Case report

DIFFUSE INFILTRATIVE LUNG DISEASES REVEALING CAVUM CANCER: ABOUT A CASE

ABSTRACT

Diffuse infiltrative lung diseases (ILDs) are a heterogeneous group of pulmonary pathologies, primarily characterized by involvement of the pulmonary interstitium. Diffuse infiltrative lung disease can be caused by inflammatory, infectious, drug-induced, toxic, or neoplastic factors. Undifferentiated carcinoma of the cavum (UCNT), although rare, can be responsible for ILDs, particularly in endemic areas and in cases of Epstein-Barr virus infection.

The clinical case presented describes a 68-year-old patient with a history of dizziness and smoking who developed progressive respiratory symptoms accompanied by ENT signs. Clinical examination and imaging studies revealed diffuse infiltrative lung disease with no identified infectious cause. A diagnosis of undifferentiated carcinoma of the cavum was made following a biopsy of a nasopharyngeal mass. Treatment included radiotherapy and chemotherapy, which led to regression of the lung lesions.

The discussion highlights the complexity of diagnosing PID of neoplastic origin, emphasizing the importance of a multidisciplinary approach and early management. Early detection of underlying causes, particularly in severe forms, is essential for a favorable prognosis.

INTRODUCTION :

Diffuse infiltrative lung diseases (DILs) constitute a heterogeneous group of pulmonary pathologies characterized by diffuse involvement of the lung parenchyma, primarily affecting the interstitium but also involving the alveoli and distal airways. They represent a major diagnostic and therapeutic challenge due to their etiological diversity and often unpredictable course. DILs can result from multiple causes, including inflammatory, infectious, drug-induced, toxic, and neoplastic processes. Accurate identification of the underlying etiology is essential to guide therapeutic management and improve patient prognosis.

In this context, neoplastic forms of DILs constitute a unique entity. Direct tumor infiltration, paraneoplastic inflammatory reactions, and complications related to oncological treatments can all contribute to the development of interstitial lung disease. Among these etiologies, undifferentiated carcinoma of the cavum (UCNT) is a rare but not exceptional tumor, particularly in certain regions where it is endemic and frequently associated with Epstein-Barr virus infection. This cancer, often diagnosed late due to non-specific initial symptoms, may be accompanied by pulmonary manifestations that can be attributed either to tumor dissemination or to a secondary systemic inflammatory response.

The clinical case presented illustrates a complex diagnostic situation in which a patient being treated for chronic vertigo developed progressive respiratory symptoms, associated with a deterioration in general condition and systemic manifestations suggestive of an underlying

inflammatory process. The discovery of ILD on chest CT led to a thorough investigation, revealing an undifferentiated carcinoma of the cavum. This case highlights the importance of a multidisciplinary approach integrating pulmonology, oncology, and immunology to establish an accurate diagnosis and optimize therapeutic management.

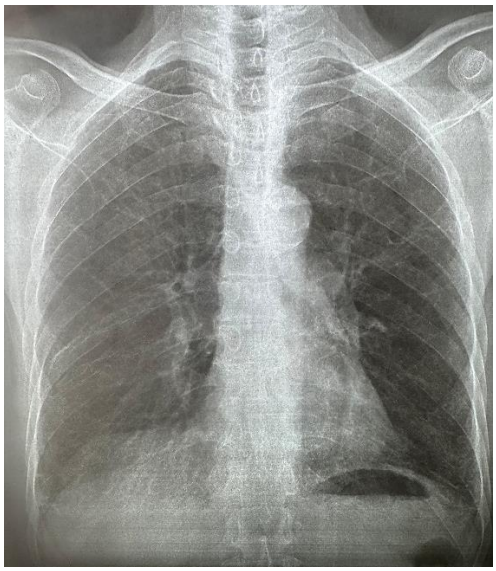
The objective of this article is therefore to discuss the relationship between ILD and neoplastic pathologies, highlighting the pathophysiological mechanisms involved and the diagnostic strategies to distinguish the various potential causes of ILD in the context of cancer. A better understanding of these interactions is essential to avoid diagnostic delays and improve the care of patients facing these complex pathologies.

CASE REPORT :

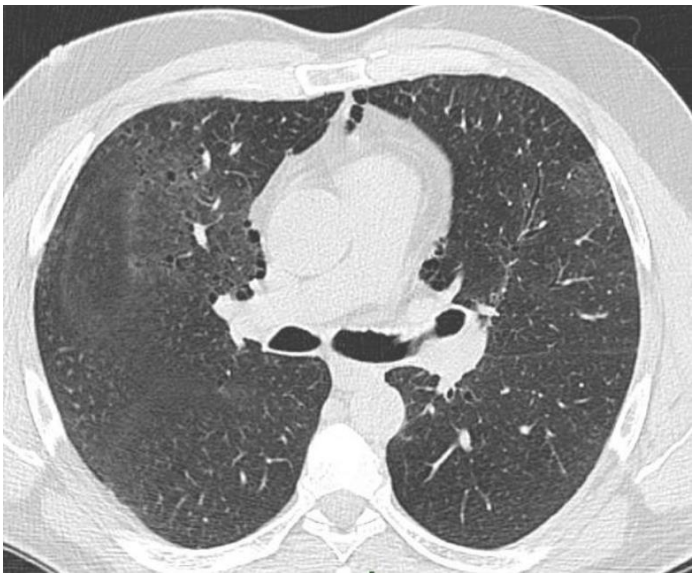
This was a 68-year-old patient with a 10-year history of rotary vertigo under anti-vertigo medication (acetylleucine), who had been treated for COVID-19 infection 6 months earlier. The patient's history of toxicity included chronic active smoking estimated at 55 pack-years and chronic alcoholism, which he had stopped 22 years earlier. The patient's history dates back three months. He presented with exertional dyspnea (NYHA stage II), a dry cough, and episodes of mild hemoptysis, without chest pain or desaturation. He also reported chronic rhinorrhea, episodes of epistaxis, bilateral hearing loss, subjective dry mouth, and Raynaud's phenomenon, well described in its three phases: ischemic phase (white phase), cyanotic phase (blue phase), and recovery phase (red phase), with no associated joint involvement. All this is taking place in a context of deterioration in the general condition, marked by a weight loss of 18 kg in six months and night sweats.

On clinical examination, the patient was in good general condition, eupneic at 18 cycles per minute, and had digital clubbing. Palpation of the lymph nodes revealed a 0.8 cm long-axis adenopathy located in the left carotid region. Pulmonary auscultation revealed bilateral wheezing. Capillaroscopy also revealed, as part of Raynaud's phenomenon, a mild nonspecific microangiopathy.

A chest X-ray demonstrated an interstitial syndrome. A high-resolution thin-slice chest CT scan showed bilateral, symmetrical, nonsystematic diffuse opacities, suggesting nonspecific micronodules, as well as septal thickening, consistent with diffuse infiltrative pneumonia. Bronchoscopy revealed first-degree diffuse inflammation with no other visible abnormalities. Bronchoalveolar lavage revealed lymphocytic fluid with mild neutrophilia (macrophage at 64.7%, neutrophilic polymorphonuclear cells at 7.6%, eosinophilic polymorphonuclear cells at 4%, lymphocytes at 23.7%), with no signs of hemorrhage, neoplastic cells, or identified pathogens.



Chest X-ray showing interstitial syndrome.



Chest CT scan showing diffuse infiltrative lung disease

The immunological workup was positive for antinuclear antibodies at 160 (threshold <80) with nucleolar appearance + granular cytoplasmic fluorescence, anti-DNA antibodies were positive, anti-RNP/Sm antibodies were positive, anti-SSA antibodies were positive, and recombinant anti-Ro52 antibodies were strongly positive.

Given the ENT signs (hearing loss, epistaxis, posterior rhinorrhea, vertigo, and cervical lymphadenopathy) and general signs (asthenia, weight loss, and night sweats), an ENT examination with rhinocavoscopy was performed, revealing free and normal-appearing nasal cavities, and a mass was visualized in the nasal cavity at the expense of the superior wall extending to the choanae. Biopsy of this mass confirmed an undifferentiated carcinoma of the nasal cavity, UCNT type.

A cervicothoracoabdominopelvic CT scan described this mass as a thickening of the posterolateral wall of the nasopharynx, more marked on the left, filling the tubal orifices, isodense, heterogeneously enhanced after injection of contrast agent, delineating areas of necrosis. This thickening measured 34 mm in maximum thickness. Laterally, it extended towards the prestylian space and encompassed the left internal carotid artery over 180°, which nevertheless remained permeable. Posteriorly and to the left, it extended towards the hypoglossal canal, which was widened compared to the contralateral side, with doubt about an extension towards the posterior cerebral fossa. Posteriorly and superiorly, it was in intimate contact with the clivus responsible for cortical lysis. Anteriorly, it extends towards the choanae and fills the posterior part of the nasal fossae and comes into contact with the middle meatus with loss of the separating border. Anteriorly and to the left, it extends towards the pterygopalatine cleft. Laterally on the left and right, it extends towards the prestylian spaces. Inferiorly, it extends towards the posterolateral walls of the oropharynx. This description was compatible with a locally advanced nasopharyngeal tumor process that measured 34 mm in maximum thickness, without other lesions of secondary appearance.

This carcinoma of the cavum was classified in our patient as T4NxM0 following extension to the clivus with cortical lysis, a widened hypoglossal canal with suspected neurological involvement,

the prestylian space and pterygopalatine cleft with significant lateral extension, the posterior cerebral fossa suspected with possible intracranial involvement, and the oropharynx and nasal cavities affected with extension to the upper airways.

The patient was discussed with oncologists and then underwent oncological management with 35 sessions of radiotherapy, as well as concomitant cisplatin-based chemotherapy. The progression was marked by a regression of radiological signs in favor of diffuse infiltrative pneumonitis.

DISCUSSION :

Diffuse parenchymal lung diseases or interstitial lung diseases (ILDs) embrace a large number of conditions, with a wide range of causes, clinical manifestations, and imaging and pathological features, as well as variable outcomes. It is a group of heterogeneous pulmonary pathologies, where interstitial involvement is predominant. The pulmonary alveolar walls are infiltrated by various combinations of inflammatory cells, fibrosis, and proliferation of certain cells that make up the normal alveolar wall (1).

The overall prevalence of ILD is estimated to be up to 76.0 cases per 100,000 people in Europe and 74.3 cases per 100,000 in the United States. Sarcoidosis, connective-tissue disease (CTD)–associated ILDs, and IPF are the most common fibrotic ILDs, with an estimated prevalence of 30.2, 12.1, and 8.2 cases per 100,000, respectively (2).

Interstitial lung diseases can result from various causes such as inflammatory, infectious, drug-induced, toxic or neoplastic processes. Among the neoplastic etiologies, undifferentiated carcinoma of the cavum (UCNT) can be (as shown in our case report) a rare but significant cause of pulmonary involvement, particularly in endemic regions and in patients with Epstein-Barr virus (EBV) infection. Pulmonary infiltration in this setting can result indirectly from a paraneoplastic systemic inflammatory response. The clinical case presented illustrates this diagnostic complexity, with a patient presenting respiratory symptoms associated with an alteration of the general condition and ENT signs suggestive of nasopharyngeal pathology.

Respiratory symptoms such as dyspnea, dry cough, and hemoptysis, although nonspecific, raised concerns about interstitial lung disease. Chest CT revealed diffuse infiltrative lung disease, a radiological pattern often observed in ILD, but not specific to a specific etiology. The diagnostic approach required a thorough investigation, including bronchoscopy and bronchoalveolar lavage, which ruled out an infectious origin or other acute pulmonary pathology. Immunological examination revealed the presence of antinuclear antibodies and autoimmune profiles that also point towards a systemic pathology such as connective tissue disease or paraneoplastic syndrome. Many factors are able to trigger auto-immunity and autoimmune diseases, and neoplasms are one of them. Neoplasms represent a type of abnormal and excessive tissue or cell growth and can have a benign (benign tumour) or malignant (cancer) form (3).

However, ENT signs, including hearing loss, epistaxis, rhinorrhea, and cervical lymphadenopathy, have been crucial in the discovery of undifferentiated carcinoma of the cavum, also known as nasopharyngeal carcinoma (NPC). This type of cancer, often diagnosed late due to nonspecific symptoms, may be accompanied by respiratory manifestations secondary to local tumor extension or lymph node metastases. The tumor extension observed

on CT, with involvement of the clivus, hypoglossal canal, posterior cerebral fossa, and upper airways, is consistent with TNM stage T4, indicating locally advanced cancer. These features echo the literature, where local extension of cavum tumors can be marked by bone and nerve invasion, thus complicating the prognosis.

For decades, nasopharyngeal carcinoma (NPC) has been endemic in indigenous populations in East and Southeast Asia, the Arctic, North Africa, and the Middle East (4). It's incidence among males is double or triple that among females in most populations (5). In high-risk populations, in contrast, NPC incidence exhibits a single peak at approximately ages 45–59 years, followed by a plateau or a modest decline (6).

The International Agency for Research on Cancer (IARC) classifies tobacco smoking and poor oral health as an established cause of NPC (7). Also, EBV infection and its ubiquitous presence in NPC strongly indicates its involvement in NPC pathogenesis (8)

Definitive diagnosis is made by endoscopic-guided biopsy of the primary nasopharyngeal tumour. Radiotherapy (RT) is the mainstay of treatment and is an essential component of curative-intent treatment of non-disseminated NPC (9).

The treatment of this type of cancer is mainly based on a combination of radiotherapy and concomitant chemotherapy. Concurrent chemoradiotherapy (CRT) is recommended for patients with advanced local or regional NPC. Radiotherapy, particularly intensity-modulated radiotherapy (IMRT), is the cornerstone of treatment for locally advanced carcinomas of the cavum. For chemotherapy the most commonly used regimen is cisplatin 100 mg/m2 every 3 weeks with concomitant RT (11). Cisplatin-based chemotherapy has shown a significant benefit in terms of survival and local control (10), as shown by the case of the patient who benefited from regression of lung lesions after treatment. The multimodal approach is essential to improve the prognosis and limit the local and systemic complications associated with this pathology.

The management of PID of neoplastic origin, particularly cavum carcinomas / nasopharyngeal carcinoma, requires a rigorous diagnostic approach, integrating clinical, radiological, histological and immunological elements. A multidisciplinary approach including pulmonology, oncology, and radiotherapy is crucial to optimize management and improve therapeutic outcomes. Early recognition of pulmonary infiltration in cavum carcinoma, although rare, remains essential to avoid diagnostic delays and to ensure management adapted to the severity of the disease.

CONCLUSION :

interstitial lung diseases (ILDs) requires precise identification of its cause, whether inflammatory, infectious, toxic, or neoplastic. Diagnosis is based on imaging tests, and treatment depends on the underlying etiology. When associated with neoplasia, management combines tumor treatment and advanced respiratory management. Early detection and appropriate management are crucial to improve prognosis, particularly in severe forms where lung transplantation may be necessary. This case illustrates the importance of a comprehensive evaluation in the face of diffuse infiltrative lung disease associated with ENT symptoms, to avoid overlooking an underlying neoplastic etiology. Multidisciplinary collaboration is essential for optimal care of these patients.

BIBLIOGRAPHICAL REFERENCES :

1. Wijsenbeek, M · Cottin, V, Spectrum of fibrotic lung diseases, *N Engl J Med*. 2020; 383:958-968, DOI: 10.1056/NEJMra2005230
2. Duchemann B, Annesi-Maesano I, Jacobe de Naurois C, et al. Prevalence and incidence of interstitial lung diseases in a multi-ethnic county of Greater Paris. *Eur Respir J* 2017 ;50:1602419-1602419.
3. Maley, C., Aktipis, A., Graham, T. *et al*. Classifying the evolutionary and ecological features of neoplasms. *Nat Rev Cancer* **17**, 605–619 (2017). https://doi.org/10.1038/nrc.2017.69
4. Muir CS, Nasopharyngeal cancer–a historical vignette CA Cancer J Clin 1983 ;33:180–5, https://doi.org/10.3322/canjclin.33.3.180
5. ray F, Colombet M, Mery L, Piñeros M, Znaor A, Zanetti R, et al, editors. Cancer incidence in five continents, Vol. XI (electronic version). Lyon: International Agency for Research on Cancer; 2017. Available from: https://ci5.iarc.fr.
6. Ellen T. Chang, Weimin Ye, Yi-Xin Zeng, Hans-Olov Adami; The Evolving Epidemiology of Nasopharyngeal Carcinoma. *Cancer Epidemiol Biomarkers Prev* 1 June 2021; 30 (6): 1035–1047. https://doi.org/10.1158/1055-9965.EPI-20-1702
7. IARC. The evaluation of carcinogenic risks to humans. Volume 100E. Personal habits and indoor combustions. Lyon, France: International Agency for Research on Cancer (IARC): 2012. p.1–538.
8. N. Raab-Traub, Epstein–Barr virus in the pathogenesis of NPC, E.S. Robertson (Ed.), Epstein–Barr virus Wymondham, Caister Academic Press, Norfolk (2005), pp. 71-92. https://doi.org/10.1016/S1044579X0200086X
9. Bossi, P. et al., Nasopharyngeal carcinoma: ESMO-EURACAN Clinical Practice Guidelines for diagnosis, treatment and follow-up, Annals of Oncology, Volume 32, Issue 4, 452 – 465. https://doi.org/10.1016/j.annonc.2020.12.007
10. Blanchard Pierre et al. Chemotherapy and radiotherapy in nasopharyngeal carcinoma: an update of the MAC-NPC meta-analysis. 2015. The Lancet Oncology, Volume 16, Issue 6, 645 – 655. https://doi.org/10.1016/S1470-2045(15)70126-9
11. Lee, A.W.M., Tung, S.Y., Ng, W.T., Lee, V., Ngan, R.K.C., Choi, H.C.W., Chan, L.L.K., Siu, L.L., Ng, A.W.Y., Leung, T.W., Yiu, H.H.Y., O'Sullivan, B. and Chappell, R. (2017), A multicenter, phase 3, randomized trial of concurrent chemoradiotherapy plus adjuvant chemotherapy versus radiotherapy alone in patients with regionally advanced nasopharyngeal carcinoma: 10-year outcomes for efficacy and toxicity. Cancer, 123: 4147-4157. https://doi.org/10.1002/cncr.30850