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RCR RADIOLOGY CASE REPORTS

Case Report

Metastatic pulmonary calcification: First report of pulmonary calcium suppression using dual-energy CT ☆

Ana Fehrmann[a], Jorge Garcia Borrega[b], Jasmin Holz[a], Nadav Shapira[c,d], Jonas Doerner[a], Boris Boell[b], David Maintz[a], Tilman Hickethier[a,]*

[a] *Department of Radiology, University Hospital of Cologne, Kerpener Str. 62, D-50937 Cologne, Germany*
[b] *Department I of Internal Medicine, Intensive Care Unit, University Hospital of Cologne, Cologne, Germany*
[c] *Philips Healthcare, Haifa, Israel*
[d] *Department of Radiology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA*

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ABSTRACT

Metastatic pulmonary calcification is an underdiagnosed metabolic lung disease characterized by diffuse calcium deposition in the lungs, often associated with secondary hyperparathyroidism due to chronic renal failure. A 31-year-old man with chronic renal failure initially presented with diffuse pain symptoms, deterioration of general condition, and respiratory insufficiency. Noncontrast-enhanced computed tomography of the chest was performed using a spectral-detector-based dual-energy CT. It showed multiple, centrilobular, ground-glass opacities, and nodules, ultimately leading to the diagnosis. Calcium suppression proved to be highly useful to classify the pulmonary alterations.

Introduction

Metastatic pulmonary calcification (MPC) is a well-known and often underdiagnosed long-term complication of end-stage renal disease with secondary hyperparathyroidism [1,2]. It is a metabolic lung disease seen at autopsy in 60%-75% of patients with renal failure and is characterized by diffuse interstitial calcium deposition in the lungs [1,3–5].

Abbreviations: CaSupp-I, calcium suppression index; CT, computed tomography; MonoE, monoenergetic; MPC, metastatic pulmonary calcification; ROI, region of interest; SDCT, spectral-detector CT.

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* *Corresponding author.*
E-mail address: Hickethier@radiologie-ac.de (T. Hickethier).

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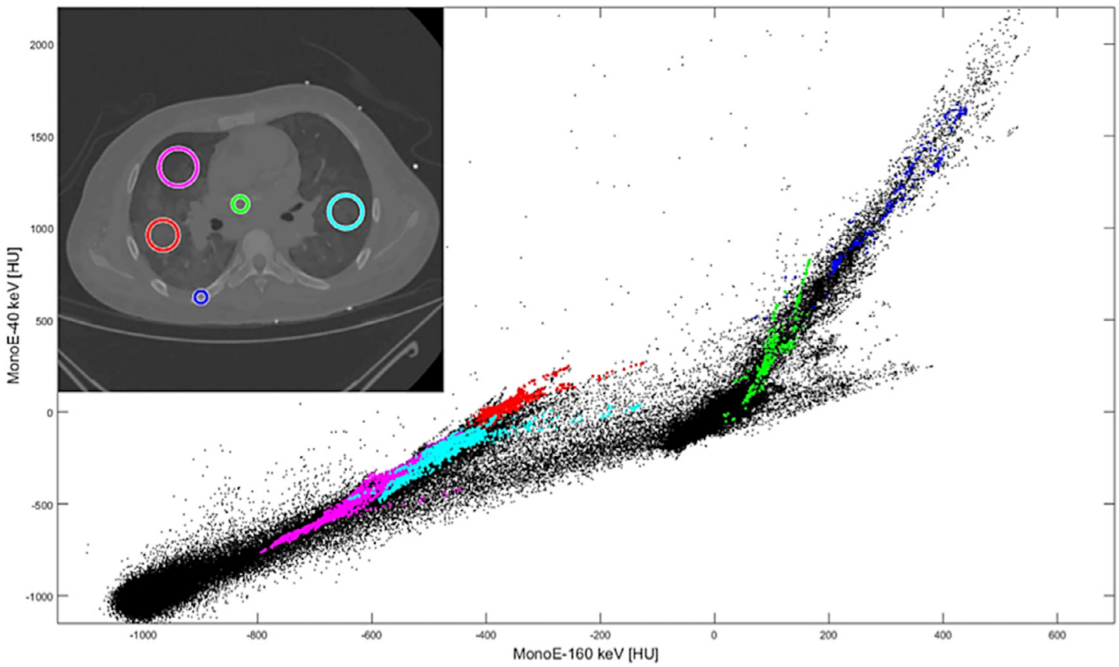

Fig. 1 – Dual-energy CT can provide virtual monoenergetic attenuation values at different keV values for each image voxel. In this scatter plot, the attenuation value at 40 keV of each voxel in the image insert (top-left, MonoE-70 keV spectral result—which has an image impression like a conventional CT image) is plotted versus its attenuation value at 160 keV. Voxels within the ROIs shown on the image insert result in corresponding clusters on the scatter plot where the slope of each cluster represents the material composition and the extent of the cluster along the slope represents the different material densities within the cluster. Such an analysis enables material separation from which one can learn, for example, that the nonpulmonary calcification (green) contains more calcium by percent mass, than the rib (blue) or that the magenta, cyan, and red voxels contain elevated amounts of calcium. In our case, a linear fit was applied to find the slope representing all magenta, cyan and red voxels. From this slope, we identified the optimal calcium suppression index, which controls the calcium percent mass of the target material to be suppressed.

Case report

A 31-year-old man initially presented to an external hospital with diffuse pain, increasing need for help, reduced mobility due to increasing weakness, and shortness of breath, so that he needed oxygen supplementation via nasal cannula. He had a longstanding history of chronic renal disease with multiple unsuccessful kidney transplants, temporary hemodialysis, and peritoneal dialysis for the last 12 months.

A computed tomography (CT) scan of the chest revealed extensive diffuse ground-glass opacifications, initially interpreted as atypical or acute eosinophilic pneumonia. A medical therapy with high-dose co-trimoxazole (trimethoprim/sulfamethoxazole; due to a suspected pneumocystis pneumonia) was initiated but did not lead to improvements. In the course of an unsuccessful bronchoalveolar lavage, the patient had to be resuscitated and intubated. He was transferred to an intensive care unit where he continued to require ventilation due to a persistent respiratory insufficiency. He was finally transferred to our hospital where a new CT thorax examination was performed to clarify the current pulmonary status. Noncontrast-enhanced examination was performed on a spectral-detector CT (SDCT; IQon, Philips Healthcare).

Conventional reconstruction of the CT images showed symmetrical, parenchymal, multiple, centrilobular fluffy ground-glass opacities, and calcified nodules. Additionally, extensive calcifications of trachea and main bronchi, vascular structures in thoracic soft tissue, coronary arteries and aortic valve were present, as well as cardiac calcifications lining the interior atrial walls. The spine had a "rugger-jersey" appearance, a distinctive pattern for hyperparathyroidism [6]. Lymphadenopathy and pleural effusions were not present.

Based on these findings and the calcium-specific dual-energy analysis (see below), as well as the negative sputum cultures for fungal and mycobacterial infection, the diagnosis of MPC was made. At the intensive care unit in our center, based on the diagnosis, the co-trimoxazole therapy was discontinued and the patient received daily hemodialysis and could be weaned from mechanical ventilation. He received oxygen supplementation with a high-flow cannula until he was finally transferred to our general ward where he only needed oxygen through a nasal cannula.

Discussion

Suspicion of MPC mainly relies on imaging findings. Standard chest radiographs are insensitive to small calcifications and changes are not specific [7,8]. CT is much more accurate for the detection and characterization of parenchymal opacities with an excellent sensitivity for calcifications [9].

Three characteristic CT patterns have been described in literature: (1) diffuse or patchy centrilobular ground-glass opacities with or without foci of calcification, (2) confluent dense parenchymal consolidations with lobar distribution, (3) multiple 3- to 10-mm diameter calcified nodules, sometimes with associated peripheral reticular opacities [7–10]. Calcifications are common and present in various forms: they may be punctate within nodular opacities, ring-like or diffuse [8,9]. They may be distributed diffusely throughout the lungs or they may show a lower or upper lung predilection [9]. Some studies report an upper lung predominance [1,7], which may be associated with a local alkaline environment due to a higher ventilation-perfusion ratio at the apex compared with the base, resulting in a precipitation of calcium-phosphate products [3,11].

A frequently associated and characteristic finding is a calcification of vessels in the chest wall, bronchial walls and myocardium [1,7].

However, the most common CT finding of fluffy, poorly defined, partially confluent nodules or consolidation is not specific for MPC, resulting in diagnostic uncertainty.

This patients' examination was performed on a SDCT, which allows generating additional, so-called spectral results of each examination, either prospectively or retrospectively. Using this additional spectral information, tissues with different elemental compositions, which may be indistinguishable visually (and also in Hounsfield unit measurements), can be differentiated through their attenuation profiles at different energy levels [12]. For calcium, a specific algorithm was recently introduced, which allows for generation of images in which the calcium contribution to the total attenuation is suppressed with an ability to modify the targeted calcium composition weight using different calcium suppression indices (CaSupp-I) [13]. For the purpose of pulmonary diagnosis, a CaSupp-I of 30 was calculated to be appropriate using the analysis shown in Figure 1.

In the calcium-suppressed images, the bilateral, diffuse ground-glass opacities as well as the parenchymal calcifications "vanished" (Fig. 2,2a, b). Pulmonary infiltrations of different etiologies, like pulmonary edema or pneumonia, for example, are unaffected by calcium suppression. This allowed a clear differentiation and confirmed the suspected calcific nature of the ground-glass opacities. To our knowledge, this is the first reported case of calcium-suppressed chest imaging to diagnose and confirm MPC.

It is very important for the radiologist to be able to reliably detect MPC in chest CT examinations because it is a frequently missed complication in patients with chronic kidney disease. This could be facilitated in the future by using dual-energy-based calcium-specific images for diagnosis and follow-up.

Therapy is aimed at the optimal treatment of the underlying causes, since no specific treatment of MPC itself is known. However, patients with pronounced pulmonary symptoms may require immediate therapeutic measures, such as normalizing hypercalcemia and hyperphosphatemia. This can be achieved with bisphosphonate or phosphate binders while Cinacalcet or even parathyroidectomy (in the absence of response to drug treatment) may be considered as hyperparathyroidism treatment [3,5]. Especially in fulminant courses like the one reported here, where the patient has developed MPC despite undergoing peritoneal dialysis, hemodialysis should be initiated to rapidly normalize hypercalcemia and hyperphosphatemia and prevent further progression of MPC. Additionally, there may be a need for urgent kidney transplantation.

Overall, MPC is regarded to be a potentially reversible condition, since both the morphologic pulmonary changes and respective symptoms can recede under early and appropriate therapy [14].

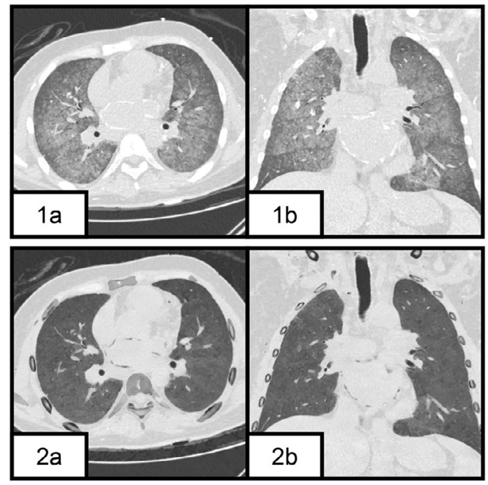

Fig. 2 – 1: Conventional reconstructions in axial (a) and coronal (b) orientation of the second CT scan of the patient showing diffuse ground-glass opacities. 2: Calcium-suppressed reconstructions of the same raw data as in 1. The diffuse ground-glass opacities disappeared indicating that they consist of calcium. Also, atrial calcifications disappear in the calcium-suppressed images.

REFERENCES

[1] Chung MJ, Lee KS, Franquet T, Muller NL, Han J, Kwon OJ. Metabolic lung disease: imaging and histopathologic findings. Eur J Radiol 2005;54(2):233–45.

[2] Faubert PF, Shapiro WB, Porush JG, et al. Pulmonary calcification in hemodialyzed patients detected by technetium-99m diphosphonate scanning. Kidney Int 1980;18(1):95–102.

[3] Chan ED, Morales DV, Welsh CH, McDermott MT, Schwarz MI. Calcium deposition with or without bone formation in the lung. Am J Respir Crit Care Med 2002;165(12):1654–69.

[4] Conger JD, Hammond WS, Alfrey AC, Contiguglia SR, Stanford RE, Huffer WE. Pulmonary calcification in chronic dialysis patients. Clinical and pathologic studies. Ann Intern Med 1975;83(3):330–6.

[5] Belém LC, Zanetti G, Souza AS Jr, Hochhegger B, Guimarães MD, Nobre LF, et al. Metastatic pulmonary calcification: state-of-the-art review focused on imaging findings. Respir Med 2014;108(5):668–76.

[6] Wittenberg A. The rugger jersey spine sign. Radiology 2004;230(2):491–2.
[7] Hartman TE, Müller NL, Primack SL, Johkoh T, Takeuchi N, Ikezoe J, et al. Metastatic pulmonary calcification in patients with hypercalcemia: findings on chest radiographs and CT scans. AJR Am J Roentgenol 1994;162(4):799–802.
[8] Lingam RK, Teh J, Sharma A, Friedman E. Case report. Metastatic pulmonary calcification in renal failure: a new HRCT pattern. Br J Radiol 2002;75(889):74–7.
[9] Belém LC, Souza CA, Souza AS Jr, Escuissato DL, Hochhegger B, Nobre LF, et al. Metastatic pulmonary calcification: high-resolution computed tomography findings in 23 cases. Radiol Bras 2017;50(4):231–6.
[10] Kuhlman JE, Ren H, Hutchins GM, Fishman EK. Fulminant pulmonary calcification complicating renal transplantation: CT demonstration. Radiology 1989;173(2):459–60.
[11] Alkan O, Tokmak N, Demir S, Yildirim T. Metastatic pulmonary calcification in a patient with chronic renal failure. J Radiol Case Rep 2009;3(4):14–17.
[12] McCollough CH, Leng S, Yu L, Fletcher JG. Dual- and multi-energy CT: principles, technical approaches, and clinical applications. Radiology 2015;276(3):637–53.
[13] Neuhaus V, Lennartz S, Abdullayev N, Große Hokamp N, Shapira N, Kafri G, et al. Bone marrow edema in traumatic vertebral compression fractures: diagnostic accuracy of dual-layer detector CT using calcium suppressed images. Eur J Radiol 2018;105:216–20.
[14] Peungjesada S, Baskin MH, Winer-Muram HT. Metastatic pulmonary calcification. Appl Radiol 2016;45(1):31–3.