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Pneumologia

Unusual cause of bronchiolitis obliterans in an immunosuppressed patient

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Abstract

English:

Bronchiolitis obliterans organizing pneumonia (BOOP) is a diffuse interstitial lung disease, currently classified as cryptogenic organizing pneumonia (COP) when idiopathic, respectively organizing pneumonia (OP) in case of a specified etiology.

We present the case of a 48-year-old patient, former smoker (20PY), diabetic, who accused moderate dyspnea, persistent febrile syndrome. The chest radiography showed multiple areas of condensation distributed bilaterally diffusely and the laboratory data revealed an important inflammatory syndrome. More than 100 colonies of Candida albicans were isolated from the sputum, therefore antifungal therapy was initiated. The computer tomography scan (CT scan) highlighted multiple micronodular and nodular lesions, some with tendency of excavation and hydroaeric level present and a polyseptate lesion in the right lower lobe; no proliferative elements were found during bronchoscopy and the bronchoalveolar lavage was non-specific; To obtain a final diagnosis, a CT-guided transthoracic needle biopsy was performed and the histological examination was compatible with organized pneumonia.

Keywords

organizing pneumonia • areas of condensation • Candida Albicans • polyseptate lesions • CT-guided transthoracic needle biopsy

Cauză neobișnuită a bronșiolitei obliterante la un pacient imunosuprimat

Rezumat

Romanian:

Bronșiolita obliterantă cu pneumonie organizată (BOOP) este o boală pulmonară interstițială difuză, actualmente clasificată ca pneumonie organizată criptogenică (COP) când este idiopatică, respectiv ca pneumonie organizată (OP) în cazul unei etiologii specificate.

Prezentăm cazul unui pacient în vârstă de 48 de ani, fost fumător (20PY), diabetic, care a acuzat dispnee moderată și sindrom febril persistent. Radiografia toracică a evidențiat multiple zone de condensare distribuite bilateral și difuz, iar datele de laborator au relevat un sindrom inflamator important. Din sputa au fost izolate mai mult de 100 de colonii de Candida albicans, motiv pentru care a fost inițiat tratamentul antifungic. Tomografia computerizată (CT) a evidențiat multiple leziuni micronodulare și nodulare, unele cu tendința de excavație și nivel hidroaeric prezent, precum și o leziune poliseptată în lobul inferior drept; bronhoscopia nu a evidențiat elemente proliferative și lavajul bronhoalveolar a fost nespecific. Pentru a obține un diagnostic final, s-a efectuat o biopsie percutanată ghidată CT, iar examinarea histologică a fost compatibilă cu pneumonie organizată.

Cuvinte-cheie

pneumonie organizată • zone de condensare • Candida Albicans • leziuni poliseptate • biopsie transtoracică ghidată CT

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Introduction

First described in the 1980's as a distinct lung disease entity [1], bronchiolitis obliterans with organizing pneumonia (BOOP) is a rare inflammatory lung disorder characterized by clinical symptoms like coughing and shortness of breath in some patients, as well as, flu-like illness in others. The disease onset is typically in the fifth or sixth decade of life, with males and females affected equally [2], [3]. Because organizing pneumonia is the predominant mechanism and bronchiolitis obliterans is only a secondary finding, the BOOP terminology was removed, being, currently, categorized as cryptogenic organizing pneumonia (COP) when the cause is unknown and respectively, organizing pneumonia (OP) in case of a specified etiology.

As previously mentioned, OP has a distinctive pathological pattern, yet it is linked to conditions or diseases that are well-documented. Some of these entities include connective tissue diseases, infections, malignancies, drugs, radiation, transplantation and aspiration [2]. Furthermore, organizing pneumonia is a serious condition that has non-specific radiographic findings and clinical signs.

OP is a reversible inflammatory and fibroproliferative process that does not disrupt the underlying lung architecture [3],[4]. The histopathological abnormalities result in alveolar organization, characterized by recruitment and proliferation of fibroblasts and myofibroblasts within the alveolar lumen to form fibroinflammatory buds (Masson bodies) [3], [5], [6].

We report a case of Candida Albicans associated organizing pneumonia that resolved under the initial antifungic treatment, without the need of corticotherapy after the histopathological confirmation of OP; this is an uncommon condition, with only a few occurrences recorded worldwide.

Case presentation

We describe the case of a 48-year-old patient, former smoker (20PY), with habitual ethylism, without occupational airborne exposure, with no allergies, who was transferred from the "Dr. N. Paulescu" National Institute to "Marius Nasta" Pneumophtiziology Institute of Bucharest, Romania, for moderate dyspnea, persistent febrile syndrome and fatigue.

The medical history of the patient started with a hospitalization in a territorial hospital, for acute urinary retention, treated with urinary catheterization. The laboratory tests indicated hyperglycaemia, leading to the patient's initial diagnosis of type 1 diabetes mellitus. Later on, a suspicion of bilateral bronchopneumonia was raised, therefore he was transferred to our hospital.

On admission, the chest radiography showed multiple areas of condensation distributed diffusely bilaterally (Figure 1) and the laboratory data revealed leukocytosis with neutrophilia, an important inflammatory syndrome and moderate anemia. Broad-spectrum antibiotic treatment was initiated, but without significant improvement.

In order to discover a potential underlying infectious cause, we continued the investigations with the sputum smear microscopy, which was acid-alcohol resistant bacillus (BAAR) negative, while the sputum cultures for Mycobacterium tuberculosis (MTB) were also negative and the sputum GeneXpert MTB/RIF was undetectable. Meanwhile, the culture from the sputum were positive for Candida Albicans (>100 colonies).

The antifungal treatment with Itraconazole 100 mg/day was added, with the amelioration of clinical symptomatology. In this setting, granulomatosis with polyangiitis, secundary pulmonary determinations and pulmonary mycosis were considered possible diagnosis.

Moreover, functional respiratory tests were performed, highlighting an obstructive ventilatory dysfunction (Table 1).

Taking into consideration the chest X-ray unspecific abnormalities, the next step was performing computer tomography scan (CT scan) of the chest with contrast, which showed multiple micronodular and nodular lesions, some with tendency of excavation and hydroaeric level present and a polyseptate lesion in the right lower lobe of 6.5/5.5 cm in diameter (Figure 2).

Afterwards, flexible bronchoscopy revealed no proliferative elements and the bronchoalveolar lavage (BAL) identified nonspecific cellularity (also including no tumoral cells).

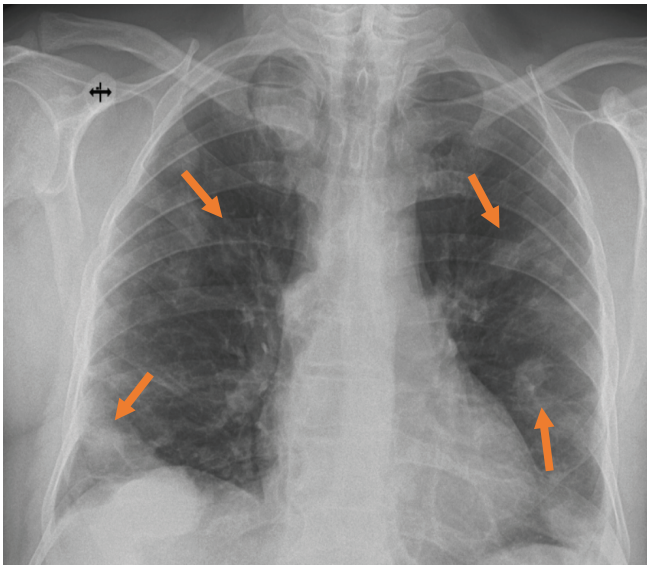

Figure 1. Chest X-ray aspect of multiple areas of condensation distributed diffusely bilaterally, normal costodiaphragmatic angles.

Table 1. Functional respiratory tests indicating lower values of FEV1, FVC and FEV1/FVC <70%.

Functional parameter	Numerical value	%
FVC	3.28 L	74.5
FEV1	2.23 L	62.3
FEV1/FVC	-	68.16%
MEF50	1.67 L	35.1
DLCO	5.08	50.3
KCOc	0.93	62.1

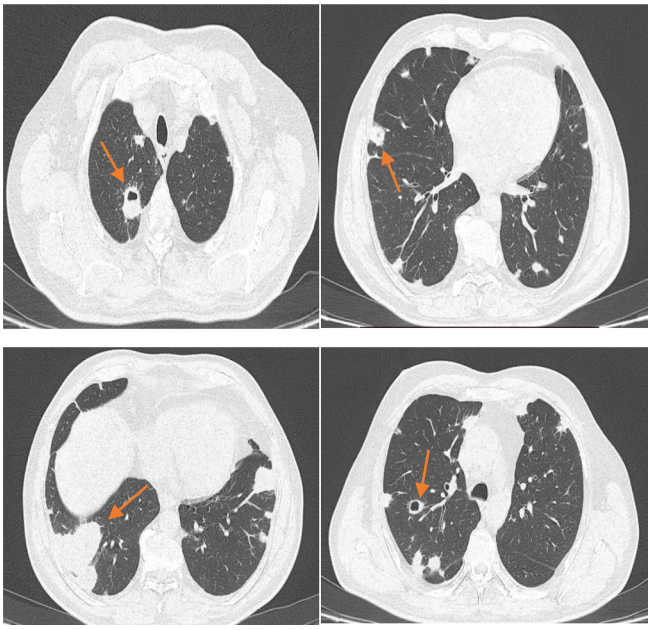

Figure 2. CT scan of the chest aspect of micronodular and nodular lesions, some with the tendency of excavation and hydroaeric level present and a polyseptate lesion in the right lower lobe.

The bronchial aspirate was BAAR negative, with negative MTB culture. Similar to the fungal sputum examination, colonies of Candida Albicans were isolated from the bronchial aspirate.
Furthermore, due to the uncharacteristic aspect of the CT scan, in order to obtain a final diagnosis, a CT-guided transthoracic needle biopsy was performed from the pseudotumoral proliferation in the right lower lobe (Figure 3) and the histological examination was compatible with organized pneumonia (BOOP lesions) - pulmonary parenchymal tissue structure altered by diffuse interstitial inflammatory infiltrate, with dispersed lymphocytic content and edema (Figure 4), associated with endoluminal buds of granulation tissue composed of exudative elements such as fibrin, fibroblasts, and components of connective tissue (Masson bodies) in the alveolar ducts and alveoli (Figure 5); no tumoral cells were found.
As previously mentioned, after the initiation of the antifungal therapy, significant clinical improvement was shown and the treatment was continued for an additional 7 days, after the patient was released from the hospital.

Figure 3. CT-guided transthoracic needle biopsy fragments from the pseudotumoral proliferation in the right lower lobe.

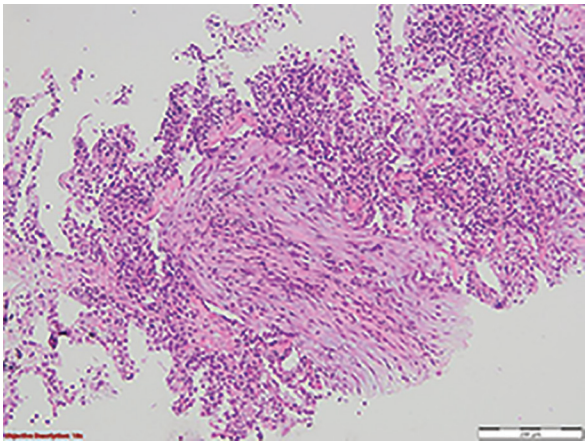

Figure 4. Pulmonary parenchymal tissue structure altered by diffuse interstitial inflammatory infiltrate associated with ductal and endo-alveolar areas of fibro-granular proliferation (HE staining, x 200).

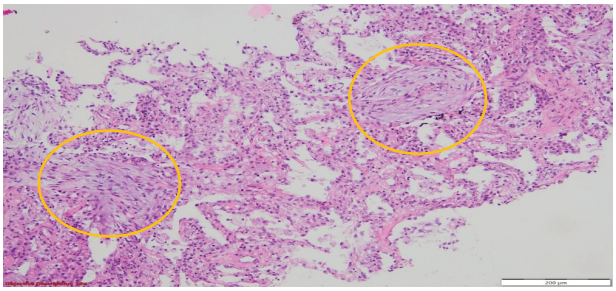

Figure 5. Multiple Masson bodies, difuse interstitial lymphocytic inflammatory infiltrate (HE staining, x 200).

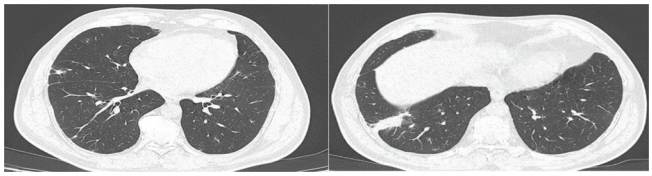

Figure 6. CT scan of the chest highlighting the almost complete resolution of the nodular and micronodular lesions.

After a month, the patient's reevaluation revealed no symptoms, clinical and biological examinations were within normal ranges, and the repeated spirometry pinpointed the complete remission of the obstructive ventilatory dysfunction. The control CT scan demonstrates the remission of the nodular and micronodular lesions (Figure 6).

Discussions

Our understanding of organizing pneumonia, which is now a well-established entity, has continued to expand as a result of histological and radiological progress. It can occur in clinical scenarios associated with other systemic inflammatory conditions, transplantation, medication exposure, infections, radiotherapy, malignancy or autoimmune diseases. [7], [8].

As far as the pathology is concerned, OP is initiated by lung injury: the alveolar epithelium reacts to produce granulation tissue [9], [10], [11] that can be associated with an interstitial inflammatory infiltrate, which is why OP is classified as an interstitial lung disease [12], [13].

The vast majority of patients have subacute onsets and respond well to corticosteroid therapy. The clinical picture of OP, as described in the medical literature, generally consists of non-specific signs and symptoms, reflecting also the underlying pathology. However, relapses are frequently seen when corticosteroids are tapered or discontinued [14]. Despite that, only a few research studies have looked into the causes of OP relapse.

The key feature in this case was the OP diagnosis of a young diabetic patient, occurring in the context of a fungal infection with Candida albicans, requiring confirmation by histopathological examination, with favorable clinical and imaging course, even without associated systemic corticotherapy.

Taking under consideration the variability of the differential diagnoses and the non-specific radiological abnormalities, we found it difficult to establish an earlier diagnosis. OP's standard radiological form consists of fluctuating multifocal parenchymal consolidations.

In over 70% of cases, OP produces focal sub-pleural and/or peribronchovascular consolidation areas, often bilateral and asymmetrical [15],[16],[17]. This may be associated with ground glass opacities or areas of traction bronchiectasis (reversible under steroid treatment) or an air bronchogram sign. [16],[18].

When multifocal parenchymal consolidation is present, a variety of differential diagnoses may be taken into account, including bronchioloalveolar carcinoma, eosinophilic pneumonia [19], pulmonary mycosis, multifocal pneumonia, OP, alveolar hemorrhage, and ANCA-associated vasculitis.

The nodular type of OP, which has a single or several nodules or masses, may be another radiological aspect of the disease. OP can present in the form of solid, mixed density or more rarely ground glass nodules [20], [21]. When there is an underlying malignancy/ infection or when the nodules are widespread or peribronchovascular, the diagnosis of OP will rarely be considered at first. Excavated nodules are also rarely found in OP.

As pointed out, we performed a CT-guided transthoracic needle biopsy that was suggestive for an organizing pneumonia, in context of the fungal infection with Candida Albicans.

Conclusions

The diagnosis of organizing pneumonia should be considered in all cases of an imaging aspect of focal/diffuse lung lesions, especially in immunosuppressed patients with fungal infections, in which the histopathological examination is crucial.

The most common etiologies of OP associated mycotic infections described in the literature are Aspergillus spp., Pneumocystis carinii, Cryptococcus Neoformans, while Candida albicans remains a very rare cause of organized pneumonia.

Funding

None.

Informed Consent Statement

Informed consent was obtained from all subjects involved in the study.

Data Availability Statement

Data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

The authors declare no conflict of interest.

References

1. Cordier JF. Cryptogenic organising Pneumonia. Eur Respir J. 2006;28:422–46. doi: 10.1183/09031936.06.00013505. [Pub Med] [CrossRef] [Google Scholar].
2. Drakopanagiotakis F, Paschalaki K, Abu-Hijleh M, et al. Cryptogenic and secondary organizing pneumonia: clinical presentation, radiographic findings, treatment response, and prognosis. Chest. 139:893–900. 201. [PubMed] [Google Scholar].
3. Drakopanagiotakis F, Polychronopoulos V, Judson MA. Organizing pneumonia. Am J Med Sci. 2008;335:34–9. doi: 10.1097/MAJ.0b013e31815d829d. [PubMed] [CrossRef] [Google Scholar].
4. Epler GR. Bronchiolitis obliterans organizing pneumonia. Semin Respir Infect. 1995;10:65–77. [PubMed] [Google Scholar].
5. Colby TV. Pathologic aspects of bronchiolitis obliterans organising pneumonia. Chest. 1992;102:38–43. doi: 10.1378/chest.102.1_Supplement.38S. [PubMed] [CrossRef] [Google Scholar].
6. Dogan D, Ocal N, Yucel O, et al. Cryptogenic organizing pneumonia diagnosed with transbronchial parenchymal biopsy: a case report with accompanying histopathological images. J Turgut Ozal Med Cent. 2016;23:81–3. doi: 10.5455/jtomc.2015.2648. [CrossRef] [Google Scholar].
7. Oymak FS, Demirbas HM, Mavili E, et al. Bronchiolitis obliterans organizing pneumonia. Clinical and roentgenological features in 26 cases. Respiration. 2005;72:254–62. doi: 10.1159/000085366. [PubMed] [CrossRef] [Google Scholar].
8. A.G. Davison, B.E. Heard, W.A. McAllister, M.E. Turner-Warwick, Cryptogenic organizing pneumonitis, Q J Med, 52 (1983), pp. 382-394.
9. G.R. Epler, T.V. Colby, T.C. McLoud, C.B. Carrington, E.A. Gaensler, Bronchiolitis obliterans organizing pneumonia, N Eng J Med, 17 (1985), pp. 152-158.
10. American Thoracic Society/European Respiratory Society, International multidisciplinary consensus classification of the idiopathic interstitial pneumonias, Am J Respir Crit Care Med, 165 (2002), pp. 277-304.
11. D.M. Geddes, BOOP and COP, Thorax, 46 (1991), pp. 545-547.
12. B.J. Roberton, D.M. Hansell, Organizing pneumonia: a kaleidoscope of concepts and morphologies, Eur Radiol, 21 (2011), pp. 2244-2254.
13. G.R. Epler, Bronchiolitis obliterans organizing pneumonia, 25 years: a variety of causes, but what are the treatment options? Expert Rev Respir Med, 5 (3) (2011), pp. 353-361.
14. A. Gómez-Gómez, R. Martínez-Martínez, M.B. Gotway, Organizing pneumonia associated with swine-origin influenza A H1N1 2009 viral infection, Am J Roentgenol, 196 (1) (2011), pp. 103-104.
15. American Thoracic Society/European Respiratory Society International Multidisciplinary Consensus Classification of the Idiopathic Interstitial Pneumonias. Am J Respir Crit Care Med. 2002;165:277–304. https://doi.org/10.1164/ajrccm.165.2.ats01. [PubMed] [Google Scholar].
16. Wells AU. Cryptogenic organizing pneumonia. Semin Respir Crit Care Med. 2001;22:449–59. https://doi.org/10.1055/s-2001-17387. [PubMed] [Google Scholar]
17. Katzenstein AL. Katzenstein and Askin's surgical pathology of non-neoplastic lung disease. 4th ed. Philadelphia, Pa: Saunders Elsevier; 2006. p. 18. [Google Scholar].
18. Kligerman SJ, Franks TJ, Galvin JR. From the Radiologic Pathology Archives. Radiographics. 2013;33:195175. https://doi.org/10.1148/rg.337130057. [PubMed] [Google Scholar].
19. R. Gudavalli, E. Diaz-Guzman, A.V. Arrossi, J.T. Chapman, A.C. Mehta, Fleeting alveolar infiltrates and reversed halo sign in patients with breast cancer treated with tangential beam irradiation, Chest, 139 (2) (2011), pp. 454-459.
20. Ponnuswamy A, Mediratta N, Lyburn ID, Finnerty JP. False positive diagnosis of malignancy in a case of cryptogenic organising pneumonia presenting as a pulmonary mass with mediastinal nodes detected on fluorodeoxyglucose-positron emission tomography: a case report. J Med Case Reports. 2009;3:124. https://doi.org/10.1186/1752-1947-3-124. [PMC free article] [PubMed] [Google Scholar].
21. Erdogan Y, Ozyurek BA, Özmen Ö, et al. The Evaluation of FDG PET/CT Scan Findings in Patients with Organizing Pneumonia Mimicking Lung Cancer. Mol Imaging Radionuclide Ther. 2015;24:60–5. https://doi.org/10.4274/mirt.03016. [PMC free article] [PubMed] [Google Scholar].