## REVIEW

3621  Autoimmunity as the comet tail of COVID-19 pandemic  
_Talotta R, Robertson E_

3645  Gender medicine: Lessons from COVID-19 and other medical conditions for designing health policy  
_Machluf Y, Chaiter Y, Tal O_

## MINIREVIEWS

3669  Complexities of diagnosis and management of COVID-19 in autoimmune diseases: Potential benefits and detriments of immunosuppression  
_Georgiev T, Angelov AK_

## ORIGINAL ARTICLE

### Retrospective Study

_D’Urbano F, Fabbri N, Koleva Radica M, Rossin E, Carcoforo P_

3697  Somatostatin receptor scintigraphy in the follow up of neuroendocrine neoplasms of appendix  
_Saponjski J, Macut D, Sobic-Saranovic D, Ognjanovic S, Bozic Antic I, Pavlovic D, Artiko V_

3708  Efficacy of stool multiplex polymerase chain reaction assay in adult patients with acute infectious diarrhea  

3718  Comparison of gemcitabine plus nab-paclitaxel and FOLFIRINOX in metastatic pancreatic cancer  
_Han SY, Kim DU, Seol YM, Kim S, Lee NK, Hong SB, Seo HI_

3730  Shear wave elastography may be sensitive and more precise than transient elastography in predicting significant fibrosis  
_Yao TT, Pan J, Qian JD, Cheng H, Wang Y, Wang GQ_

3743  Radioactive $^{125}$I seed implantation for locally advanced pancreatic cancer: A retrospective analysis of 50 cases  
_Li CG, Zhou ZP, Jia YZ, Tan XL, Song YY_

3751  Active surveillance in metastatic pancreatic neuroendocrine tumors: A 20-year single-institutional experience  

3763  Clinical efficacy of tocilizumab treatment in severe and critical COVID-19 patients  
_Zeng J, Xie MH, Yang J, Chao SW, Xu EL_
## Contents

**World Journal of Clinical Cases**  
Semimonthly Volume 8 Number 17 September 6, 2020

<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>3774</td>
<td>Phosphatidylinositol-3,4,5-trisphosphate dependent Rac exchange factor 1 is a diagnostic and prognostic biomarker for hepatocellular carcinoma</td>
<td>Cai Y, Zheng Q, Yao DJ</td>
</tr>
<tr>
<td>3804</td>
<td>Portal gas in neonates; is it always surgical? A case report</td>
<td>Altokhais TI</td>
</tr>
<tr>
<td>3808</td>
<td>Large lingual heterotopic gastrointestinal cyst in a newborn: A case report</td>
<td>Lee AD, Harada K, Tanaka S, Yokota Y, Mima T, Enomoto A, Kogo M</td>
</tr>
<tr>
<td>3814</td>
<td>Osteochondral lesion of talus with gout tophi deposition: A case report</td>
<td>Kim T, Choi YR</td>
</tr>
<tr>
<td>3835</td>
<td>Diagnosis of an actively bleeding brachial artery hematoma by contrast-enhanced ultrasound: A case report</td>
<td>Ma JJ, Zhang B</td>
</tr>
<tr>
<td>3841</td>
<td>Lung adenocarcinoma harboring rare epidermal growth factor receptor L858R and V834L mutations treated with icotinib: A case report</td>
<td>Zhai SS, Yu H, Gu TT, Li YX, Lei Y, Zhang HY, Zhen TH, Gao YG</td>
</tr>
<tr>
<td>3847</td>
<td>Gastroduodenitis associated with ulcerative colitis: A case report</td>
<td>Yang Y, Li CQ, Chen WJ, Ma Zh, Liu G</td>
</tr>
<tr>
<td>3853</td>
<td>Majocchi’s granuloma caused by <em>Trichophyton rubrum</em> after facial injection with hyaluronic acid: A case report</td>
<td>Liu J, Xin WQ, Liu LT, Chen CF, Wu L, Hu XP</td>
</tr>
</tbody>
</table>
Contents

Semimonthly Volume 8 Number 17 September 6, 2020

3859 Novel deletion mutation in Bruton’s tyrosine kinase results in X-linked agammaglobulinemia: A case report

3867 Multidisciplinary treatment of life-threatening hemoptysis and paraplegia of choriocarcinoma with pulmonary, hepatic and spinal metastases: A case report
   Lin YY, Sun Y, Jiang Y, Song BZ, Ke LJ

3875 Diagnostic value of ultrasound in the spontaneous rupture of renal angiomyolipoma during pregnancy: A case report
   Zhang T, Xue S, Wang ZM, Duan XM, Wang DX

3881 Gallbladder sarcomatoid carcinoma: Seven case reports
   Qin Q, Liu M, Wang X

3890 Surgical strategy used in multilevel cervical disc replacement and cervical hybrid surgery: Four case reports
   Wang XF, Meng Y, Liu H, Hong Y, Wang BY

3903 Diagnosis and treatment of an elderly patient with 2019-nCoV pneumonia and acute exacerbation of chronic obstructive pulmonary disease in Gansu Province: A case report
   He TP, Wang DL, Zhao J, Jiang XY, He J, Feng JK, Yuan Y

3911 Diagnosis and treatment of mixed infection of hepatic cystic and alveolar echinococcosis: Four case reports
   A JD, Chai JP, Wang H, Gao W, Peng Z, Zhao SY, A XR
ABOUT COVER

Editorial board member of World Journal of Clinical Cases, Dr. Elia de Maria is Adjunct Professor of Arrhythmology Lab in the Cardiology Unit, Ramazzini Hospital in Carpi, Italy. He graduated in Medicine and Surgery from the University of Napoli in 1999, continuing on to obtain specialization in Cardiology in 2003. He also holds the distinction of High Degree Master in Electrophysiology and Cardiac Stimulation. Since 2005, he has practiced as a Permanent Consultant Cardiologist in the Italian Public Hospitals, and since 2015 as an External Contract Professor in the Faculty of Medicine and Surgery of University of Verona. His clinical and research interests encompass pharmacological therapy in acute and chronic cardiac conditions, temporary and definitive pacing, thoracentesis and pericardiocentesis, and hemodynamic monitoring. (L-Editor: Filipodia)

AIMS AND SCOPE

The primary aim of World Journal of Clinical Cases (WJCC, World J Clin Cases) is to provide scholars and readers from various fields of clinical medicine with a platform to publish high-quality clinical research articles and communicate their research findings online.

WJCC mainly publishes articles reporting research results and findings obtained in the field of clinical medicine and covering a wide range of topics, including case control studies, retrospective cohort studies, retrospective studies, clinical trials studies, observational studies, prospective studies, randomized controlled trials, randomized clinical trials, systematic reviews, meta-analysis, and case reports.

INDEXING/ABSTRACTING

The WJCC is now indexed in Science Citation Index Expanded (also known as SciSearch®), Journal Citation Reports/Science Edition, PubMed, and PubMed Central. The 2020 Edition of Journal Citation Reports® cites the 2019 impact factor (IF) for WJCC as 1.013; IF without journal self cites: 0.991; Ranking: 120 among 165 journals in medicine, general and internal; and Quartile category: Q3.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: Yan-Xia Xing; Production Department Director: Yan-Xiaojian Wu; Editorial Office Director: Jin-Lei Wang.
Lung adenocarcinoma harboring rare epidermal growth factor receptor L858R and V834L mutations treated with icotinib: A case report

Shu-Sen Zhai, Hui Yu, Tian-Tian Gu, Yan-Xia Li, Yan Lei, Hai-Yan Zhang, Tong-Huan Zhen, Yun-Ge Gao

Abstract

BACKGROUND
Epidermal growth factor receptor (EGFR) tyrosine-kinase inhibitors are widely used for the treatment of non-small-cell lung cancer with EGFR mutations. However, patients with rare, even compound EGFR mutations have different responses to EGFR-tyrosine-kinase inhibitors, which bring uncertainty to clinical treatment.

CASE SUMMARY
A 45-year-old female patient presented with a 3-mo history of cough and white sputum without chest pain. Chest computed tomography revealed lung space-occupying lesions and multiple lymphadenectasis. Bronchoscopy and pathology suggested lung adenocarcinoma. Compound variation of EGFR gene (exon 21 L858R/V834L) was detected in both tissue and circulating tumor deoxyribonucleic acid samples. As a result of next-generation sequencing and her family’s wishes, the patient was given oral treatment with icotinib hydrochloride (125 mg/d, tid) from March 21, 2019 and has achieved stable disease for the last 1 year.

CONCLUSION
Non-small cell lung adenocarcinoma with EGFR L858R/V834L was treated successfully with icotinib, and it may be a new medication treatment option.

Key words: Icotinib hydrochloride; Epidermal growth factor receptor L858R/V834L; Non-small cell lung cancer; Stable disease; Case report
INTRODUCTION

Non-small cell lung cancer (NSCLC) is one of the leading causes of cancer mortality. Epidermal growth factor receptor (EGFR) gene mutations in lung adenocarcinoma account for about 48% of patients. EGFR gene exon 19 single nucleotide polymorphism and deletion variation is a common type of mutation\(^1\). However, non-EGFR Del19/L858R rare mutations account for 23% of cases, mainly composed of exon 20ins, G719X, de novo T790M and L861Q combined with the classic mutation of the compound mutation. For the rare compound mutations of EGFR, there have been some drug studies. For example, first-generation EGFR tyrosine kinase inhibitors (TKIs) are effective for G719X, 21L861Q and the compound mutations carrying sensitive mutations, but more data are needed for efficacy against 20S768I\(^2,3\). The second-generation EGFR-TKIs have a wider spectrum. They are effective for G719X, S768I, L861Q and complex mutations, and studies have shown a significant increase in progression-free survival compared to first generation EGFR-TKIs\(^4\). The third-generation EGFR-TKIs have shown some therapeutic effect in small phase II studies, but this needs to be verified\(^5\).

The molecularly targeted drug for lung cancer, icotinib hydrochloride (Kemena), is a small anticancer drug with completely independent intellectual property rights in China. The drug was approved by the China Food and Drug Administration on June 7, 2011 for the first-line treatment of patients with locally advanced or metastatic NSCLC with sensitive mutations in the EGFR gene. According to the phase III clinical trial and BRAIN studies, compared with the control group, progression-free survival and objective response rates were significantly prolonged in patients with EGFR mutation treated with icotinib, adverse reactions were significantly reduced and the safety was acceptable\(^6\). Here, we report a case of NSCLC with rare EGFR L858R/V834L compound mutation who was treated with icotinib. The treatment was effective, and there was no sign of resistance to icotinib.

CASE PRESENTATION

Chief complaints

A 45-year-old woman presented to the outpatient department of our hospital complaining of hoarseness and a cough with sputum.

History of present illness

Since December 2018, the patient had had cough and sputum without obvious inducement, a small amount of white phlegm, no fever, no chest tightness, no shortness of breath and no headache.
History of past illness
Her past medical history was unremarkable.

Personal and family history
No specific personal history of disease was recorded.

Physical examination
Her mental state was good. She had a hoarse voice. Superficial lymph nodes were not affected, heart and lung auscultation were normal, liver and spleen were not enlarged and neither lower limbs had edema.

Laboratory examinations
Routine blood examination, liver and kidney function and electrolyte test indicators were, normal and carcinoembryonic antigen was 17.6 ng/mL (reference value < 5 ng/mL). Blood gases were normal. Laryngoscopy suggested vocal cord paralysis.

Imaging examinations
Lungs were examined by computed tomography (CT) (mediastinal window) on March 12, 2019. A soft tissue mass shadow was found in the left lower hilum of the lung; the boundary of the shadow was not clear, and it measured about 27.5mm × 26.8 mm; and the three-stage CT value was about 56/68/81 Hu. Multiple swollen lymph nodes were found in the left supraclavicular area and mediastinum, and the largest was about 11.6 mm × 27.2 mm and was located beside the aortic arch. A small amount of liquid density shadow was seen in the left thoracic cavity. CT examination (pulmonary window) revealed a mass shadow in the left lower lung dorsal segment, with coarse margin, pleural traction and dorsal bronchial occlusion. Multiple small nodules < 10 mm were found in both lungs, with clear boundaries; ground-glass nodules, 17.2 mm × 18.2 mm, were found in the right upper lung, some of which were high density. Magnetic resonance imaging of the head was normal, and abdominal CT was normal.

Further diagnostic work-up
To determine potential therapeutic methods, with the patient’s consent, tissue samples from lung bronchoscopy and whole blood as a control were subjected to next-generation sequencing using by a 757-gene panel (Yucebio, Shenzhen, China). Compound variation of EGFR gene (exon 21 L858R/V834L) was detected in both tissue and circulating tumor deoxyribonucleic acid samples (Figure 1A). Immunohistochemistry showed that EGFR expression in tumor tissue was positive, and programmed death-ligand 1 expression was < 1% (total cholesterol < 1%) (Figures 1B and C).

FINAL DIAGNOSIS
CT examination showed lung space occupying lesions and multiple lymphadenectasis. Bronchoscopy and pathology were performed in the outpatient department. The results were: CT4N3M1, stage IV lung adenocarcinoma (according to American Joint Cancer Committee, 8th edition), with both lungs, mediastinal and left periclavicular lymph nodes metastasis (Figure 2).

TREATMENT
As a result of the tests and her family’s wishes, the patient was treated with oral icotinib hydrochloride (125 mg/d, tid) from March 21, 2019.

OUTCOME AND FOLLOW-UP
In the course of treatment, the patient’s condition gradually improved, hoarseness lessened, no adverse drug reaction occurred and carcinoembryonic antigen gradually decreased by 5.6 ng/mL. Lung CT examination showed that multiple small pulmonary nodules gradually reduced and disappeared, mediastinal lymph node metastasis decreased and periclavicular lymph node metastasis decreased and
Figure 1  Next generation sequencing result and immunoassay of epidermal growth factor receptor and programmed death-ligand 1. A: Next generation sequencing result of the patient’s tissue sample, showing variation in epidermal growth factor receptor exon 21; B: Epidermal growth factor receptor immunoassay; C: Programmed death-ligand 1 immunoassay.

Figure 2  Representative images of hematoxylin and eosin-stained lung adenocarcinoma. A and B: The tumor cells were characterized by the variation in nucleus size and shape, the deep staining and the increased nucleoplasm index, which was marked by a closed curve; Also, hematoxylin and eosin staining showed that the tumor cells invaded the surrounding tissue (A: 100 × and B: 200 ×).

disappeared (Figure 3). No abnormality was found by head magnetic resonance imaging examination. At present, we continue to treat her with icotinib hydrochloride with regular follow-up in the outpatient clinic.

DISCUSSION

The somatic variant of EGFR V834L is a rare mutation. Only three cases have previously been found in lung adenocarcinoma, but little is known about its clinical significance. None of the cases reported targeted therapy of EGFR L858R/V834L complex mutation. In 2018, a study assessed the efficacy of first-generation of EGFR-TKI icotinib in patients with NSCLC carrying rare EGFR mutations and found that icotinib had clinical benefit for patients with rare, especially complex mutations\(^8\). In two previous reports containing cases of EGFR L858R/V834L, gefitinib and erlotinib were used for treatment of patients, and there was no targeted drug treatment for EGFR L858R/V834L patients\(^9\). Coincidentally, the cases with EGFR V834L mutation also had EGFR L858R mutation. In addition, in 2018, Li et al\(^{11}\) found that a patient with
NSCLC who progressed to multilne therapy carried an EGFR L858R/V834L complex mutation when the disease progressed slowly from 2012 to 2016. After 2016, the relapse time was shortened, and the driver mutation changed to EGFR 19 del. The authors speculated that this complex mutation might be related to a relatively inactive disease state[11].

In our case, the patient carried a somatic compound mutation of EGFR V834L/L858R, and there are no specific reports of drug treatment of such patients at present. After treatment with icotinib, multiple nodular lesions continued to be alleviated, and the clinical efficacy was evaluated by achievement of stable disease, suggesting that icotinib has some therapeutic effect on NSCLC with EGFR V834L/L858R compound mutation. The wild-type amino acid in EGFR position 834, valine, and mutation-type amino acid leucine are both hydrophobic, and leucine only has an additional C-H group compared to valine, which may have little effect on the protein structure (Figure 4A and B). According to the structure of EGFR protein and considering that positions 834 and 858 are close in the spatial structure of the protein (Figure 4), they may have some effect on the drug binding of some EGFR-TKIs[12]. Therefore, it is necessary to carry out targeted drug therapy for NSCLC patients with this rare complex mutation.

**CONCLUSION**

In this case of NSCLC with EGFR V834L/L858R complex mutation, icotinib achieved good clinical efficacy. However, this treatment needs to be validated in a larger population.
Figure 4 Structural analysis of epidermal growth factor receptor L858R and V834L mutants.

REFERENCES


