



Assmann-Redeker Infiltrate: Current Reassessment of a “Classic” Radiological Sign of Post-Primary Tuberculosis

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Abstract

M. Tuberculosis is the responsible of a respiratory chronic disease that spreads through the respiratory tract and has the lungs as primary target. The increase of new cases, mainly due to migratory flows, has led to the reappearance of aspects of the disease that are now forgotten. The aim of this paper is focusing on a typical radiological sign indicative of progressive post-primary disease, actually no more considered in recent scientific literature, but well known to radiologists at the beginning of the 20th century: The infiltrate of Assmann-Redeker. The recognition of this sign makes it possible the recognition of cases of early post-primary disease and the immediate implementation of the correct therapeutic procedure. Our paper consists of a series of four cases admitted to the Policlinico Umberto I in Rome, in which these findings were not initially recognized. Retrospectively this radiological sign was found on the chest X-ray. All Patients underwent chest CT to compare this finding. Diagnostic confirmation was finally obtained through laboratory investigations and one case histology proven, after surgery.

Abbreviations

CT: Computer Tomography; WHO: World Health Organization; TB: Tuberculosis; SARS-CoV-2: Severe Acquired Respiratory Syndrome Coronavirus 2; PA: Posterior Anterior; LL: Latero-Lateral

Introduction

Tuberculosis (TB) is a chronic infectious disease caused by *Mycobacterium tuberculosis*, a *Bacillus* that spreads through the respiratory tract and most commonly has the lungs as target organs (80%).

According to data released in the World Report on Tuberculosis of 2018 by the World Health Organization (WHO) [1], this is one of the top ten deadly diseases worldwide and is the leading cause of death from a single pathogen. In 2014, the WHO proposed a global strategy to end tuberculosis epidemics around the world, estimating a 75% reduction in the death rate from tuberculosis in 2025 and 95% in 2035 [2].

However, one of the main obstacles to achieving this objective is represented by the migratory phenomenon, with great difficulty in visualizing an epidemic outbreak, making its management more complex and demanding. The epidemic is influenced by several factors, such as high mobility, low socioeconomic status, poor hygiene, and poor accessibility to the health service, which involves a prolonged time for the diagnosis and treatment of tuberculosis, favoring the spread of the disease.

The migrant population is, therefore, subject to a higher risk of tuberculosis, constituting high challenges for the prevention and control of the disease.

Although TB is not a rare disease, the reduced knowledge of some indications, that was once well known and then forgotten, can lead to a delayed diagnosis. While the Gohn's complex, the characteristic tuberculous caverns, or the Miliary dissemination belong to common knowledge, there are less known but still characteristic findings of tuberculous disease that must return to a distant part of the cultural background of the radiologist specialist.

We intend to highlight in particular, a radiological sign of progressive post-primary disease, the infiltrate of Assmann-Redeker, now almost totally disappeared from modern literature despite the frequency, in the course of tuberculous disease, have not decreased at all.

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Materials and Methods

We considered four cases which underwent diagnostic evaluation in our Institute in a period ranging from 2017 to 2020. All the radiological investigations suggesting tuberculous diseases were re-evaluated and integrated with the anamnestic and clinical data - laboratories.

The specific X-ray findings were:

- Hazy infiltrative areas with mainly apical localization (so-called Assman-Redeker infiltrate)
- Focal areas of translucency referable to cavitation
- Pleural effusion

The specific CT findings were

- Consolidation and cavitation
- Lymphadenopathy
- Involvement of the airways
- Pleural effusion [3,4]

Finally, diagnostic confirmation with culture was obtained.

Case Series

Case 1

Man with recurrent syncopal episodes and marked weight loss: A 59 years old man was admitted in the emergency room complaining about some recurrent syncopal episodes preceded by dizziness. Smoking habit and marked weight loss of about 30 kg in the last six months have also reported.

The preliminary chest X-ray examination showed an area of consolidation at the left mid-upper field, adhering to the lateral pleura and extending to the perihilar area (Figure 1a).

Based onto the medical history, the case was suspected for lung cancer. Following investigations were performed:

- Brain CT: No significant findings.
- Chest CT: Extensive area of consolidation at the left upper lobe compatible with cancer (Figure 1b).

The patient underwent biopsy; the pathologist report was "Diffuse lymphomonocytic infiltrate with extensive perivascular fibrous transformation".



Figure 1A: Images in a 59-year-old man who presented with recurrent syncopal episodes preceded by dizziness. X-ray Posterior- Anterior (PA) and Latero-Lateral (LL) scan: Area of consolidation at the level of the left mid-upper field, adhering to the lateral pleura and extending up to the perilar area.

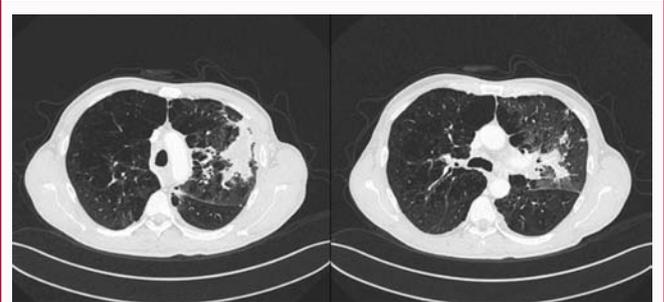


Figure 1B: Images in a 59-year-old man who presented with recurrent syncopal episodes preceded by dizziness. Axial thin-section unenhanced CT scan shows extensive area of consolidation at the level of the left upper lobe referable to the newly formed process.



Figure 1C: Images in a 59-year-old man who presented with recurrent syncopal episodes preceded by dizziness. X-ray check after a month shows increase in the consolidation area, involving all the upper left lobe.

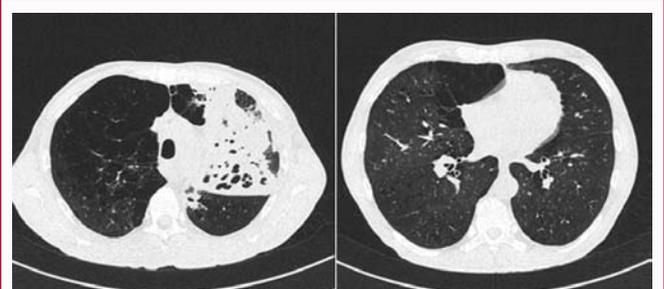


Figure 1D: Images in a 59-year-old man who presented with recurrent syncopal episodes preceded by dizziness. Axial thin-section collimated unenhanced CT image shows a complete structural subversion of the left upper lobe with lingular sparing.

A chest X-ray a month later showed: An increase of the consolidation area was evident, extensively involving all the upper left lobe (Figure 1c):

The following CT shows a complete parenchymal subversion of the left upper lobe with lingular sparing (Figure 1d).

During hospitalization, the serological investigations performed revealed an HIV infection. The previous diagnosis has been then reconsidered as a tubercular disease and the therapy changed to a specific antibiotic therapy with isoniazid, ethambutol, rifampicin and Pyrazinamide for six months.

A CT examination, 7 months later, clearly showed the resolution of the pulmonary consolidation therefore to be attributed to

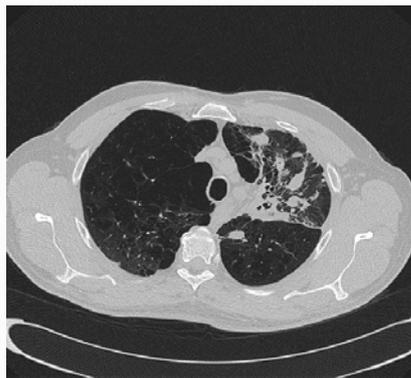


Figure 1E: Axial thin section CT image, post-therapy.

reactivation of the bacillus in a patient with immunosuppression (Figure 1e).

Case 2

Young man with suspected SARS-CoV-2 pneumonia: A 22-years-old man from Asia come to the Emergency Room for suspected Severe Acquired Respiratory Syndrome Coronavirus 2 infection (SARS-CoV-2), with hyperpyrexia (T:39°C) and respiratory symptoms (cough, cold, and sneezing). The medical history: was negative for major disease.

On CT scan, a consolidation with almost complete hepatization of the entire right upper lobe in the residual aerated parenchyma is observed and the presence of "bronchiectasis cystic areas" with a maximum size of 7 mm is described. Further consolidations are



Figure 2A: Images of the 22-year-old man of Asian origin, who presented with fever and respiratory symptoms. CT axial scans show an almost complete "hepatization" of the entire right upper lobe; in the spared portion of the lung the presence of "bronchiectatic cystic areas" was described.

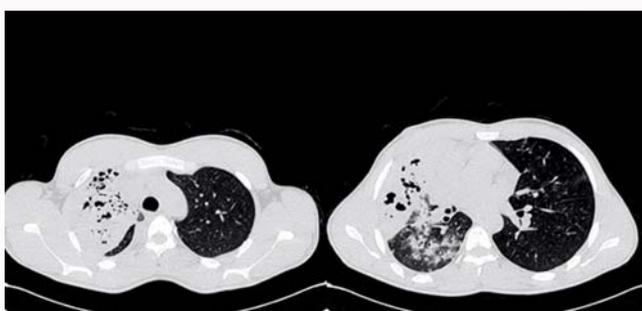


Figure 2B: Images of the 22-year-old man of Asian origin, who presented with fever and respiratory symptoms. CT axial scans after three weeks shows some cavitations in the right upper lobe.

found in the middle lobe, right lower lobe, lingular segment, and left upper lobe. The first suspect is for COVID-19 infection so empirical anti-inflammatory and antibiotic therapy is undertaken (Figure 2a).

In absence of clinical improvement, three weeks later (Figure 2b), chest CT scan was performed. The radiological findings showed a severe worsening, with the aerated part at the level of the right upper lobe replaced by some small cavitations. The overall picture described is indicative of Assmann-Redeker infiltrate. The diagnosis has been confirmed by sputum test. The patient has undergone specific therapy with the combination of four antibiotics: Isoniazid, ethambutol, rifampicin and pyrazinamide for the first six months.

Case 3

Woman with productive cough and hemoptysis: A 46-year-old woman was admitted to emergency room for productive cough and hemoptysis. The patient reported Kaposi's sarcoma from 2007, diabetes, and a previous right upper lobar infection not well defined.

The chest X-ray showed a big opacity in the right apical area and shift of the ipsilateral hemidiaphragm (Figure 3a).

CT confirmed the complete atelectasis of the right upper lobe with cavitation in the context (Figure 3b). Diagnosis of tuberculosis has been confirmed by sputum test.

The patient worsened with an increase of cavitation and necrosis phenomena; then an infection due to *Aspergillus* spp. arises (Figure 3c).



Figure 3A: Images in a 46-year-old woman who presented with fever and productive cough. X-ray shows an area of subversion of the lung parenchyma in the right apical area.

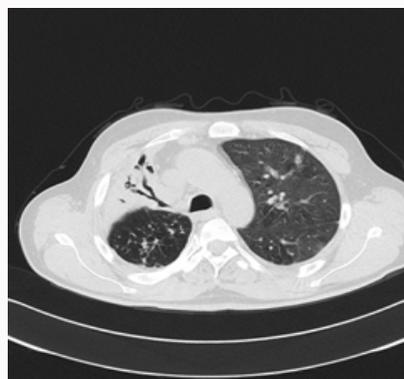


Figure 3B: Images in a 46-year-old woman who presented with fever and productive cough. Axial thin-section collimated unenhanced CT image shows a complete atelectasis of right upper lobe and the presence of cavitation areas in the context.

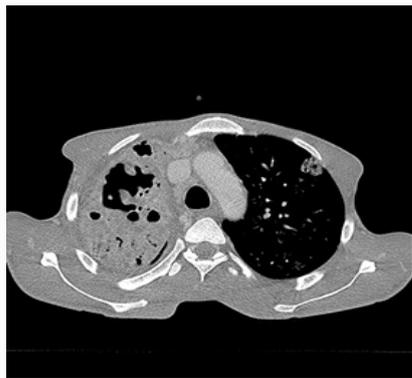


Figure 3C: Images in a 46-year-old woman who presented with fever and productive cough. Axial thin-section unenhanced CT scan shows an increase in cavitative and colliquative phenomena, with super infection with *Aspergillus* spp.

In this case the only way to limit the expansive infective process was deemed to be to a superior lobectomy according to the advice of the thoracic surgeon. The histology confirmed Tuberculosis and *Aspergillus* co-infection.

Case 4

Young man with cough and dyspnea with unknown medical history: The last case is a 19-years-old man of Somali origin, admitted in our hospital after a humanitarian flight. He presented cough and dyspnea but most of his medical history remained unknown due to the language barrier.



Figure 4A: Images in a 19-year-old man with unknown exposure history who presented with fever and cough. X-ray scans shows opacity in the left apical area with widespread hypodiaphania of the remaining parenchyma as per pleural effusion.

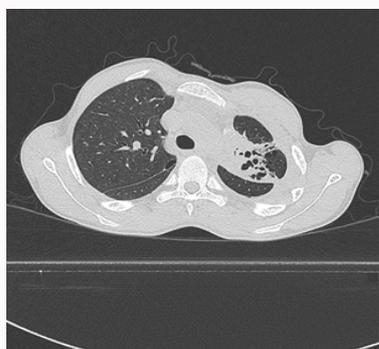


Figure 4B: Images in a 19-year-old man with unknown exposure history who presented with fever and cough. Axial thin-section collimated unenhanced CT image shows apical consolidation with small cavitation phenomena with a "breadcrumb" appearance.



Figure 5: X-ray and CT CASE 1. The area of opacity at the level of the left upper lobe, corresponding to an Assmann-Redeker infiltrate, was initially considered a heteroplastic process.

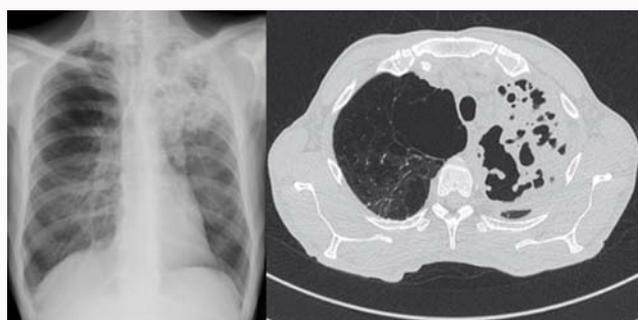


Figure 6: A month later - Case 1. Worsening is evident. On the X-ray, the appearance of a coarse opacity with poorly defined margins is observed, due to the presence of cavitative phenomena which are confirmed by CT examination.

Due to the poor documentation available the patient had been initially treated with a nonspecific antibiotic therapy.

The chest X-ray described an irregular opacity in the left apical area, with diffused hypodiaphania of the remaining parenchyma, probably due to pleural effusion (Figure 4a).

The CT scan, performed four days later, confirmed apical consolidation with small cavitations (the so called "breadcrumb appearance"). This typical finding, in this case, is immediately identified as post-primary TB with apicodorsal reactivation of the left upper lobe (Assmann-Redeker infiltrate) (Figure 4b).

Results and Discussion

Chest X-ray is commonly the first radiological examination in patients with a suspected tuberculous disease. It is the first level of investigation with the highest degree of appropriateness. In all cases of consolidation involving the upper lobes or the upper segments of the lower lobes, associated with mediastinal lymphadenopathy or cavitation, the diagnosis of TB must be considered [5].

Primary tuberculosis is mainly common in the pediatric population, although in low prevalence areas the adult population may represent more than a quarter of cases. This is because in many cases, primary tuberculosis has few or no symptoms; more often, only HIV patients can show clear signs of disease at this stage [6].

The radiographic features described in the literature are:

- Lymphadenopathy which is the most common sign of primary TB, present in about one-third of cases.
- Pulmonary consolidation, often not so different from other bacterial forms.

- Pleural effusion, typically unilateral, present in about 25% of adult cases [7].

The Literature shows that chest X-ray has a high sensitivity but low specificity [5].

Post-primary tuberculosis, on the other hand, represents the evolution of the disease after a variable long latent period. This is mainly due to a partially competent immune system which leads to the reactivation of the *Bacillus*, with consequent dissemination.

At this stage, a typical sign well known to radiologists, especially in the pre-antibiotic era but less considered in recent literature, is the so-called early Assmann-Redeker infiltrate. This sign (also called "precocious subclavicular physiogenic infiltrate") was described during the 1930s by Assmann and was considered one of the earliest signs of post-primary disease in adults until the 1950s, even before manifesting symptoms [8]. The importance of early diagnosis of this aspect of post-primary TB lies in the finding, widely documented since the time of the first description, of an evolution of the infiltrate towards the much more extensive and severe caseous phlebitis, in case of delay in the introduction of therapy [9].

The infiltrate is described as a rounded opacity, mainly located at the infraclavicular level in correspondence with the upper lobes. The size may be variable and are not related to symptoms, while the density is similar to the hilar shadows but it never reaches the density of the mediastinum [9]. The description given by Assmann concerned plain chest radiography. The evolution in caseous pneumonia was expressed with an extension of opacity to the whole lobe and the appearance of numerous small areas of cavitation, which provide the typical aspect defined as "breadcrumb".

In the CT era, as evident from literature, this infiltrate has never been distinguished by the severe post-primary TB, although this particular aspect may differentiate the advanced disease in which more extensive cavitations, present in about 50% of cases, represent the most characteristic sign [7].

The Assmann-Redeker infiltrate can be observed in CT as an area of parenchymal consolidation with blurred edges, mainly localized at the level of the posterior segments of the upper lobes and with a multiloculated appearance like a "crumb of bread".

Our first case is emblematic of the incorrect clinical/therapeutic management. In fact, the patient was initially considered oncological, thus conditioning the evolution of his disease. If a differential diagnosis with TB were immediately considered, prompt action would have been taken; avoiding the patient's worsening (Figure 5).

In the second case, the small cavitations due to caseous necrosis have been erroneously referred as cystic bronchiectasis. To rejoin the studies conducted by Assman at the beginning of the 20th century, in this case, the evolution of the disease was, precisely, what he described with the use of traditional radiology alone: Cavitation phenomena, typical of uncontrolled post-primary TB [9] (Figure 6).

Learning Points

- The Assmann-Redeker infiltrate at chest X-ray presents as a rounded opacity, mainly located at the infra-clavicular level in the upper lobes with variable size and a density similar to the hilum, observed in patients in an early stage of post-primary tuberculosis.
- CT scan, the second level exam, often reveals a typical lobar pneumonia with many areas of cavitation. This specific aspect is generally described as breadcrumb appearance.
- When all these findings are presents, related to typical TB symptoms, radiologists should consider this infectious disease at first.

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