Strauss; connective tissue diseases like rheumatoid disease, ruptured hydatid and malignancy. A constellation of imaging features including wall thickness, number of lesions, distribution/site,
adjacent GGO/nodules/consolidation, satellite lesions, internal contents, fluid level and the background lung need to be considered to reach a diagnosis.

Amongst lung malignancies, squamous cell carcinoma is the most common type to present as cavitary mass while adenocarcinomas rarely show true cavitation due to lack of frank necrosis and relative preservation of lung architecture. Adenocarcinomas however show areas of pseudocavitation due to presence of air in the patent smaller bronchi and preserved intra-alveolar air.

IMAC is a special subtype of invasive adenocarcinoma lung that is more common in females, non-smokers and presents at a younger age. When these tumors are multifocal, they are frequently multiobar and lower lobe predominance is seen.[2,5]. On CT, IMAC usually appear as consolidation with air bronchogram (commonest) or multifocal solid and subsolid (ground glass) nodules or masses which tend to be bronchocentric.[2,6]. Due to abundant mucin production, large areas of pseudocavitation may be seen. They have low FDG uptake[7] due to large amount of mucin and for same reason show less contrast enhancement frequently depicting the “CT angiogram sign”.

Previously IMAC was termed as Mucinous Broncho-alveolar Carcinoma however the term BAC has now been removed from recent adenocarcinoma classification. BAC by definition was for non-invasive tumors while IMAC though predominantly show lepidic spread, frequently have areas of frank invasion. GGO is an indicator of lepidic spread while the solid component correlates with invasion. IMAC are frequently EGFR negative and may show k-RAS mutation, therefore having a poorer prognosis.[8]. IMAC presenting as cavity is rare and to the best of our knowledge only two cases have been described previously.[9,10]. Cavitation in adenocarcinoma may be caused by obstruction of the distal bronchus by tumour cells creating a check-valve mechanism or alveolar rupture due to tumour proliferation or mucus retention[9].

A detailed review of the previously reported cases and all the imaging studies of our case enabled us to come up with a peculiar finding common to all, which we intend to refer to as the “Tambourine sign”.

On CT, IMAC usually appear as consolidation with air bronchogram (commonest) or multifocal solid and subsolid (ground glass) nodules or masses which tend to be bronchocentric. Due to abundant mucin production, large areas of pseudocavitation may be seen. They have low FDG uptake due to large amount of mucin and for same reason show less contrast enhancement frequently depicting the “CT angiogram sign”.

Previously IMAC was termed as Mucinous Broncho-alveolar Carcinoma however the term BAC has now been removed from recent adenocarcinoma classification. BAC by definition was for non-invasive tumors while IMAC though predominantly show lepidic spread, frequently have areas of frank invasion. GGO is an indicator of lepidic spread while the solid component correlates with invasion. IMAC are frequently EGFR negative and may show k-RAS mutation, therefore having a poorer prognosis.[8]. IMAC presenting as cavity is rare and to the best of our knowledge only two cases have been described previously.[9,10]. Cavitation in adenocarcinoma may be caused by obstruction of the distal bronchus by tumour cells creating a check-valve mechanism or alveolar rupture due to tumour proliferation or mucus retention[9].

A detailed review of the previously reported cases and all the imaging studies of our case enabled us to come up with a peculiar finding common to all, which we intend to refer to as the “Tambourine sign”.

“Tambourine” sign refers to an irregular cavitary lesion with adjacent thick walled undistorted bronchioles within wall of the lesion and adjacent to it. The appearance resembles the musical instrument tambourine where the irregular cavity wall corresponds to the ring of the instrument, while the thick walled dilated bronchioles within the wall correspond to the metallic jingles. The cavity wall itself though irregular, may not be thick (as in

---

**Table 1** The clinical work-up and evaluation from onset till diagnosis.

<table>
<thead>
<tr>
<th>Year</th>
<th>Work-up and Evaluation</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>2008: Figure 1</td>
<td>Blood counts, sputum for AFB, fungal elements, Connective tissue and vasculitis workup, ACE, hydatid serology and ESR was normal</td>
<td>Treated as respiratory tract infection, cavity was considered post infective</td>
</tr>
<tr>
<td>2010: Figure 1</td>
<td>Repeat blood work up inconclusive; sputum that showed heavy growth of S. viridans but negative for AFB, fungal, atypical mycobacteria and nocardia. PFT: Normal</td>
<td>Treated with antibiotics as superadded streptococcal infection</td>
</tr>
<tr>
<td>2012: Figure 2</td>
<td>Repeat work up inconclusive, Multiple BAL and FOB: Negative. CT showed progression. ECHO: Normal LV function, no vegetations. TBLB: Chronic inflammatory cells with some fibrosis</td>
<td>Given empirical ATT, no response. Later tracazol and steroids were added with some benefit. After that patient was on routine usage of inhaled steroids (formoterol + budesonide) with only occasional cough dyspnoea and chest discomfort. Advised LLL lobectomy but refused</td>
</tr>
<tr>
<td>2014: Figure 2</td>
<td>Laboratory and clinical workup negative. USG guided biopsy from LLL solid component done x/o IMAC</td>
<td>Started on Pemetrexed and Carboplatin</td>
</tr>
</tbody>
</table>

---

**Figure 1** The clinical work-up and evaluation from onset till diagnosis. BAL: Bronchoalveolar lavage; TBLB: Transbronchial lung biopsy; ACE: Angiotensin converting enzyme; EGFR: Epidermal derived growth factor receptor; PFT: Pulmonary function test; AFB: Acid fast bacilli; ESR: Erythrocyte sedimentation rate; GGO: Ground glass opacity; ATT: Anti tubercular therapy.

---

Verma R et al. Lung cavity “Tambourine sign”
Figure 2  Initial and two year follow-up computed tomography imaging. Chest radiograph (A) and CT (B) in 2008 (first study) show well-defined thin-walled (4 mm) irregular cavitary lesion (arrow head) in superior segment of left lower lobe. Thick walled bronchioles (dotted arrows) are seen near the edge and within the wall of cavity with adjacent ground glass giving rise to "Tambourine" sign; (C) depicts the musical instrument "tambourine" for comparison; subsequent radiograph (D) and CT (E and F) in 2010 shows increase in size and wall thickness of the cavity. Note the adjacent bronchioles (thin white arrows) entering into the cavity wall. CT: Computed tomography.

Figure 3  Disease progression with development of soft tissue. Chest CT study of 2012 lung window (A and B) shows multiple new cavitating nodules in RUL (A) and increase in size of LLL cavity with development of internal septations (arrows) (B). No solid nodules or GGO or consolidation is seen. Current CECT images (2014: C to E) demonstrate further increase in size of the lesions and multiple new lesions having internal septations and development of significant soft tissue component in LLL cavity (solid arrows). Also note the "Tambourine" sign in RLL cavities as well (encircled cavity in C). LLL: Left lower lobe; RUL: Right upper lobe; GGO: Ground glass opacity; CECT: Contrast-enhanced computed tomography.
the initial CT in the index case). Prominent thick walled undistorted bronchi are caused by tumour cell infiltration and desmoplastic reaction. Presence of internal septations and surrounding GGO (indicating lepidic spread of the tumor) further increase the likelihood of malignancy in such a lesion. When viewed in retrospect, both of the previously described cases as well as our patient showed “Tambourine” sign in all the CT examinations.

Paucity of malignant cells in such large amount of mucin may make IMAC difficult to detect on BAL cytology as well as on TBLB. Though adenocarcinomas are usually aggressive, unusually slow growing lesions have also been reported. This along with other confounding factors (Table 1) delayed the diagnosis in the index case. Adenocarcinoma may develop in a pre-existing cavity; however the index case was likely to be harbouring malignancy right from the onset. This is because the LLL cavity showed suspicious features on the first CT itself (“tambourine” sign) and progressively increased in size and wall thickness on subsequent imaging, along with development of multifocal lesions. The unusual feature in our case was atypical radiological appearance of the lesion as a thin-walled cavity, repeated negative cytology/biopsy and unusual slow growth.

Summary and conclusion
The purpose of this article is to highlight an additional radiological sign which could raise suspicion of malignancy in a lung cavity. An irregular cavitary lesion with adjacent thick walled undistorted bronchioles within wall of the lesion and adjacent to it (“Tambourine” sign) is suspicious for malignancy and needs extensive work-up even if the cavity is relatively thin walled. Internal septations, surrounding GGO, lower lobe location, multifocality, normal background lung without any obvious airway disease, fibrosis and scarring may further point towards underlying malignancy (IMAC), provided the work-up for other differentials is negative (as in our case). Any increase in size or wall thickness prompts aggressive management by early surgical removal even when repeated BAL or biopsy is negative (Table 2).

COMMENTS
Case characteristics
Cough, shortness of breath and occasional hemoptysis.

Clinical diagnosis
Respiratory tract infection.

Differential diagnosis
Reactivated kochs.

Laboratory diagnosis
Was confusing and non contributory.
Imaging diagnosis
Initially lung cavity with tambourine sign initially later developed soft tissue.

Pathological diagnosis
Invasive mucinous adenocarcinoma.

Treatment
Premetrexed and carboplatin combination chemotherapy and radiotherapy for bone metastasis.

Related reports
Being thin walled cavity with no significant soft tissue repeat biopsies may be negative hence surgical excision may be considered when extensive workup is inconclusive.

Term explanation
The cavity resembles “Tambourine” on computed tomography, that refers to the musical instrument seen as thin walled cavity in background of normal lung with prominent and thick walled undistorted bronchi draping and entering the cavity walls.

Experience and lesson
This imaging finding has been retrospectively observed in previous similar reported cases of Invasive mucinous adenocarcinoma presenting as cavity and hence the classical appearance need to be focussed and re-emphasised. Close follow-up is very helpful in such cases.

REFERENCES

P- Reviewer: Aggarwal D  S- Editor: Ji FF  L- Editor: A  E- Editor: Li D