

Brain Miliary Dissemination Pattern by Lung Adenocarcinoma: Case Report

Patrón de diseminación miliar cerebral por adenocarcinoma pulmonar: Presentación de caso

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Summary

The case of a male patient of 56 years who consulted for long-standing respiratory symptoms initially focused as pulmonary stationary tuberculosis, with stationary evolution and neurological deterioration and histopathologic diagnosis of lung adenocarcinoma as well as scanographic findings compatible with brain metastatic lesions in miliary pattern. In addition to the clinical and imaging case, a review of the literature is done with magnetic resonance imaging findings for differential diagnosis of miliary brain tuberculosis given the similarities in the imaging findings.

Resumen

Se trata de un paciente de 56 años de edad quien consultó por síntomas respiratorios de larga evolución inicialmente enfocados como tuberculosis pulmonar, con evolución estacionaria, deterioro neurológico y diagnóstico histopatológico de adenocarcinoma pulmonar, así como hallazgos radiológicos compatibles con lesiones metastásicas cerebrales en patrón miliar. Además de la descripción clínica e imaginológica del caso se efectúa una revisión de la literatura con los hallazgos por resonancia magnética, para realizar el diagnóstico diferencial con tuberculosis miliar cerebral en razón de las semejanzas imaginológicas.

Introduction

Metastatic cerebral dissemination occurs in 25-35% of cancer patients. Primary tumors with central nervous system (CNS) dissemination include the lung, breast, skin (melanoma), kidney, and gastrointestinal tract, the latter two of which develop brain metastases more frequently (40% and 28% respectively) (1). The best diagnostic study for brain metastases is magnetic resonance imaging (MRI) where they are seen as spherical lesions, with perilesional edema localized at subcortical cortical junction. Miliary pattern brain metastases are, in most cases, secondary to a primary lung neoplasm with subsequent impairment of neurologic status associated with dementia, disorientation, and rarely coma progression, and, unlike non-miliary metastases, may not enhance with the contrast medium (2).

Clinical case

A 56-year-old male patient from an urban area with a history of smoking 20 packs / year) suspended in the last 2 years, with no other history of importance, with a clinical history of 3 months of evolution consisting of occasional dry cough associated with nocturnal diaphoresis, asthenia, adynamia and weight loss. In the last 15 days prior to the visit he developed progressive dyspnea until rest and persistent wet cough, in addition the relatives indicate episodes sporadic alterations in the state of consciousness with spontaneous recovery, without other associated symptoms. At admission to the emergency department, pulmonary auscultation is reduced vesicular murmur without other findings relevant to physical examination, normal serum laboratories for age, chest X-ray entry (Figure 1) on the basis of which is suspected of infectious process type pulmonary tuberculosis miliary vs. pulmonary mycosis. Extension studies included 6 negative smear

microscopes for acid-fast bacilli, serology, and HIV-negative ELISA. Transthoracic echocardiography records severe circumferential pericardial effusion with systolic collapse of the right cavities. Pericardiocentesis was performed with drainage of 700 cm³ of blood fluid. He had bilateral pleural effusion. Cultures and cytologies of the pericardial and pleural fluid were negative; normal fiberoptic bronchoscopy was with negative bronchioloalveolar lavage cultures. Bronchial mucosa biopsy showed atypical bronchial lesion; it was suspected granulomatous infectious process (pulmonary pericardial tuberculosis), neoplastic process was not ruled out. The clinical evolution was stationary. Thoracic computed tomography (CT) was performed (Figure 2) with which it was decided to perform diagnostic pulmonary thoracoscopic lobectomy and representative samples for histopathological study (Figure 3). Subsequently, the patient presented deterioration of the neurological state, considered as a process not associated with delirium, for which a brain magnetic resonance (MRI) study was performed (Figures 4 and 5). The results of the lung biopsy were: moderately differentiated adenocarcinoma, with areas of comedocarcinoma with vascular invasion, lymphatic and visceral pleura, negative for granulomatous disease. The patient progresses morbidly with deterioration of the neurological and respiratory state and dies.

Discussion

Tuberculosis continues to be one of the most important pathologies. It is the second leading cause of death in the world due to infectious disease after the human immunodeficiency virus and predominates in immunocompromised patients. It has a high risk of mortality and neurological sequelae. According to WHO global reports on tuberculosis 2013-2015, 8.6 million new cases were reported in 2012 (3), with a decline in incidence rates by 2015 of 1.5% per year (4); in general,



Figure 1. Portable chest X-ray, anteroposterior projection with multiple micronodular opacities and right parahilar localization mass that erases the right contour of the mediastinum.

about 1.9 million people are infected each year with *Mycobacterium tuberculosis* and approximately 1% of cases develop dissemination to the CNS, with a worse prognosis than in other dissemination sites (5). Cerebral tuberculosis typically presents with headache, low-grade fever and neurological targeting; some patients may experience epileptic seizures and meningeal syndromes, and even in patients with initial respiratory symptoms and exposure to the bacillus, this entity should be included and studied within differential diagnoses (5).

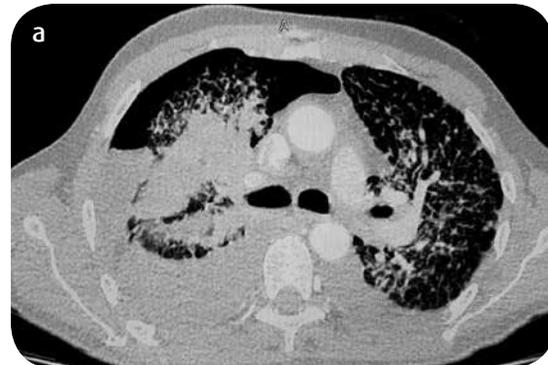


Figure 2. Chest CT in the pulmonary window: a) axial cuts, b) coronal and c) sagittal reconstructions: mass of right parahilar location and spiculated contours associated with multiple micronodular opacities and miliary distribution in both lung parenchyma. In the axial section, in addition, a right pneumothorax chamber is identified.

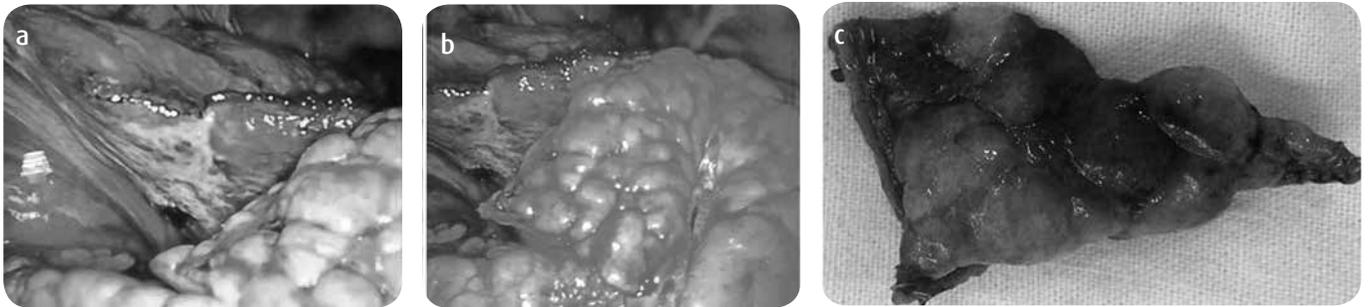


Figure 3. a and b). Images taken during the lobectomy in pulmonary wedge by videothoracoscopy. At the level of the minor fissure: below the middle lobe of the nodular surface, above the upper lobe with broad scarring region and diffuse anthracosis. c) Surgical part in wedge of the right lower lobe, nodular lung parenchyma and areas of congestion.

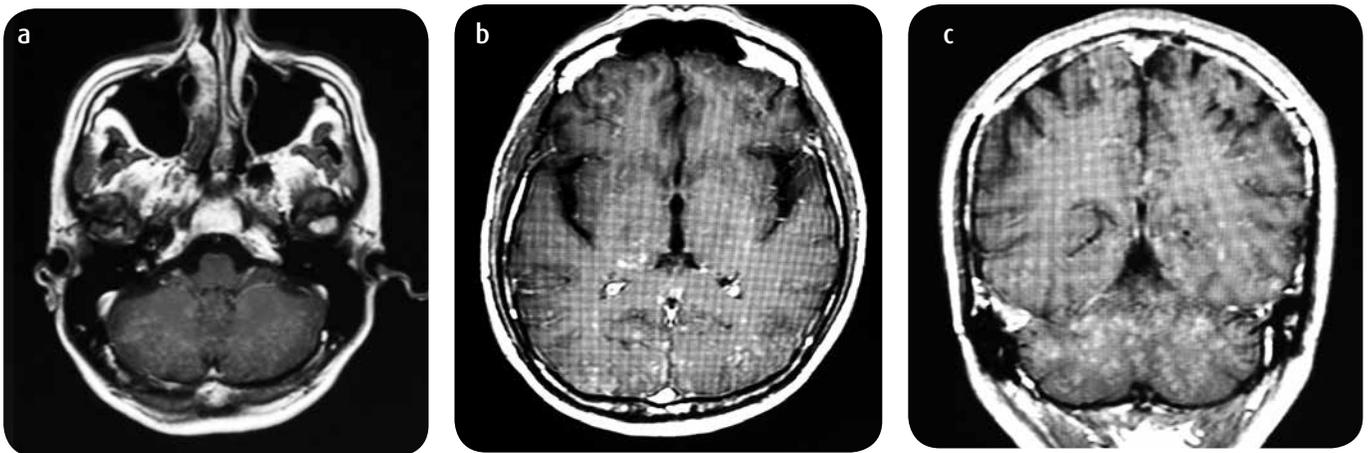


Figure 4. MRI sequence with T1 information with contrast medium: a and b) axial sections and c) coronal reconstruction, showing small foci of subcortical nodular enhancement supra and infratentorial, without white matter edema or meningeal enhancement.

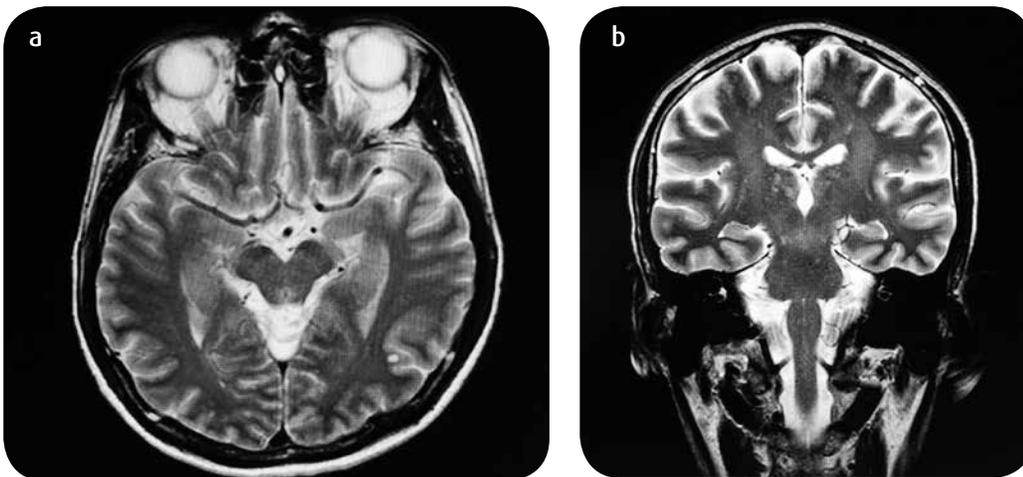


Figure 5. MRI sequences with T2 information: a) axial plane and b) coronal: High subcortical signal of micronodular appearance corresponding to the areas of enhancement in sequences with T1 information is identified.

Meningeal tuberculosis is the most common form, but it also presents as diffuse cerebral tuberculosis, such as exudative basal meningitis or localized forms, such as tuberculomas, abscesses, or cerebritis. In children it is usually infratentorial, whereas in adults predominates the supratentorial location. CT and MRI findings differ according to presentation in the CNS, compromise of meninges, associated cerebral infarcts or tuberculomas may be

found. In general, brain MRI is superior to CT to define lesions in basal ganglia, brain stem or to assess spinal cord involvement (6).

CT scan of the skull with contrast medium should be performed initially in the evaluation of all patients with suspected tuberculosis in the CNS, with a sensitivity of 99% and specificity of 85.7% for cerebral tuberculoma, reported up to 10-30% of the cases (6, 7).

Miliary tuberculosis is a rare extrapulmonary disease, more frequent in immunosuppressed patients, and is usually the result of hematogenous dissemination of lung infection and in the majority of cases due to *Mycobacterium tuberculosis* infection (8). There are few descriptions of cases of cerebral miliary tuberculosis with cerebral CT studies within limits of normality, but with MRI findings of diffuse nodular lesions and predominance in the posterior fossa, suggesting small tuberculomas. These tuberculomas generally measure less than 2 millimeters in diameter, are usually not identified in sequences with simple T1 information, so that only small high signal foci are observed in sequences with T2 information that present punctate enhancement with paramagnetic contrast in sequences with information T1 with contrast medium (9).

Cerebral metastasis

More than 50% of brain tumors correspond to metastases. This is one of the most serious complications of cancer due to its incapacitating neurological symptoms; in the United States the relationship between brain metastases and primary brain neoplasm is 10: 1 and the probability of developing brain metastases from a primary is 48% for melanoma, 32% for lung, 21% breast, 11% renal cell tumor and 6% gastrointestinal. In the first two cases are usually multiple lesions and in the others, single lesions; differential diagnoses include primary brain tumors, abscesses, neurosarcoidosis, CNS angitis and demyelination, without overlooking opportunistic infections of the CNS (1, 2).

The incidence of this type of metastasis has been increasing given the major early extension studies in which MRI is included. Localization frequencies are described in the cerebral hemispheres in about 80% of the cases, 15% in the cerebellum and 5% in the cerebral stem and basal ganglia (1,10); solitary metastatic lesions are present in 50% of the cases and, to a lesser extent, as multiple lesions, up to 30% are found with three or more metastatic nodules (11).

Cerebral metastases in the cerebral CT are seen as lesions of medium or low signal, located in the cortico-subcortical union, with perilesional edema in variable degree, associated in some cases with intracranial (spontaneous) hemorrhage; in studies with contrast medium there is intense, nodular enhancement, which can best be observed in larger lesions and studies with late phases at 5 and 10 minutes; however, small or localized lesions in the brain stem or posterior fossa may not be clearly seen (11).

MRI findings with contrast media are more specific and sensitive, both for diagnosis and for evaluation of response to treatment, and include: lesions with ring enhancement surrounded by vasogenic edema of preference in cortical-subcortical junction, which in T1-enhanced sequences are medium or low signal (melanomas are observed with high signal); in FLAIR sequences, moderate-high lesions with halo with striking high signal, and diffusion sequences usually without evidence of restriction are observed. Some imaging findings may suggest that the lesions do not have a metastatic origin, for example, enhancement in demyelinating pathology is usually presented as a "C" rather than a complete ring, even in cases of tumor recurrence. postradiation cerebral necrosis may be indistinguishable in CT and MRI, in which case complementary studies are suggested by metabolic techniques, such as positron emission tomography (PET). In this case, in the first case, there

is an increase in the cellular enhancement of glucose and in the second, hypometabolic images (2).

Carcinomatous encephalitis

Cerebral metastases with a miliary pattern are a rare presentation of brain metastases and are characterized by perivascular nodules of diffuse miliary distribution, also described as carcinomatous encephalitis, first reported in 1951 (12). They are shown as multiple lesions, small and of high intensity in the cerebral cortex and in the basal ganglia that enhance with the contrast medium (Gd-DPTA). Perivascular miliary metastases (carcinomatous encephalitis) may not enhance and be confused with inflammatory or infectious processes, such as vasculitis or tuberculosis, within differential diagnoses (2).

The literature describes cases of patients with clinical symptoms that initially show respiratory symptoms with a diagnosis of pulmonary neoplasia and subsequent deterioration of the neurological state (compatible with brain metastases) with clinical and imaging improvement after oncological treatment (3).

Conclusions

Cerebral miliary lesions detected and characterized by MRI are an infrequent, very characteristic, but not pathognomonic, finding of an infectious disease caused by *Mycobacterium tuberculosis*, common in our country. However, we must not forget the metastatic carcinoma of the lung primary encephalitis, which is indistinguishable from an imaginary point of view. We recommend to always consider the data of clinical history that can orient towards one pathology or another, being very important the interaction between the different groups of specialists and the multidisciplinary management.

CT, even with multidetector equipment, is a very low sensitivity study for the detection of cerebral compromise in this pathology; however, we recommend its use for the complementary evaluation of the thorax, which is of vital importance in the differential diagnosis.

Finally, it is essential to use the contrast medium during the MRI study, since it is the contrasted phase that best delimits and characterizes the miliary lesions.

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