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CASO CLÍNICO/CLINICAL CASE

Pneumonia Lipídica Exógena – um diagnóstico não suspeito

Exogenous Lipoid Pneumonia – unsuspected diagnosis. A case report

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RESUMO

Uma mulher de 49 anos de idade foi internada no Serviço de Pneumologia com febre, tosse e dispneia. A radiografia de tórax mostrava condensação bilateral, atingindo predominantemente os segmentos posteriores dos lobos superiores e inferiores. A

ABSTRACT

A 49-year-old woman was admitted to hospital with fever, cough and dyspnea. The chest radiographs showed bilateral consolidation, more severe on right side, predominantly affecting posterior segments of upper and lower lobes. The thoracic CT

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tomografia axial computorizada do tórax revelava opacidades nodulares bilaterais cujos aspectos variavam desde um padrão em vidro fosco até um padrão alveolar confluente em áreas de maior densidade. A fibrobroncoscopia revelou sinais inflamatórios generalizados. O exame directo e cultural para o bacilo de Koch foram negativos. Após lavado brocoalveolar e biópsia pulmonar transbrônquica inconclusivos procedeu-se a uma biópsia pulmonar cirurgica. O exame histológico revelou tratar-se de uma pneumonia lipídica. Posteriormente obteve-se a informação de que a doente utilizava parafina líquida em gotas nasais desde há cerca de 10 anos.

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Palavras-chave: Pneumonia lipídica exógena; TAC torácica; Biópsia pulmonar.

scan detected bilateral opacities ranging from ground glass pattern to alveolar nodules coalescing in larger areas of dense consolidation. Bronchoscope examination revealed generalised inflammatory signs. Stains and cultures were negative. After inconclusive bronchoalveolar lavage and transbronchial lung biopsy, an open lung biopsy was performed. Histological examination showed an unexpected finding of lipoid pneumonia and thereafter information of use of liquid paraffin nose drops, during the preceding 10 years, was obtained.

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Key-words: Exogenous lipoid pneumonia; Thoracic CT scan; Open lung biopsy.

INTRODUCTION

Lipoid Pneumonia (LP), first described by Laughlen (1) in 1925, may be classified as exogenous, endogenous or idiopathic (2). Exogenous lipoid pneumonia (ELP) is a particular form of aspiration pneumonia that results from the long-term inhalation of oil-based substances. Even though it may also be acute, ELP is most frequently a chronic disease. It mostly commonly presents in elderly patients with predisposing factors, such as gastrooesophageal reflux, neuromuscular or psychiatric disorders (3) or in patients without organic disease, who have regularly taken the mineral oil liquid paraffin at night for chronic constipation (4). Respiratory disease results from repeated small aspirations. A similar condition can result from the use of oily nasal drops, although such medication is rarely used nowadays (5). Mineral oil is relatively inert, and once in the alveolar space, the oily substances are emulsified by lung lipase, resulting in a foreign body reaction that causes little acute inflammation. Fat droplets are absorbed into alveolar macrophages. These enter the interstitium and coalesce to form fat-laden giant cells, which eventually aggregate and are surrounded by fibrosis(4).

Commonly the condition presents as an interstitial pneumonia in a dependent lobe. Occasionally it appears radiological as a mass with a spiculated appearance resembling a peripheral tumour (paraffi--noma) (6). Rarely, repeated widespread aspiration can cause diffuse pulmonary fibrosis (7).

Clinically, most patients are asymptomatic; few cases only present with cough, dyspnea and chest pain (8,9). Fever, weight loss, cough, dyspnea were the most frequent symptoms reported by Gondouin and al. (3) in a retrospective study of ELP. Because symptoms are absent or nonspecific and the roentgenographic findings simulate other disease, exogenous lipoid pneumonia is often unrecognised (10). We report a case of a patient in whom exogenous pneumonia resulted from intranasal application of liquid paraffin nasal drops.

CASE REPORT

A 49-year-old Chinese nonsmoking woman was referred to the pneumology department at Centro

Hospitalar Conde S. Januário with low-grade fever, cough and mild dyspnea. Past medical history disclosed that the patient had essential hypertension and diabetes mellitus controlled by medication and diet. In 1988 was diagnosed nasopharyngeal carcinoma (NPC) and she received radiotherapy.

In 1993, she presented with productive cough and episodes of fever. Pulmonary tuberculosis was then diagnosed by chest radiography without bacteriologic proof and a three-drug antituberculous regimen was irregular administered for two years.

She was admitted at other institution in November 1997 with persistent fever, weight loss, progressive dyspnea and, again a three-drug antituberculous regimen of isoniazid, riphampicin and ethambutol associated with ciprofloxacin and ceftazidime was administered. However, after two weeks of treatment, she still had fever every day and, in view of economic problems, was transferred to our hospital.

On admission, the axillary temperature was 37,6º C, the blood pressure was 132/75mm Hg, the pulse was 102 beats per minute and the respiratory rate was 26 breaths per minute. The physical examination revealed a moderate finger clubbing. Chest auscultation revealed a decrease of bilateral breath sounds and dry crackles over the upper right and lower left lung. Cardiac examination was normal. There was no hepatosplenomegaly or ankle oedema Results of her examination were otherwise completely normal.

The results of a complete blood count are presented in Table I.

The levels of urea nitrogen, creatinine, electrolytes, glucose, bilirubin, aspartate aminotransferase, and alanine aminotransferase were normal. The urine was normal. Tests for human immunodeficiency virus (HIV 1 and 2) antibodies, rheumatoid factor were negative. A tuberculin skin test was negative. The results of serum protein electrophoresis are presented in Table II. Three blood cultures specimens were sterile.

Room air arterial-blood gas measurements showed a pH of 7.43, PCO2 of 34.7 mm Hg, and a Pa02 of 73.3 mm Hg. Pulmonary function tests gave an FVC 1.161

TABLE I

Haematological Findings

Variable	Observed value
Hematocrit (%)	34
Haemoglobin (g/dL)	11.6
White-cell count (per mm^3)	8 600
Differential count (%)	
Neutrophils	79
Lymphocytes	16
Monocytes	2.7
Eosinophils	1.2
Erythrocyte sedimentation rate (mm/hr)	130
Platelet count (per mm^3)	483 000
Prothrombin time	Normal
Partial-thromboplastin time	Normal

TABLE II

Serum electrophoresis

Variable	Observed Value (g/l)
Protein	86.1
Albumin	29
Globulin	
α 1	3.7
α 2	1.0
β	14.2
γ	29.2

(53% predicted), FEV 1 of 1.151 (62% predicted) and TLC 2.991 (83% predicted) The lung diffusing determined by the single breath carbon monoxide method was 84% predicted. An electrocardiogram was normal.

Radiographs of the chest (Fig. 1) showed bilateral consolidation, without loss of volume, more severe on right side, predominantly affecting posterior segments of upper and lower lobes. There was no enlargement of mediastinic silhouette. An abdominal ultrasonographic examination was normal. The evaluation by computed tomographic (CT) demonstrated small-enlarged lymph nodes in the precarinal region. On the lung window (Fig. 2) was detected bilateral opacities ranging from ground-glass pattern (in zones less affected of upper lobes) to alveolar nodules coalescing in larger areas of

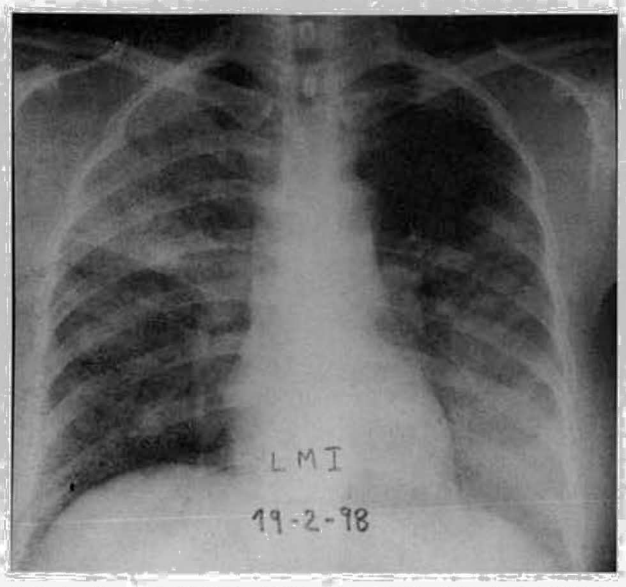

Fig. 1 – Posteroanterior chest radiograph showing bilateral interstitial infiltrates predominantly in lower lung fields

branches. However, the subpleural zones were also affected on areas where the consolidation was denser. The plain CT scan shows also air bronchogram and spontaneous angiogram sign, but there was no stretching, spreading, or narrowing of the involved bronchovascular ramifications. On thin section CT it is possible detect, even on areas of dense consolidation, small cystic air spaces with thick walls, mainly on subpleural zones and around the main bronchovascular branches. High resolution CT scan also revealed welldefined areas of ground-glass attenuation with superimposed septal wall thickening (crazypaving pattern).

Two flexible bronchoscope examinations revealed the mucous of all bronchial tree to be erythematous. Cytological examinations and the specimens from transbronchial lung biopsy were nondiagnostic.

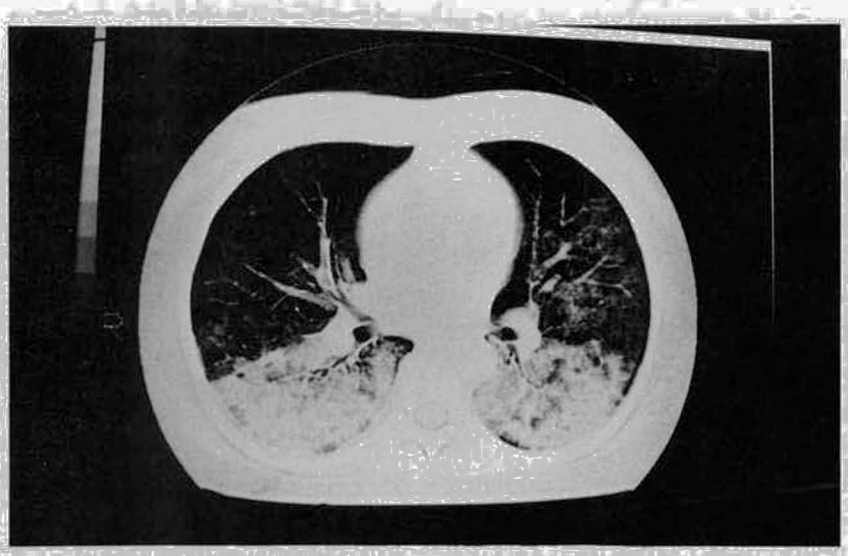

Fig. 2 – Computed tomogram showed bilateral alveolar nodules coalescing in larger areas of dense consolidation of lower lobes

dense consolidation (on apical and posterior segment of lower lobes). Even in areas of ground-glass opacity the attenuation measurements did not reveal fat density. The most part of subpleural zone was spared, as well as the region around the main bronchovascular

Bronchoalveolar lavage was performed and the differential count revealed 49% macrophages, 27 nercent lymphocytes, 24 percent neutrophils. Microscopic examination of specimens of bronchial washings showed *Candida albicans and Klebsiella pneumoniae.*

Fluconazole and ciprofloxacin were administered intravenously.

Because clinical synptoms and repeated x-ray films of the chest remained unchanged we proposed an open lung biopsy. Histology specimen (Fig. 3) revealed numerous lipid-laden macrophages; multinucleated giant cells in the large distorted alveolar spaces and interstitial fibrosis, consistent with the diagnosis of exogenous lipoid pneumonia. No other abnormal cells were seen.

On further direct questioning the patient referred that, since ten years ago after the radiotherapy, she had been taking mineral oil liquid paraffin nasal drops (Fig. 4) regularly, because she felt mild difficult of swallowing and dry nose. The patient stopped taking mineral oil nasal drops and received 30 mg oral prednisolone per day.

Fig. 4 – The bottle with liquid paraffin nasal drops

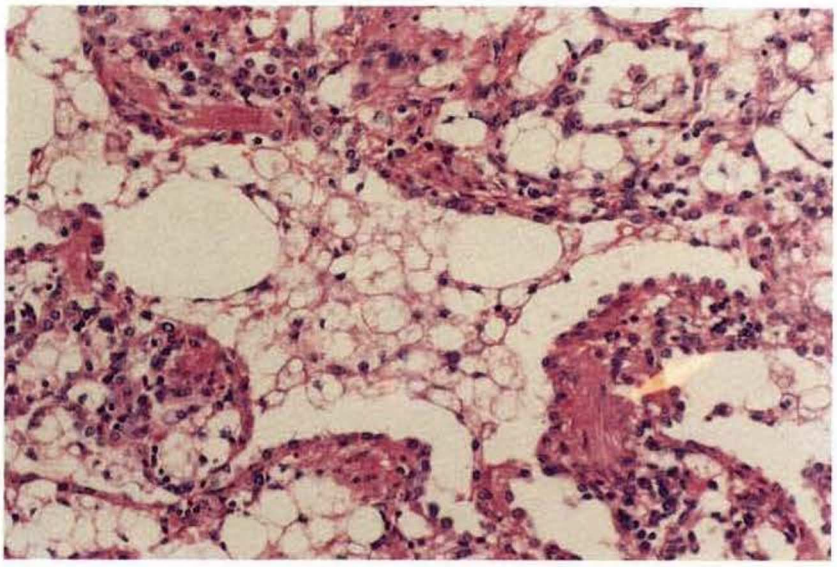

Fig. 3 – Open lung biopsy showing numerous alveolar macrophages with multiple clear vacuoles. Interstitial fibrosis and cell inflammatory infiltrates are noted (hematoxylin-eosin)

DISCUSSION

ELP is an uncommon lung disorder, more prevalent in adults than in children. It is known to mimic many pulmonary diseases and the diagnosis is often difficult, particularly in the absence of predisposing factor (11,12) Clinically, most patients are asymptomatic, few cases only present with cough, sputum,

dyspnea, hemoptysis, and chest pain. Secondary bacterial infection may occur (13). There is no classic chest radiographic appearance and it may be diffuse airspace infiltration or localised consolidation simulating tumour (14). Pulmonary involvement in our patient was distinguished by its diffuse pattern, which are only rarely reported (15,16). A specific history of lipoid aspiration is rarely obtained unless specifically sought. Most cases of mineral oil aspiration are discovered incidentally at autopsy, or on open lung biopsy for investigation of abnormal chest radiograph. The most relevant imagiologic findings, in our case, were those related with the distribution of the lesions, the association of alveolar and interstitial pattern and low density consolidation. The distribution of the parenchymal lesions, showing involvement of dependent zones of the lungs suggests an aspiration mechanism. When this mechanism is implicated, the consolidation can be bilateral, but is more severe on basal and posterior segments of the right lobe, as was observed in our case. The pulmonary opacification consisted mostly of parenchyma consolidation associated with areas of ground-glass opacities showing septal thickening superimposed. The association of alveolar and interstitial findings is not surprising when we consider the pathologic substract of LP. The alveolar filling is caused either by exudation of blood plasma in alveoli (17) or by masses of alveolar macrophages vacuoled with lipoid material (18). The interstitial lesion results from the inability of interstitial macrophages to degrade the oil phagocytozed (17). This leads to a chronic inflammatory process evolving in foreign-body-like reaction; and, eventually, in "end-stage lung" (8,17).

In spite of the fact that we can not detect fat density, we noticed that the areas of homogeneous consolidation did not obscure the margins of vessel - "positive angiogram sign". The CT angiogram sign - that is, the ability to see normal pulmonary vasculature within parenchymal consolidations, initially reported as specific for the diagnosis of bronchioloalveolar cell carcinoma is able to occur whenever the low attenuation of the consolidation outlines the pulmonary vessels. These situation take places when mucin (as in bronchioloalveolar cell carcinoma) or fat (in lipoid pneumonia) is the cause of complete filling of the air spaces.

Contrasting with our findings, in bronchioloalveolar cell carcinoma there is, usually stretching or spreading of the vessels. In any case, the stability of the lesions was not compatible with an aggressive pathogenic agent, either infectious or neoplastic. The key to diagnosis lies with the demonstration of fat droplets in sputum and expectorated macrophages, in lavage fluid (19,20) Fibreoptic bronchoscopy with bronchoalveolar lavage has a high diagnostic yield (21) and, in some cases, lavage may be therapeutic (16,22). Percutaneous fine needle aspiration biopsy, biopsy specimen obtained via bronchoscopy, or open lung biopsy is often required for histologic confirmation diagnostic (2,11).

In our case, despite two-bronchoalveolar lavage and two-transbronchial lung biopsy, only the open lung biopsy specimen showing plentiful foamy macrophages was consistent with lipoid pneumonia. Treatment of lipoid pneumonia involves identification and removal of the initiating agent, oxygen therapy and oral steroids with or without antibiotics (23,24).

ELP often presents diagnostic challenges and the diagnosis was difficult to establish without a history of prolonged consumption of medications containing mineral oil, or other evidence of disorders of deglutition or gastro-oesophageal reflux. Though bronchoscopy with bronchioloalveolar lavage and transbronchial biopsy now offers a safer route to histological diagnosis, the imaging findings could contribute to elicit the suspicion. Actually, a distribution compatible with aspiration and the association of criteria suggesting low density consolidation with interstitial alterations must arouse the possibility of ELP.

Recently reported cases of exogenous lipoid pneumonia resulting from the use of oil based products (25,26,27) suggest that more cases can occur. The physicians and patients need to be aware of the hazards of use of these products and should try to stop this habit.

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