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1 June 2019

https://doi.org/10.1016/j.pulmoe.2019.09.010
2531-0437/

Community-acquired *Klebsiella pneumoniae* liver abscess: a case complicated by metastatic lung abscesses

To the Editor,

A 74-year-old caucasian male, presented with a two-week history of fever, shivering, right scapular pain and dry cough. His medical history recorded high blood pressure, smoking and alcohol drinking. He had no recent history of antibiotic use, hospitalization or travelling to foreign countries. On admission he was sweaty and febrile, without any other significant alterations on physical examination. Laboratory analyses detected hypocapnia, elevated white blood count, C-reactive protein level as well as elevated liver enzymes. Chest X-ray revealed faded round densities on both lungs while abdominal ultrasound showed an hyperreflective liver with an oval, hypoechoic and heterogenic lesion (7.3×3.9 cm). Patient was hospitalized and started on doxicicline. Abominal MRI confirmed the nodular lesion in the the IV/VIII segments of the liver, with fluid and internal septae (Fig. 1). Simultaneously, the patient was diagnosed with diabetes mellitus and Kp resistant only to ampicillin was isolated in 2 blood cultures. The antibiotic was changed to amoxicillin-clavulanic acid plus metronidazole and the patient became afebrile and without pain. Percutaneous drainage was not executed due to high risk related to subphrenic location. Subsequent contrast CT-scan also revealed multiple nodules on both lungs, mostly peripheral, the bigger ones being cavitated and were considered as septic pulmonary emboli (Fig. 2). The patient was discharged after 2 weeks, antibiotics were continued until 8 weeks and no recurrence has been reported after 2 years .

We believe that this patient had a distinctive form of community acquired *Klebsiella pneumoniae* (Kp) infection causing liver abscess and complicated with septic metastatic pulmonary emboli, forming abscesses.

Liver abscess due to *Klebsiella pneumoniae* (KLA) is a distinct syndrome characterized by monomicrobial liver abscess, almost exclusively acquired in the community and in the absence of hepatobiliary disease. It is strongly associated with diabetes mellitus and Asian ethnicity and has a higher probability of complicating with metastatic infection sites than liver abscesses of other etiologies.[2] Some particularly virulent strains expressing hypermucoviscous phenotype are responsible for this invasive syndrome, despite not being naturally resistant to antibiotics.[3] It was geographically confined to Southeast Asia until the past decade, when other reported cases indicate the emergence of this syndrome worldwide.[3] In up to 11–12% of cases, KLA can be complicated with other septic metastatic lesions.[3]

Our patient was Caucasian and a 74-year-old male, consistent with published demographic data.[3] He fulfilled the requested diagnosis criteria for KLA[2,5,6]; 1. Clinical symptoms and laboratory findings of liver abscess: fever, chills, referred scapular pain, elevation of white-blood cell count and C-reactive protein, abnormal liver function tests; 2. Compatible imaging: as in this case, KLA has distinctive imaging features, being more often single, solid in appearance and septated, comprising multiple non-communicating locules; 3. Isolation of Kp in blood culture/abscess aspiration culture: although serotyping was not conducted, antimicrobial susceptibility of Kp isolated in blood culture meets the characteristic pattern of virulent KLA, described to be resistant to ampicillin and ticarcillin/carbenicillin but susceptible to all other antibiotics.[2,3,5]

That this patient had no underlying hepatobiliary disease, no previous hospitalizations or antibiotic use having acquired Kp in the community, also favored this diagnosis. Furthermore, he was simultaneously diagnosed with diabetes mellitus, the most common host risk factor for KLA.[3] Metastatic complications are more frequent in KLA than liver abscesses of other etiologies[2]; They can occur in up

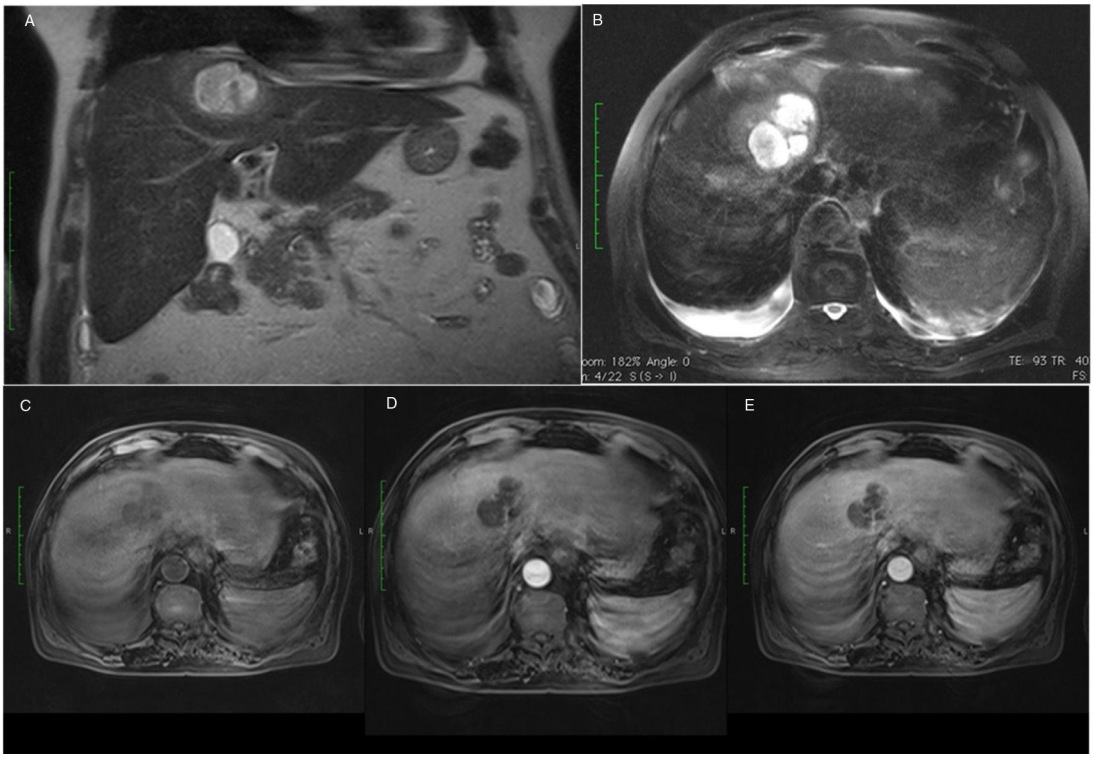

Fig. 1 Abdominal MRI (A) Coronal plan, T2 HASTE sequences – nodular lesion in the IV/VIII segments of the liver (B) Axial plan, T2 FS weighted sequences – hypersignal with fluid and internal septae (C) before gadolinium injection (non-enhancement phase) (D) after gadolinium injection, arterial phase – without contrast enhancement (E) after gadolinium injection, portal phase- peripheral contrast enhancement of the lesion.

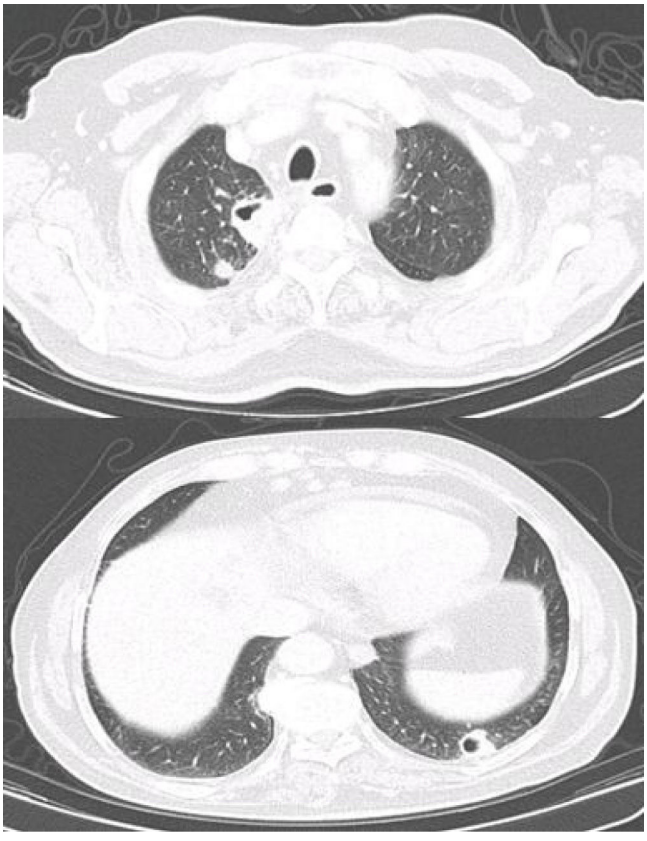

Fig. 2 Thoracic CT scan – axial plan – multiple peripheral nodules of both lungs, the bigger ones, cavitated.

to 11–12%, most commonly as endoftalmitis and meningites but SPE is a rare complication and it is generally present at hospital admission.[3–6] Our patient met SPE diagnostic criteria: had dry cough and hypocapnia, lung infiltrates, KLA as the embolic source, other potential explanations for lung infiltrates excluded and lung infiltrates resolved after appropriate antimicrobial therapy.[5,6] A broad spectrum of CT-scan findings can be present but less commonly compatible with lung abscesses.[6]

In conclusion, we describe a case of KLA with high clinical importance since it is the second case reported in Portugal [1], and the only one with the exceptionally rare complication of lung abscesses.[3,4,7] This case is an additional proof of the emergence of this syndrome worldwide. In cases of multiple lung abscesses with an acute presentation with dry cough in diabetic patients Kp should be considered, since it may be the first manifestation of serious underlying infection.

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24 June 2019

https://doi.org/10.1016/j.pulmoe.2019.08.006
2531-0437/

rs1573858 GATA-2 homozygote variant associated with pulmonary alveolar proteinosis, cytopenia and neurologic dysfunction

Dear editor,

Pulmonary alveolar proteinosis (PAP) is a syndrome characterized by the accumulation of alveolar surfactant. Although auto-immune PAP is responsible for 90% of all cases, association with genetic abnormalities has also been established.[1,2]

The authors present the case of a 43 years old non-smoker female. She has a previous medical history of idiopathic CD4 lymphocytopenia, idiopathic segmental dystonia, lymphedema and septicaemia due to parvovirus B19. Two years ago, she was treated for *Pneumocystis jiroveci* pneumonia with cotrimoxazol with clinical resolution.

Ten months ago, she was admitted to Hospital for dyspnea with acute respiratory failure. She was assumed to have had acute cardiac failure with good response after diuretic treatment. After discharge, the echocardiogram was normal but in this context she performed a thoracic computed tomography scan which showed diffuse pulmonary ground-glass opacities and slight thickening of the interlobular septa — ''*crazy-paving*'' pattern (Fig. 1). At this time, she was referred to our Department of Thoracic Diseases due to these imaging findings and chronic respiratory insufficiency. She performed bronchoalveolar lavage that evidenced rare alveolar macrophages in an amorphous granular background with proteinaceous material; the cytopathological study was negative for malignant tumour cells and microbiological study showed no pathogenic microorganisms. Routine blood tests reported: hemoglobin 9.0 g/dL, platelets 59,000/μL, leukocytes 3100/μL, neutrophils 1181/μL, lymphocytes 1160/μL and monocytes 40/μL. Results were positive (1:320) for antinuclear antibodies (ANA), and negative for anti-neutrophil cytoplasmic antibodies (ANCA) and anti-extractable nuclear antigens (ENA) antibodies. Anti-granulocyte-macrophage colony-stimulating factor (anti-GM-CSF) antibodies were negative. A required genetic test for GATA-2 gene mutation identified a rs1573858 homozygote, benign variant. Although this mutation is considered not pathogenic, the whole clinical profile, except segmental dystonia, is typical of GATA-2 deficiency. Therefore, she was diagnosed with GATA-2 deficiency related PAP and whole lung lavage (WLL) was proposed. Right WLL was initially performed. A total of eight litres of warmed saline solution was instilled in the right lung and the fluid was then consecutively collected by gravity after opening an outflow tube. The procedure was aided by mechanical chest percussion. After 20 days, left WLL was performed with eight litres of saline solution (Fig. 2). There were no procedure complications and currently the patient does not require oxygen therapy.

Macrophage homeostasis is highly relevant to lung hygiene. Conditions reducing either the number or functions of alveolar macrophages would be expected to reduce their capacity to clear surfactant from the lung surface, promoting secondary PAP.[1,3]

GATA-2 belongs to a family of transcription factors that are critical regulators of gene expression in hematopoietic cells. Therefore, GATA-2 gene mutations may lead to haploinsufficiency associated with profound cytopenias. It remains unclear why but dendritic cells, monocytes, B and NK lymphoid cells are the ones mainly affected.[3,4] Given this involvement, an association between GATA-2 insufficiency and PAP is to be expected. Given the usual abundance of alveolar macrophages in bronchoalveolar lavage fluid of these patients, PAP in GATA-2 deficiency must reflect more an alveolar macrophage dysfunction than a quantitative deficit, presumably by direct effects on alveolar macrophage phagocytosis.[4] GATA-2 also interacts with different signaling cascades through modulating the expression of key receptors or transducing proteins, such as M-CSF receptor or phospholipase C.[3] *Collin et al.*[3] reported the presence of 18% of PAP and 50% of abnormal pulmonary function cases in GATA-2 deficiency while *Vinh* et al.[5] found it in 33% of patients. As expected, our patient had no