Journal of Investigative Medicine High Impact Case Reports
Volume 10: 1–4

DOI: 10.1177/23247096221084840
journals.sagepub.com/home/hic
SAGE

Organizing Pneumonia: A Clinical Challenge in a Child With Previous Rhabdomyosarcoma

Ricardo Barreto Mota, MD[1], Diogo Costa Carvalho, MD[1], Inês Azevedo, MD, PhD[1,2], Sílvia Costa Dias, MD[1], and Nuno Jorge Farinha, MD[1]

Abstract

Organizing pneumonia is a pulmonary disease of undefined etiology, with few reported cases in children. It may be secondary to chemotherapy, radiation therapy, infectious agents, or hematopoietic cell transplantation. We present a case of an 18-year-old boy who presented to a follow-up consult with respiratory symptoms at the age of 11 years, 8 years after finishing treatment for a prostatic relapse of a pelvic rhabdomyosarcoma. Chest radiography revealed nodular opacities in the left lung, the one in the left lower lobe with silhouette sign with the left hemidiaphragm. Chest computerized tomography showed 2 nodular lesions in the left upper lobe, one of them cavitated, and another nodular lesion in the left lower lobe; 2 of these nodules had surrounding ground-glass opacities. Microbiological work-up, including tuberculosis screening, was negative. Biopsy revealed findings suggestive of organizing pneumonia. He presented spontaneous resolution. This case presented a diagnostic challenge due to rarity of this condition and its indetermined association with the patient's history of rhabdomyosarcoma. With this case, the authors alert that organizing pneumonia must be considered in patients presenting with pulmonary lesions with a history of previous hematopoietic stem cell transplants, lung irradiation, or immunosuppression. Pulmonary metastases and secondary tumors must be considered as a differential diagnosis in patients with a heavily treated relapsed rhabdomyosarcoma.

Keywords

pediatrics, cryptogenic organizing pneumonia, rhabdomyosarcoma, tuberculosis

Introduction

Organizing pneumonia (OP), previously referred to as bronchiolitis obliterans with OP, is an insidious pulmonary disease of undefined etiology. It is histologically characterized by intra-alveolar granulation tissue, fibroblasts, and a connective matrix.[1] The OP is considered to be an inflammatory reaction to multiple possible triggers, including chemotherapy, radiation therapy, infectious agents, collagen vascular diseases, and hematopoietic cell transplantation.[2] The mean age of onset is usually in the sixth decade of life and it has rarely been reported in children where it is often cryptogenic. We present a case of a boy with previous history of nonalveolar rhabdomyosarcoma who presented to a follow-up consult with respiratory symptoms and nodular lesions in image studies.

Case Report

We present a case of an 18-year-old boy who had an OP at the age of 11 years, 8 years after finishing treatment for a prostatic relapse of a pelvic rhabdomyosarcoma.

At the age of 3 months, he was diagnosed with a pelvic nonalveolar rhabdomyosarcoma, treated with 7 IVA cycles (ifosfamide, vincristine, actinomycin D) followed by surgery, 2 additional IVA cycles, and 2 topotecan/cyclophosphamide cycles. Two years later, he had a prostatic relapse treated initially with cycles of topotecan and carboplatin and subsequently with doxorubicin, surgery, and brachytherapy, with no evidence of disease since then.

Eight years after finishing treatment, he presented to his general practitioner (GP) with fever (38.7°C) and posterior

[1]Centro Hospitalar Universitário de São João, Porto, Portugal
[2]University of Porto, Portugal

Received December 15, 2021. Revised January 24, 2022. Accepted February 11, 2022.

Corresponding Author:
Ricardo Barreto Mota, Department of Pediatrics, Centro Hospitalar Universitário de São João, Alameda Prof. Hernâni Monteiro, Porto 4200-319, Portugal.
Email: rjdmota@gmail.com

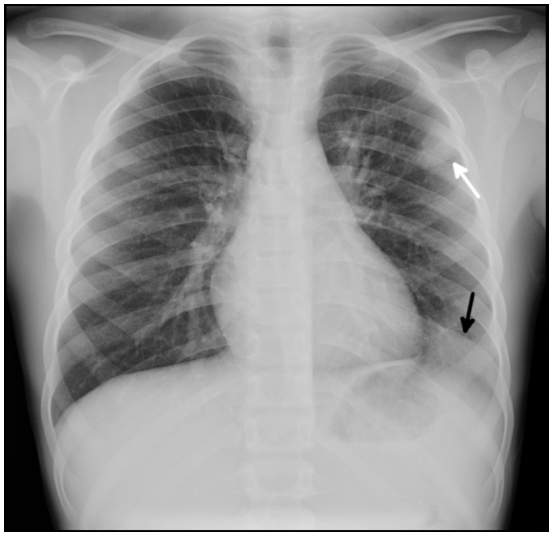

Figure 1. Frontal chest radiography showing 2 nodular opacities (arrows) in the left lung, one in the left lower lobe with silhouette sign with the left hemidiaphragm (black arrow).

thoracic pain with 3 days evolution. He had been complaining of loss of appetite and slight dry cough for the last 3 weeks. During that period, he was occasionally subfebrile, mainly in the afternoon (maximum temperature 37.6°C). His GP prescribed a 3-day course of azithromycin, with mild improvement, and referred to his oncologist. A chest radiography showed nodular opacities in the left lung, the one in the left lower lobe with silhouette sign with the left hemidiaphragm (Figure 1). He had a recent contact with a schoolmate with pulmonary tuberculosis. On observation, he had a good general status, no fever, no signs of respiratory distress, and reduced respiratory sounds in the lower half of the left hemithorax. The diagnostic work-up showed mild anemia (hemoglobin 11.6 g/dL) and leukocytosis ($15\,459 \times 10^9$/L, neutrophils $11\,340 \times 10^9$/L), platelets count of $544\,000 \times 10^9$/L, erythrocyte sedimentation rate of 79 mm/h, and C-reactive protein of 68.6 mg/L. Tuberculin test and interferon-γ release assay were negative. Serologies for *Rickettsia conorii* revealed negative immunoglobulin (Ig) G and IgM, and for *Mycoplasma pneumoniae* and *Chlamydia pneumoniae* both revealed past infection (positive IgG with negative IgM). Blood and sputum cultures were negative, as well as polymerase chain reaction assays in sputum for respiratory syncytial virus, adenovirus, influenza A and B, and parainfluenza 1, 2, and 3. Blood polymerase chain reaction assay for *Aspergillus fumigatus* and serologies for *Cryptococcus neoformans* were also negative. Chest computerized tomography (CT; Figure 2) 4 weeks after symptom onset showed 2 nodular lesions in the left upper lobe, one of them cavitated, and another nodular lesion in the left lower lobe. Two of these nodules had surrounding ground-glass opacities. The abdominal ultrasound was normal.

Bronchoscopy, bronchoalveolar lavage (BAL) from the left upper lobe, and lung endoluminal lung biopsy from the lung nodule area were performed, mainly to exclude a pulmonary relapse. Cytology of the BAL showed epithelial cells, some macrophages e some polymorphonuclear cells. No malignant cells were present. No cell count differential was performed. Immunocytochemistry for desmin and myogenin was negative. The histology showed distorted lung parenchyma with fibroblastic alveolar polyps. Pulmonary interstitium presented polymorphic inflammatory infiltrate, edema causing stretching of alveolar septi, and pneumocyte hyperplasia. No cancer cells or microorganisms were observed. The BAL was negative for all cultural studies, including bacteriology, mycology, and mycobacteriology. Polymerase chain reaction assay for *Aspergillus fumigatus*, *Candida albicans*, *Mycobacterium avium*, *Mycobacterium tuberculosis complex*, *Mycobacterium intracellulare*, nocardia, and histoplasma were negative, as well as for respiratory syncytial virus; adenovirus; influenza A and B; parainfluenza 1, 2, and 3; herpes simplex 1 and 2; and cytomegalovirus. Based on these findings, a diagnosis of OP was established.

Meanwhile, the chest pain and cough subsided. The chest radiography performed after the biopsy showed an improvement and thus no steroids were added. Pulmonary function tests performed 15 days after the biopsy were normal.

He maintained a close clinical and radiological follow-up and remained asymptomatic. Chest CT 7 weeks after the biopsy showed almost total resolution of the left nodular lesions. He stays well and free of disease after 6 years.

Discussion

This patient had a prostate relapse of rhabdomyosarcoma treated with the SIOP Mesenchymal Malignant Tumors (MMT) strategy[3,4] and he stayed in remission since the end of treatment. In the follow-up of a relapsed rhabdomyosarcoma, recurrence is the first concern when pulmonary nodules are found, but differential diagnosis with a secondary tumor, in this heavily treated patient, and with infection is mandatory.[1]

Our patient was diagnosed with OP through the presence of typical histological characteristics, namely, the presence of myofibroblasts and polymorphic infiltrate in the pulmonary connective tissue, alveolar infiltration of inflammatory cells, and general preservation of the lung architecture.[1] All the microbiological work-up, including tuberculosis investigation, was negative and our patient improved without steroids or antimicrobial therapy, except for a 3-day course of azithromycin. Short courses of macrolides had not been described in the treatment of OP. The optimal length of treatment is not well defined but usually long courses are used. Nevertheless, we cannot exclude that, in mild cases like this one, which improved spontaneously, 3 days of azithromycin had an effect.

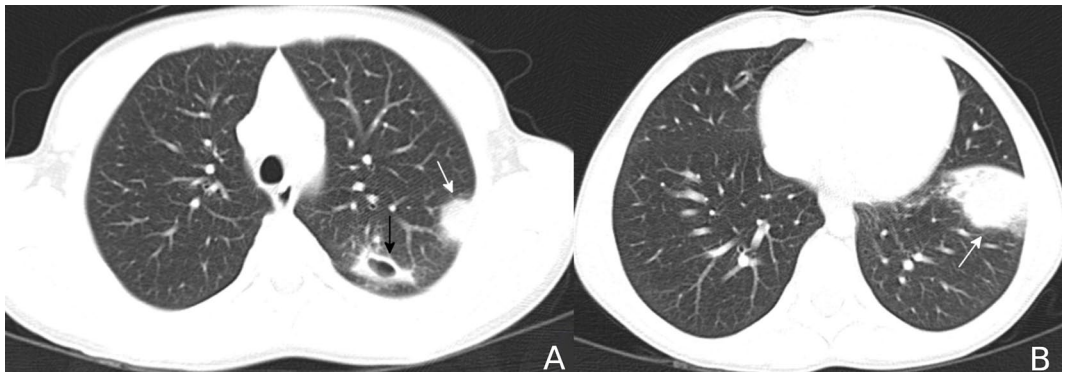

Figure 2. Chest CT (A) showing 2 nodular lesions in the left upper lobe, one with ground-glass opacity surrounding the nodule (white arrow), the other with central cavitation (black arrow), and (B) another nodular lesion in the left lower lobe also with ground-glass opacity surrounding the lesion (white arrow).
Abdominal ultrasound was normal (not shown).
Abbreviation: CT, computerized tomography.

Radiologically, the most common presentation of OP, observed in 70% of cases, consists of focal disperse nodular lesions associated with ground-glass opacities, as present in our patient, or air bronchogram. Various other nonspecific patterns, ranging from unilateral nodular, to focal peribronchial lesions, diffuse heterogeneous subpleural consolidations, migratory opacities, and reverse halo signs with ground-glass opacities surrounded by denser consolidations, may also be present. Cavitated lesions, as those observed in this patient, are very rare in OP (6%), being more frequent in pulmonary tuberculosis or in some malignant tumors, which widened our differential diagnosis.[5] Determining its etiology may be a challenging task, and when no cause is found, it is termed cryptogenic OP.[1] A study by Drakopanagiotakis et al comparing secondary and cryptogenic OP found minor differences in its clinical and radiological characteristics, reporting more severe analytical features and worse prognosis in patients with cryptogenic OP,[6] highlighting the difficulties in the differential diagnosis between these 2 pathologies. In our patient, the main etiology for secondary OP was the previous rhabdosarcoma treatment or a previous unaccounted infection.

In other pediatric sarcoma, OP has occurred after hematopoietic stem cell transplantation and lung irradiation a short time after treatment[7]; in our case, intensive chemotherapy and the deep immunosuppression might have accounted for the OP, but, due to the time lag, cryptogenic OP is more probable, and there are very few reports of OP occurring late after chemotherapy treatment.

The standard treatment for OP is corticosteroids, with variable description of dosage and duration in the literature.[1] In this case, however, we observed a regression of the lesion without steroids, a rare evolution barely described in the literature.[8] Noteworthy, he had initially received a short course of azithromycin which might have had an anti-inflammatory and therapeutic effect. It should be noted, however, that follow-up without treatment should be reserved for patients with mild clinical and radiological presentation, as was the case of our patient.[1]

This case presented a diagnostic challenge due to the rarity of this condition and its undetermined association with the patient's history of rhabdomyosarcoma. The authors stress the importance of this etiology in the differential diagnosis of pulmonary metastases and secondary tumors that are highly probable following a heavily treated relapsed rhabdomyosarcoma.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Ethical Approval

Our institution does not require ethical approval for reporting individual cases or case series.

Informed Consent

Written informed consent was obtained from a legally authorized representative(s) for anonymized patient information to be published in this article.

ORCID iDs

Ricardo Barreto Mota https://orcid.org/0000-0001-7145-7073
Inês Azevedo https://orcid.org/0000-0002-0090-8612

References

1. Cottin V, Cordier JF. Cryptogenic organizing pneumonia. *Semin Respir Crit Care Med*. 2012;33:462-475. doi:10.1055/s-0032-1325157.
2. Elbahlawan L, Rains KJ, Stokes DC. Respiratory care considerations in the childhood cancer patient. *Respir Care*. 2017;62(6):765-775. doi:10.4187/respcare.05223.
3. Jenney M, Oberlin O, Audry G, et al. Conservative approach in localised rhabdomyosarcoma of the bladder and prostate: results from International Society of Paediatric Oncology (SIOP) studies: malignant mesenchymal tumour (MMT) 84, 89 and 95. *Pediatr Blood Cancer*. 2014;61(2):217-222. doi:10.1002/pbc.24727.
4. Arndt CAS, Bisogno G, Koscielniak E. Fifty years of rhabdomyosarcoma studies on both sides of the pond and lessons learned. *Cancer Treat Rev*. 2018;68:94-101. doi:10.1016/j.ctrv.2018.06.013.
5. Long NM, Plodkowski AJ, Schor-Bardach R, et al. Computed tomographic appearance of organizing pneumonia in an oncologic patient population. *J Comput Assist Tomogr*. 2017;41(3):437-441. doi: 10.1097/RCT.0000000000000520.
6. Drakopanagiotakis F, Paschalaki K, Abu-Hijleh M, Aswad B, Karagianidis N, Kastanakis E, et al. Cryptogenic and secondary organizing pneumonia: clinical presentation, radiographic findings, treatment response, and prognosis. *Chest*. 2011;139(4):893-900. doi:10.1378/chest.10-0883.
7. Bitzan M, Ouahed JD, Carpineta L, Bernard C, Bell LE. Cryptogenic organizing pneumonia after rituximab therapy for presumed post-kidney transplant lymphoproliferative disease. *Pediatr Nephrol*. 2010;25(6):1163-1167. doi:10.1007/s00467-010-1447-8.
8. Zhou Y, Wang L, Huang M, et al. A long-term retrospective study of patients with biopsy-proven cryptogenic organizing pneumonia. *Chron Respir Dis*. 2019;16:1479973119853829. doi:10.1177/1479973119853829.