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Small cell lung cancer elevates procalcitonin levels in the absence of infection

To the Editor,

A 77-year-old man with a history of hypertension, type 2-diabetes and chronic obstructive pulmonary disease came to the Emergency Department of our hospital with visual impairment, agraphia and memory loss. Cranial computed tomography (CT) revealed a hypodense lesion in the left posterior parietal white matter (maximum diameter of 4.5 cm) with vasogenic oedema. He was admitted to hospital to complete study of the primary neoplasm for suspicion of brain metastases. On day 3 post-admission, brain magnetic resonance imaging showed three images that suggested brain metastases. On day 5, he had a fever (39 °C) due to phlebitis in his right arm, with blood analysis showing leucocytosis, neutrophilia, and elevated C reactive protein (CRP) and procalcitonin (PCT) levels (see Fig. 1). Empirical therapy was started with meropenem and daptomycin. Positivity for methicillin-susceptible S. aureus was observed in cultures of two blood samples drawn at that time, and he was de-escalated to intravenous (IV) administration of 2 g cloxacillin. On day 9, blood cultures were negative, and trans-thoracic echocardiogram showed no signs of infective endocarditis. On day 9, cervical-thoracic-abdominal-pelvic CT study revealed a cavitated pulmonary nodule that could correspond to a primary pulmonary neoplasm with mediastinal lymph node metastases. Fluorine-18 fluorodeoxyglucose positron emission tomography findings led to suspicion of brain, skeletal, mediastinal lymphatic metastases of a pulmonary neoplasm, without ruling out a multifocal septic process. On day 25, cervical-thoracic CT showed a minimal decrease in the size of the pulmonary nodule, with the disappearance of its central cavitated component and the persistence of mediastinal nodes, with no change in their size. On day 28, PCT was elevated, CRP showed a small increase, and the leukocyte count was normal (see Fig. 1), while carcinoembryonic antigen (348.5 ng/ml), specific enolase antigen (23.9 ng/ml), and pro-gastrin-releasing peptide (2022 pg/ml) levels were all elevated. A trans-esophageal echocardiogram (TEE) ruled out infective endocarditis. Finally, cytology obtained by endobronchial ultrasound (EBUS) was reported as small cell lung cancer (TTF1 +, CD56+, CD45+, P40-). From day 5, the patient was free of fever, and repeated blood cultures were negative. However, PCT levels progressively increased up to 2.14 ng/ml at hospital discharge (see Fig. 1). The patient completed 33 days of treatment with cloxacillin (until TEE and EBUS results were obtained) for suspicion of septic emboli and osteomyelitis secondary to methicillin-susceptible S. aureus bacteraemia due to the progressive elevation in PCT levels and the imaging findings. The patient was discharged with diagnoses of extensive small cell lung cancer with brain, bone and mediastinal metastases, and transient methicillin-susceptible S. aureus bacteraemia without infective endocarditis. The patient received chemotherapy with carboplatin (AUC 4) and 80% etoposide with G-CSF from day 51, and whole-brain radiotherapy from day 61.On day 92, cranial CT showed a reduction in size of the largest brain metastasis (38 x 34 mm) and disappearance of the other brain metastases; thoracic CT showed a reduction in size of the pulmonary nodule (from 11 mm to 6 mm), the disappearance of nodes and the persistence of bone metastases; there was no change in abdominal CT findings. On day 144, cranial-thoracic-abdominal CT showed no changes with respect to day 92. Finally, on day 154, C-reactive protein and procalcitonin levels were normal.

PCT has been considered an excellent marker of bacterial infection for over 20 years [1], and levels > 2.0 ng/ml have been related to sepsis [1]. A systematic review [2] on the diagnostic accuracy of PCT in bacteremia reported that the optimal and most widely used cut-off value is 0.5 ng/ml, offering a sensitivity of 76% and specificity of 69%. Nevertheless, other authors [3] reported major PCT elevations in patients with metastatic small cell lung cancer but without sepsis, as in the present patient. A study [4] of 89 cancer patients concluded that PCT may give false positive results in patients with lung cancer, especially in those with neuroendocrine cancers or multiple metastases. In this line, a study [5] of 147 patients with lung cancer observed an independent association between a serum PCT value > 0.15 ng/ml and the presence of a neuroendocrine component in the tumor, finding that the elevation of serum PCT values was significantly greater in small cell lung cancers than in pulmonary adenocarcinomas. Of particular interest in our case is that the progressive elevation of PCT, despite its specificity, was not related to bacterial infection but rather to metastatic small cell lung cancer with neuroendocrine differentiation, as previously reported [3–5]. Finally, we highlight the decrease in PCT levels produced by the cancer treatment. To our knowledge, only one article [6] has reported an association between serum PCT levels and treatment response in neuroendocrine neoplasms of the digestive system and no data have previously been published on this association in lung neoplasms, as in the present case. Further research is needed to determine the specificity of PCT in patients with small cell lung cancer and in particular to explore the potential usefulness of PCT to monitor the response to treatment in this type of lung cancer.

Authors' contributions

AJPC and VMG wrote the paper and approved submission.

Declaration of Competing Interest

None.

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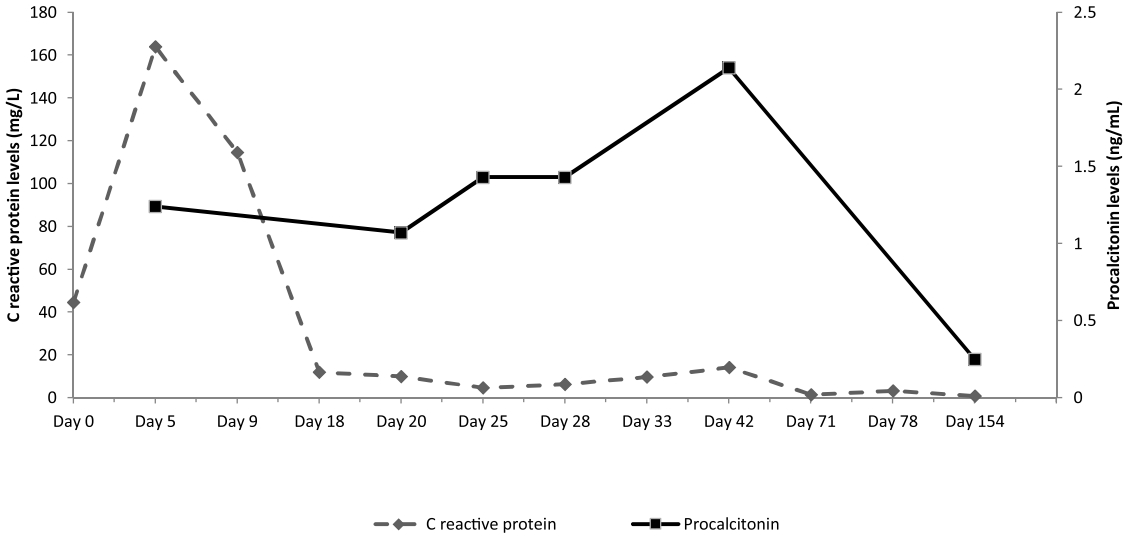

Fig. 1. C-reactive protein and procalcitonin levels during admission and after cancer treatment.

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References

[1] W. Karzai, M. Oberhoffer, A. Meier-Hellmann, K. Reinhart, Procalcitonin–a new indicator of the systemic response to severe infections, Infection 25 (1997) 329–334.
[2] S.H. Hoeboer, P.J. van der Geest, D. Nieboer, A.B. Groeneveld, The diagnostic accuracy of procalcitonin for bacteraemia: a systematic review and meta-analysis, Clin. Microbiol. Infect. 21 (2015) 474–481.
[3] P.A. Billy, L. Parmeland, S. Brunette, S. Lecordier, M. Pecquet, A major procalcitonin elevation without sepsis in a metastatic small cell lung carcinoma, Ann. Biol. Clin. (Paris) 75 (2017) 572–575.
[4] V. Avrillon, M. Locatelli-Sanchez, L. Folliet, M. Carbonnaux, E. Perino, G. Fossard, et al., Lung cancer may increase serum procalcitonin level, Infect. Disord. Drug Targets 15 (2015) 57–63.
[5] M. Patout, M. Salaün, V. Brunel, S. Bota, B. Cauliez, L. Thiberville, Diagnostic and prognostic value of serum procalcitonin concentrations in primary lung cancers, Clin. Biochem. 47 (2014) 263–267.
[6] L. Chen, Y. Zhang, Y. Lin, L. Deng, S. Feng, M. Chen, J. Chen, The role of elevated serum procalcitonin in neuroendocrine neoplasms of digestive system, Clin. Biochem. 50 (2017) 982–987.

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