La radiologia medica (2021) 126:22–28
https://doi.org/10.1007/s11547-020-01230-x

CHEST RADIOLOGY

Exogenous lipoid pneumonia: when radiologist makes the difference

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Received: 15 March 2020 / Accepted: 12 May 2020 / Published online: 25 May 2020

Abstract

Purpose To report high-resolution CT (HRCT) findings in our group of patients with exogenous lipoid pneumonia (ELP), confirmed with histopathological findings and clinical-anamnestic data, in order to describe the most common radiological patterns of this rare disorder.

Materials and methods In this retrospective study, HRCT of 10 patients with ELP were evaluated by three radiologists. Diagnosis of ELP was made through CT, bronchiolo-alveolar lavage (BAL) and a pneumological examination associated with an accurate medical anamnesis. Five patients had a histologically proven ELP, through lung biopsy. All patients had a chronic exposition to substances made of animal fat or mineral/vegetable oils.

Results In our cohort of patients with ELP, the following parenchymal patterns were observed: 8/10 patients had lung consolidation with adipose density (attenuation values < -40 HU); 10/10 patients had multiple areas of ground glass opacity; 6/10 patients had smooth thickening of interlobular septa and ground glass opacities ("crazy-paving" pattern); 2/10 patients presented nodules > 2.5 cm with spiculated margins (tumor-like); 5/10 patients showed reactive lymph nodes enlargement. The oldest lesions were characterized by bronchiectasis and fibrosis around the lipidic consolidations.

Conclusion Pulmonary alterations found in HRCT exams can be confused with other lung diseases (especially lung tumors) and they are always a challenge even for the most experienced radiologist. In our experience, although non-specific, consolidation areas with low HU values and crazy-paving pattern are frequently associated in ELP. These characteristics should alert the radiologist to consider ELP among the possible differential diagnoses, always correlating the results of CT examination with appropriate clinical-laboratory evaluations and an accurate anamnesis.

Keywords Computed tomography · Lung · Pneumonia · HRCT

Lipoid pneumonia is an uncommon condition that results from a pulmonary accumulation of lipid in the alveoli, due to the accumulation of fat-like compounds of animal, vegetable or mineral origin. This rare disorder can be either "endogenous" or "exogenous" based on the source of the lipid substances [1, 2]. The endogenous form, also called "cholesterol" or "golden" pneumonia, is caused by the accumulation of lipid substances derived from the lung itself, usually from a lipid-storage disease [3, 4]. It usually develops when destroyed alveolar cell walls release lipids that are generally contained inside lung tissue (most commonly cholesterol and derived molecules) after a damage caused by an obstructive airway lesion or a suppurative process. Chronic exogenous lipoid pneumonia (ELP) usually results from repeated episodes of aspiration/inhalation of animal fat or mineral/vegetable oils, present for example in food, radiographic contrast media or oil-based medications (such as laxatives), over an extended period [3, 5]. There is also an acute form, that is secondary to a single episode of accidental (or not) inhalation of a large quantity of lipid material over a short period of time [3]. This form usually occurs in children due to accidental poisoning or in performers (like fire-eaters)

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that use liquid hydrocarbons such as petroleum for the flame blowing [6]. First described in 1925 by Laughlen in few patients with a prolonged history of laxative ingestion or use of oil-based nose drops, nowadays some examples of chronic ELP are caused by repeated use of petroleum jelly at bedtime over a long period (for example vaseline oil), excessive use of lip balm, vaseline inhalation during the placement of nasal-gastric tubes, professional exposure to paraffine or others oily materials [1]. Other factors that can facilitate the development of chronic ELP are elder age, the presence of tracheostomy or neuro-muscular disorders, swallowing dysfunctions, gastro-esophageal reflux disease and hiatal hernia, rectal or subcutaneous administration of mineral oils [7]. Regarding the clinical manifestations, the acute form of ELP typically manifests itself as cough, dyspnea and low-grade fever [3]. Instead clinical manifestations of chronic ELP are non-specific and can manifest from asymptomatic forms (that are only identified because of an incidentally detected abnormality on radiological imaging) to severe respiratory failure [8]. Diagnosis is usually difficult because a history of oil ingestion is often missed, and the exposure is often identified only retrospectively when the diagnosis is made, after an accurate medical anamnesis [9]. Radiological diagnosis can be tricky if the radiologist does not know the prevalent CT findings. Bronchiolo-alveolar lavage (BAL) and lung biopsy, the more aggressive approach, can confirm the diagnosis: The typical histopathological findings are macrophages with intracellular lipid vacuoles. Indeed, the aim of this study is to describe the CT findings of our ELP series, confirmed with histopathological findings and clinical-anamnestic data.

Materials and methods

We retrospectively reviewed the radiological imaging of patients with non-specific clinical recalls (chronic cough, dyspnea, fever) and history of chronic use of oily substances that had a pneumological consult in the period from May 2013 to December 2019. Inclusion criteria were a multidisciplinary diagnosis of ELP (established by imaging features associated with anamnesis, histopathology and/or BAL), chronic use of oily substances, a chest CT performed at the time of diagnosis and a clinical-radiological follow-up after 6-month/1-year. Patients with diagnosis of advanced fibrotic disease were excluded. On the basis of these inclusion criteria, a total of 10 patients were selected. All patients performed a BAL and they were also subjected to a pneumological examination and a careful medical anamnesis, in order to investigate an history of oil use. Informed consent was obtained from all individual participants included in the study. Chest CT exams were performed using the same 64-row multidetector system (Sensation Siemens, Erlangen, Germany), with high resolution technique (HRCT—slice thickness 1 mm). All the scans were in inspiration phases. Images were reconstructed using a smooth reconstruction kernel (B30f) for mediastinal structures and a sharp one (B70f) for parenchymal evaluation. HRCT studies were evaluated by three expert radiologists dedicated to thoracic disease in order to radiologically define the predominant pattern of presentation; in case of discordance, a consensual agreement was reached.

Results

Results are reported in Table 1. In total, ten patients with ELP were enrolled: seven males and three females, aged 42–94, mean age 74 years. In particular, 4/10 (40%) were laryngectomized patients that underwent chronic use of lubricants for tracheostomy and 6/10 (60%) were dysphagic/elder patients: 4 of them used paraffin oil for constipation and the other 2 used lipid-containing nasal sprays and nose drops. HRCT findings showed the following prevalent parenchymal patterns: 8/10 patients (80%) had lung consolidation with adipose density (attenuation values < -40

Table 1 Patients' CT and clinical features

Gender	Age	Cause of oil inhalation	Biopsy	Consolidation	Nodule	GGO	Crazy paving
M	42	Tracheostomy	Yes	No	No	Yes	No
F	75	Tracheostomy	Yes	No	Yes	Yes	Yes
M	80	Tracheostomy	No	Yes	No	Yes	No
M	87	Elder-constipation	Yes	Yes	Yes	Yes	Yes
M	70	Elder-constipation	No	Yes	No	Yes	No
M	64	Nasal decongestionant	Yes	Yes	No	Yes	Yes
M	80	Tracheostomy	No	Yes	No	Yes	Yes
F	94	Elder-constipation	No	Yes	No	Yes	No
M	86	Elder-constipation	No	Yes	No	Yes	Yes
F	89	Nasal decongestionant	No	Yes	No	Yes	Yes

M male; *F* female; *GGO* ground glass opacitiy

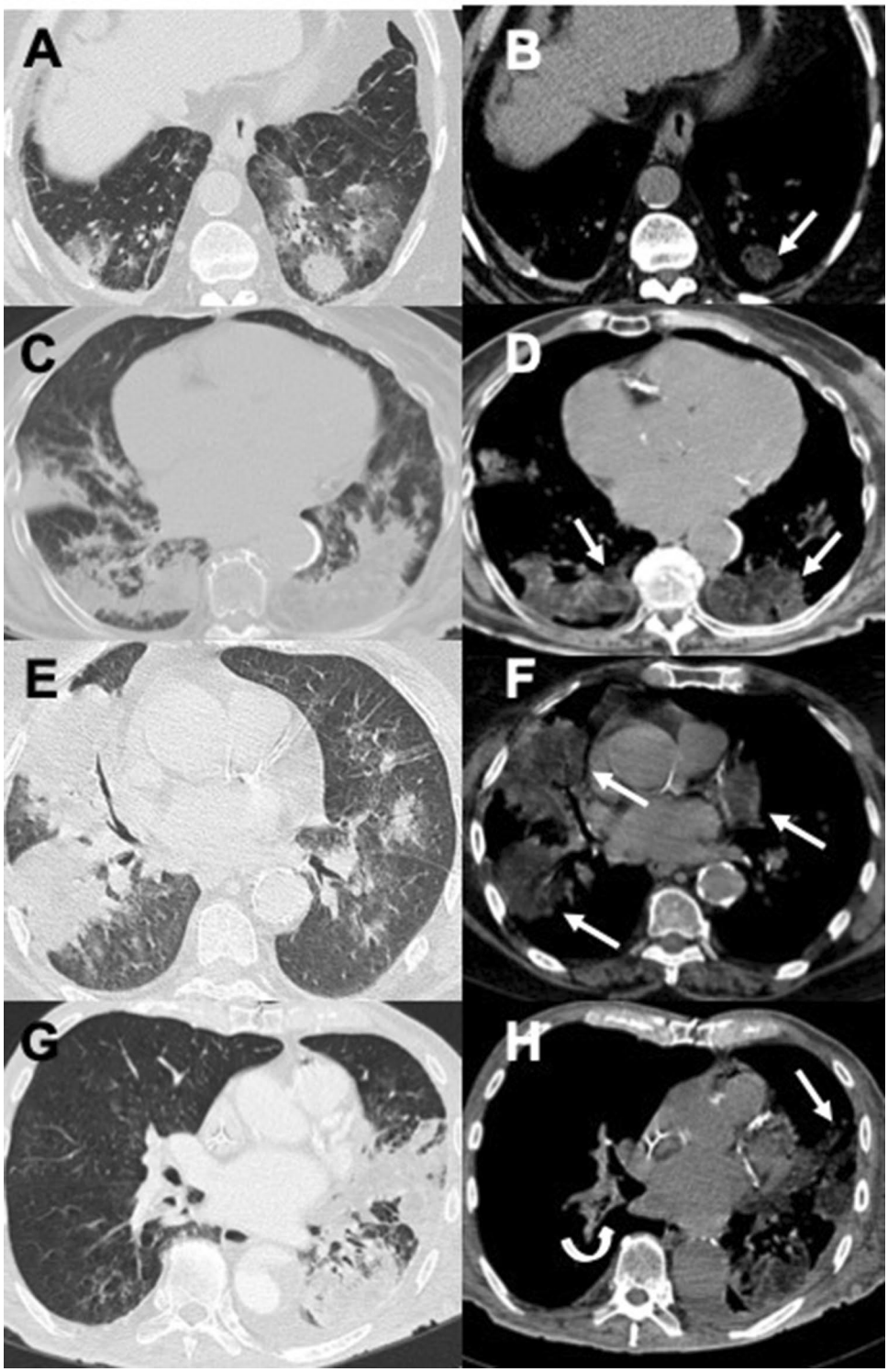

Fig. 1 CT features of ELP. Four patients of our cohort showing hypodense consolidations at baseline CT (white arrows) and diffuse ground glass opacities, both in the lower lobes and/or in the posterior segments of upper lobes. Please note patient in figure **g–h** has a replete bronchus of hypodense material (rounded arrow)

HU); 10/10 patients (100%) with multiple areas of ground glass opacity; 6/10 patients (60%) had smooth thickening of interlobular septa associated with ground glass opacities ("crazy-paving" pattern); 2/10 patients (20%) presented nodules > 2.5 cm with spiculated margins (tumor-like); 5/10 patients (50%) showed reactive lymph nodes enlargement. Regarding the localizations of pulmonary alterations, they were found in the lower lobes in all the patients (10/10) and in 4/10 of them also in the posterior segments of the upper lobes. Lung biopsy or transbronchial biopsy was performed in 5/10 patients. BAL was performed in all patients, showing macrophages with intracellular lipid vacuoles. No

patients underwent surgery primarily due to the stability of the lesions over time: No regression of lung findings was observed despite patient recommendations.

Discussion

ELP is caused in many cases by excessive use of an oily substance: animal oils caused a very active inflammatory response; mineral ones are more inert because they have no fatty acids and are rapidly destroyed by pulmonary macrophages. Vegetables oils are emulsified but not hydrolyzed by lung lipase and result in foreign body reaction. Macrophages with fatty acids and intracellular lipid vacuoles distend alveolar walls and interlobular septa [9–11]. In fact, one of the most common radiologic manifestations of chronic ELP at CT are one or multiple ground-glass or consolidative opacities, sometimes with specific fatty attenuation (values < −40 HU). These alterations usually involve one or more segments with a typically peri-broncho-vascular distribution and are predominant in the lower lobes, usually with subpleural sparing [1, 12, 13]. Furthermore, architectural distortion and thickening of the interlobular septa can be found, as well as crazy-paving pattern with a basilar predominance. Typically, chronic ELP could manifests itself as an adipose-containing mass and, even if the mass has often irregular or spiculated margins due to chronic inflammations and secondary fibrosis, the presence of fat inside the lesion is a diagnostic feature. If fat is absent, the mass or nodules of chronic ELP can be indistinguishable from primary lung cancer or pneumonia [14]. Chest radiography is often non-specific, and HRCT is mandatory to better assess lung involvement [3, 15]. In fact, HRCT is the best imaging

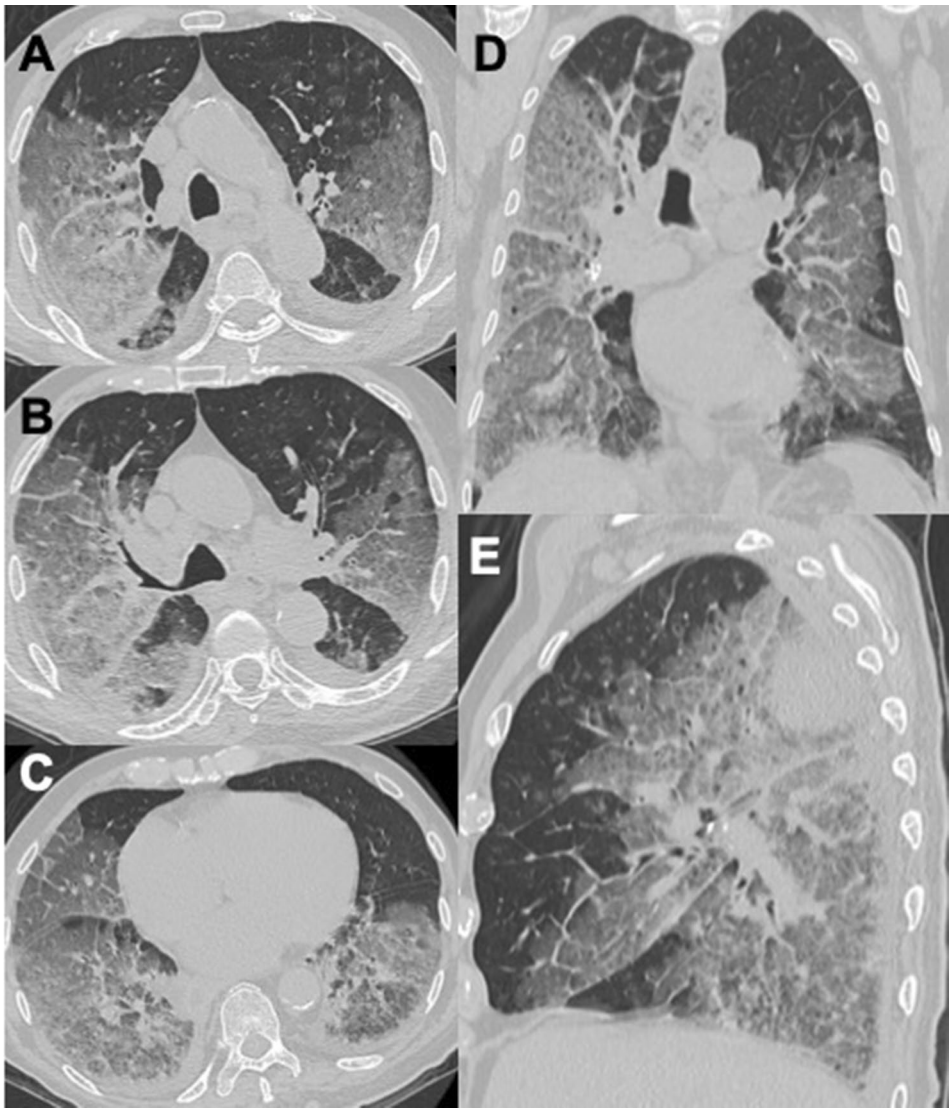

Fig. 2 Crazy paving. Example of crazy-paving pattern in an 86-year-old male with chronic use of Vaseline oil for constipation. Axial (**a–b–c**), coronal (**d**) and sagittal (**e**) reconstruction

modality for establishing the diagnosis of lipoid pneumonia. The most characteristic finding in our cohort of ELP is the presence of areas with fat attenuation value (negative attenuation values, between −30 HU and −150 HU, measured at baseline scan) in the consolidations or nodules, with or without a peripheral fibrous reaction (Fig. 1). Nevertheless, CT attenuation measurements are not always characteristic due to the averaging with attenuation values from surrounding inflammatory infiltrates [2, 16]. In fact, inflammation or superinfection can increase the attenuation coefficient, resulting in a harder diagnosis: in these cases, extensive consolidation is of lower attenuation value than expected, but its higher than subcutaneous fat [2]. Architectural distortion can be associated with consolidative opacities, as well as the thickening of interlobular septa or fibrosis in the adjacent parenchyma can occur because of the transposition of oils from the alveoli into the lung interstitium [1]. Moreover, a distinctive pattern consisting of "ground glass" opacities with associated interlobular septal thickening (the so-called crazy-paving appearance), similar to the pattern described in alveolar proteinosis or bronchoalveolar carcinoma, with a basilar predominance, has been reported in various study as a common sign in adult patients with ELP [2, 17] (Fig. 2). This pattern reflects gross and microscopic features of pathologic findings; in particular in case of lipoid pneumonia ground-glass opacities are likely to reflect the fill-in of alveoli with macrophages and the amount of inflammation, while thickened septae and centrolobular thickening reflect the inflammatory infiltrates of interstitial tissue [2]. When ELP manifest itself with the "crazy-paving" pattern, it should be put in differential diagnosis with acute or chronic eosinophilic pneumonia, alveolar proteinosis, infections (Pneumocystis or Cytomegalovirus pneumonia), organizing pneumonia and hypersensitivity pneumonia: an accurate clinical evaluation and acute or chronic onset of symptoms usually help in the differential diagnosis [12, 17–19]. In case of hypodense nodules/consolidations at CT exam, the principal differential diagnoses are hamartoma, lipoma, necrotizing pneumonia, mucinous adenocarcinoma, post-obstructive pneumonia and pulmonary infarction. It has to be remembered also that these patients are usually asymptomatic and pulmonary lesions are discovered incidentally. When the lipoid pneumonia manifests itself with architectural distortion or as

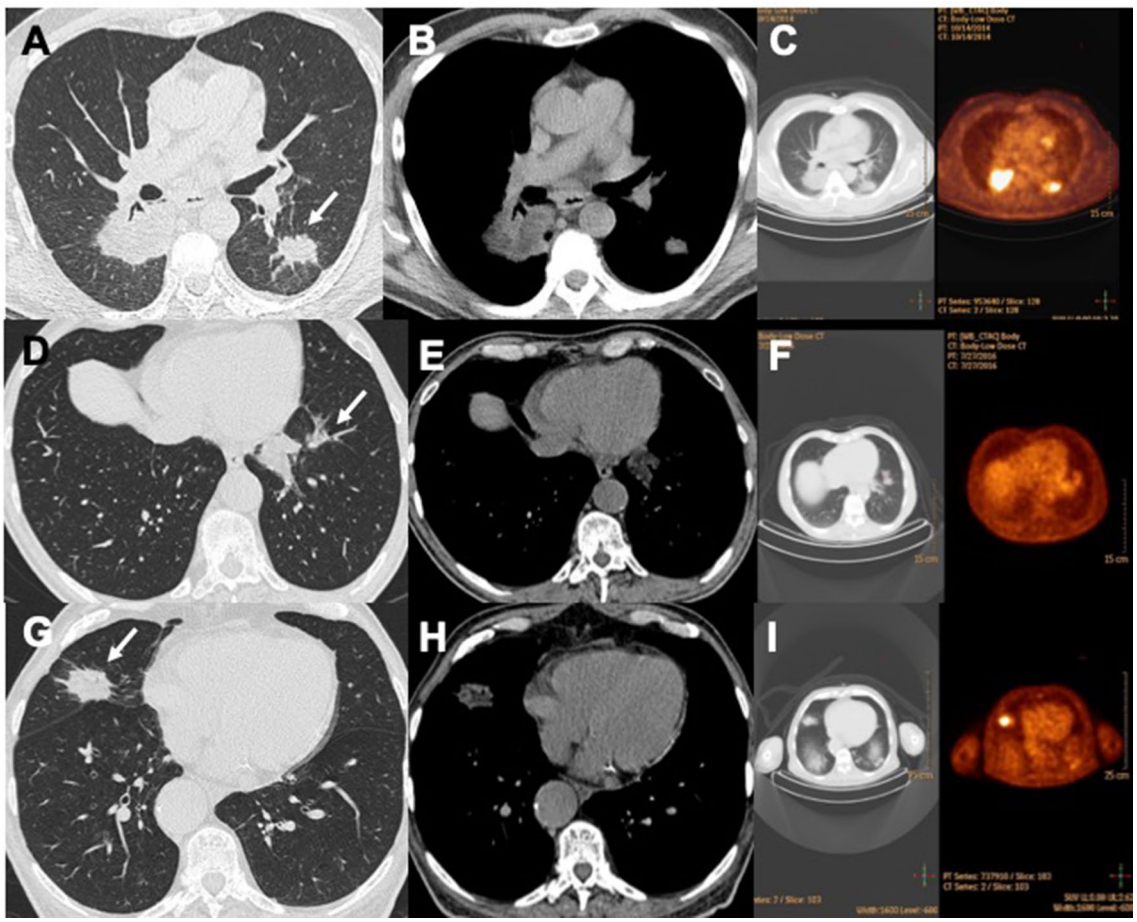

Fig. 3 PET positivity of ELP nodules/consolidations. Three examples of our patients with PET positivity of hypodense nodules (**a** and **g**) and consolidation (**d**) (white arrow)

a spiculated nodule, differential diagnosis is tricky and should be done even with primary lung cancer: usually radionuclide imaging, especially with 18F-Fluorodeoxyglucose Positron Emission Tomography (18FDG-PET), is recommended [14, 20] (Fig. 3). Unfortunately, PET scan is usually positive for a hypermetabolic lesion and often lung biopsy is mandatory. One of the most important characteristics is the lesions stability over time during the follow-up exams. Our cohort of patients confirms that consolidation with fatty-density and crazy-paving appearance are the most common findings of lipoid pneumonia. Radiologist should know CT appearance of the disease because they have a key role in the diagnosis. In fact, in all our cases, it was the radiologist who first puts the suspicion of lipoid pneumonia itself. Diagnoses were then confirmed with BAL (in the most uncertain cases also with biopsies) and with a careful anamnestic research of exposure to oily substances [21–24]. BAL has also a therapeutic role because can remove part of lipidic substances from the alveoli [25, 26]. It has to be remembered that HRCT should not be used in the routine follow-up for patients with stable disease and it should be considered in case of worsening of clinical conditions; it also true that many subjects with ELP are oncological patients (tracheostomized for laryngeal cancer) who, in any case, perform CT for their routine follow-up. In these cases, multidisciplinary approach to the disease help in reaching the diagnosis faster, setting the proper therapy and programming a personalized follow-up. This study has several limitations: first of all, the retrospective nature of the work and second the small number of patients. Nevertheless, it is known that ELP is an uncommon diagnosis and we have collected ten cases in six years in a second-level university hospital. It is important to recognize the various radiological manifestations of ELP, for a prompt an accurate diagnosis, resulting in decreasing of morbidity rates especially in the elderly, who are the majority of the affected population.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest related to the publication of this article.

Ethical approval All procedures performed in studies involvement human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

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