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Miliary tuberculosis in a patient with tuberculous mycotic aneurysm of the abdominal aorta: Case report and review of the literature

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ABSTRACT

The combination of miliary tuberculosis and tuberculous mycotic aneurysm has been described in the literature. We present the case of an 84-year-old man who was diagnosed with a mycotic aneurysm of the abdominal aorta and an adjacent soft tissue mass, after a 3- month history of fever. The patient underwent endovascular restoration of the aneurysm and was treated with broad-spectrum antibiotics. One and a half months later the fever relapsed and the chest CT scan revealed findings consistent with miliary tuberculosis and opacities of both upper lobes not present before, while the abdominal CT scan revealed an increase in the size of the para-aortic mass. Tuberculosis was documented by positive culture for *M. tuberculosis* of bronchial washing and by the CT-guided para-aortic mass biopsy. The patient received anti-TB treatment for 9 months leading to a spectacular improvement of his clinical condition and imaging findings. A review of the literature since 2008 revealed 28 more cases of tuberculous mycotic aneurysm. The treatment and outcome of all cases are described. Mycotic aneurysm of tuberculous etiology remains a reality and has a relatively good prognosis. Although miliary tuberculosis affects mortality even elderly patients may benefit from "aggressive" management and treatment.

1. Introduction

The term mycotic aneurysm is used to describe aneurysms arising from the infectious destruction of the vascular wall. They were first named by Osler in 1885 [1], who misleadingly used the term "mycotic" to describe the deterioration of the vessel that resembled a fungal growth. Mycotic aortic aneurysms are rare, as they account for 3% of aneurysms of the abdominal aorta in necrotomic preparations [2] and they are usually caused by *Staphylococcus* and *Salmonella* [2]. The first description of mycotic aortic aneurysm of tuberculous etiology dates back to 1895 and since then a limited number of cases have been published, mainly as case reports.

Miliary tuberculosis is a potentially fatal form of tuberculosis arising from the diffuse hematogenous spread of *M. tuberculosis* to various parts of the body. Its radiographic imaging in the lungs is typical and involves the appearance of multiple nodules a few millimeters in diameter (mm) in all lung fields. The combination of miliary tuberculosis and tuberculous mycotic aneurysm is described in the literature [1,3] in a limited number of patients. In this paper we describe the interesting case of an immunocompetent elderly patient with mycotic aortic aneurysm, who later developed miliary tuberculosis, eventually leading to the diagnosis of the disease.

2. Case report

A 84-year old man of Greek origin, retired farmer and former smoker, with a possible history of tuberculosis in his childhood, was admitted to hospital with low-grade fever and febrile episodes up to 38.5 °C, with concomitant weight loss of about 12Kg during the last 3 months. The clinical examination did not reveal any focal symptoms, while the chest radiograph was normal. Apart from an ESR of 100mm/1h, no remarkable findings resulted from the rest of the laboratory and imaging tests. Blood cultures were negative for bacteria and the virological control was also negative (RPR, EBV, CMV, TOXO, HIV, HBV, HCV, echo virus, coxsackie, parvo B19).

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Immunological tests (ANA, ANCA, RF, C3, C4, immunoglobulins) did not provide any abnormal findings.

In order to investigate the patient's fever, a chest CT scan was performed, which did not reveal significant findings in the lungs, apart from fibrous tissue in both apices (Fig. 1a and b) while an abdominal CT scan revealed a sacciform aneurysm of the abdominal aorta and soft tissue at the level of the left renal artery. No vertebral infection was detected and the differential diagnosis included mass, abscess and inflammatory lesion. The patient was then submitted to placement of intraluminal stent, during which no biopsy was performed.

Transesophageal echocardiography, fundoscopy, temporal artery biopsy and the thyroid gland biopsy were all normal. Moreover, a radioisotopic study performed with labeled autologous leukocytes did not detect any focus of abnormal concentration around the stent in the abdominal aorta, suggesting absence of inflammation in the area. Finally, the mantoux skin test was measured at 17mm. The patient received piperacillin/tazobactam and teicoplanin and then imipenem for a cumulative period of 20 days, and afterwards he was discharged from the hospital without being totally aferile.

One and a half months later he was readmitted suffering from fever up to 39 °C for ten days and cough with mild expectoration. He showed signs of weakness and enfeeblement as well as mild confusion and disorientation in time and space. New chest X-ray and CT-scans were performed, the findings of which indicated miliary tuberculosis and presence of opacities in both upper lobes (Fig. 1c and d). A new abdominal CT scan revealed increased size of the soft tissue in 3.5 × 2.4 × 5 cm and expansion to the ipsilateral psoas muscle (Fig. 2a and b). The head CT scan was normal and the patient did not consent to lumbar puncture.

On the basis of the new imaging findings, tuberculosis was

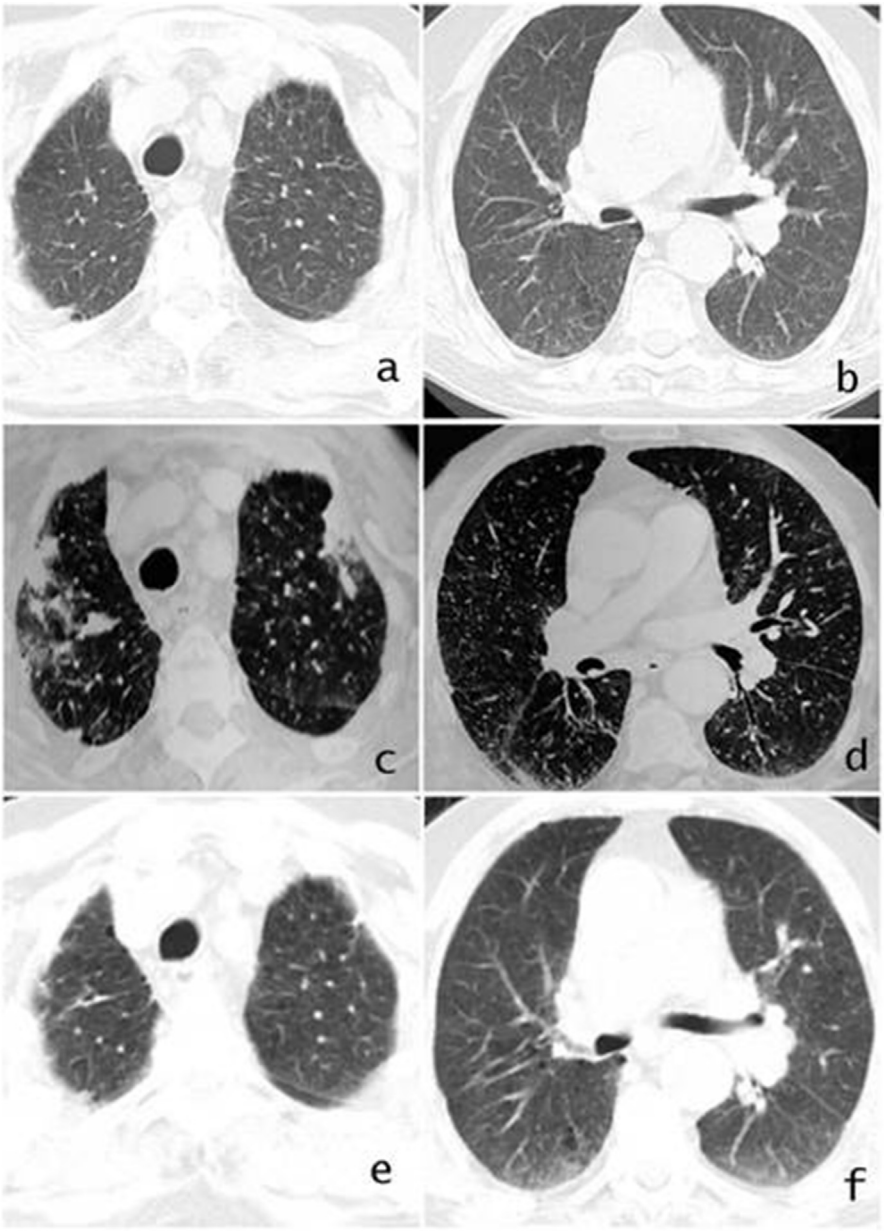

Fig. 1. Chest CT showing fibrous tissue in both apices at the beginning (a,b), miliary tuberculosis and opacities in both upper lobes (c,d) and significant improvement after anti-TB treatment (e,f).

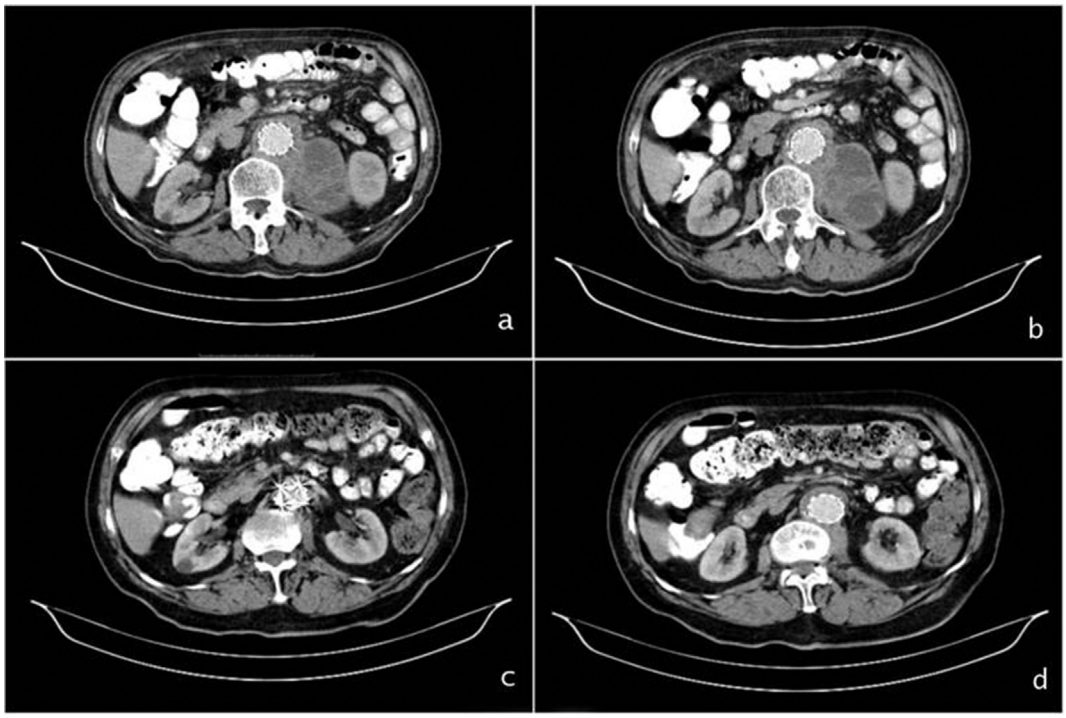

Fig. 2. Abdominal CT showing the aortic aneurysm with an endovascular graft in it and the para-arotic mass before (a,b) and after the anti-TB treatment (c,d).

strongly suspected and the patient was transferred to the Pulmonary Department. The patient underwent bronchoscopy, but the Ziehl-Neelsen stain, the molecular test for *M. tuberculosis* of the bronchial lavage, as well as sputum and urine samples, were negative. However, 10 days later the liquid culture (Bactec Mgit) of bronchial lavage proved positive for *M. tuberculosis* and the patient was started on a 4-drug regimen with rifampicin, isoniazid, ethambutol and pyrazinamide.

A few days later a needle biopsy of the mass located behind the aortic aneurysm was performed under CT guidance. The biopsy showed no signs of granulation tissue. However, the molecular test for *M. tuberculosis* rRNA was in the gray zone and the Löwenstein-Jensen culture of the tissue block eventually proved positive. The strain was sensitive to all first-line anti-tuberculosis drugs.

The patient received anti-tuberculosis treatment for 9 months (2 months rifampicin - isoniazid - ethambutol - pyrazinamide & 7 months rifampicin - isoniazid) which he completed without experiencing any side effects. During treatment he showed an impressive improvement of his clinical condition. Fever remitted completely, he regained his body weight (about 10Kg in 9 months), became functional and fully oriented. The final ESR decreased to 35mm/1hr. A significant improvement in his chest and abdominal CT scans was also noted (Fig. 1e and f and Fig. 2c and d).

3. Discussion

Mycotic aortic aneurysm of tuberculous etiology is a rare clinical entity and few series of cases have been published to date [1,4,5]. A review in 1933 included 21 [6], and another in 1965 [4] 51 cases. The numbers are surprisingly small considering the incidence of tuberculosis at that time and the fact that anti-TB drugs were first released in the early 1950s. In the longest series of cases to date, Long et al. reported 41 cases, 22 men and 19 women, with a mean age of 50 years, who were diagnosed from 1945 to 1999. In addition, Canaud et al in 2008 presented 3 patients with tuberculous mycotic aneurysm of the abdominal aorta and reported 15 more cases from 1999 to 2008 [5].

A review of the English literature from 2008 to today revealed 28 more cases (Table 1) [3,7–33], specifically 18 men and 10 women with a mean age of 44.64 ± 18.16 years (range 16–84). 7 patients had a history of pulmonary tuberculosis and had previously received anti-tuberculosis medication. Despite the small number of published cases to date, it is possible that the incidence of the disease will increase in the future due to the greater number of immunodeficient patients and to the emergence of drug-resistant tuberculosis. Other reasons that suggest a possible imminent increase is the emergence of infections by atypical mycobacteria and intravesical BCG injections for bladder cancer. Mycotic aneurysm of the aorta arising from *M. intracellulare* has been already reported [34], while in a recent review of the literature 2 of the 28 cases were due to BCG [8,12].

The pathogenesis of tuberculous aneurysms is highly interesting and includes several mechanisms. The most common origination involves infection of the vessel by an adjacent tuberculous focus, such as lymph nodes or paravertebral abscess. This is possibly the case in the patient described here. In Long's series [1], an adjacent focus was found in 75% of patients. In this review, histologically documented adjacent tuberculous focus was found in 8 patients (28%) while in 3 cases there was also an adjacent focus which was eventually identified as a collection of clots. Other pathogenetic mechanism is the direct hematogenous infection in the tunica intima or infection in the tunica media or adventitia by the vasa vasorum, as well as the autoimmune reaction induced by tuberculosis [1,5]. The tuberculous infection in the vascular wall, regardless of pathogenetic origin, results in its destruction. The necrosis of the vessel's entire thickness leads to rupture that is followed by either massive bleeding or the formation of perivascular hematoma which can maintain communication with the vascular lumen, in which case it is called pseudoaneurysm. In contrast, the expansion of the infection along the vascular wall is more likely to cause a true aneurysm [17,35]. In the present literature review, the lesions in 13 of 28 (46%) cases were described as

Table 1
Review of literature about tuberculous mycotic aneurysms since 2008.

	Age/Gender	Location	TB location	Paraaortic mass	Ps	Anti-TB treatment (months)		Surgical management	Outcome	Comments
						Before operation	After operation			
1	69/M [3]	Ab AA	Miliary TB cervical lymph nodes TB	+			4D Anti-TB	EVAR	Death	
2	56/M [7]	Ab AA					4D Anti-TB	S	Favourable	resistant to isoniazid
3	64/M [8]	Th + Ab AA					2D Anti-TB (9M)	S	Favourable	BCG due to bladder Ca - *M.bovis*
4	28/M [9]	Th AA					Anti-TB (6M)	EVAR	Favourable	
5	25/M [10]	Th AA	Pulmonary TB	clots	+		Anti-TB	S	Favourable	History of TB
6	55/M [11]	Th AA		clots			4D Anti-TB	S	Favourable	History of TB
7	58/M [12]	Ab AA		+			Anti-TB	EVAR	Favourable	BCG due to bladder Ca - *M.bovis*
8	61/M [13]	Ab AA	Miliary TB	+		Anti-TB	Anti-TB (18M)	EVAR	Favourable	Immunosupression
9	63/M [14]	Th AA	Pulmonary TB				Anti-TB (4M)	EVAR	Favourable	
10	84/M [15]	Th AA		+	+			EVAR	Favourable	History of TB Anti-TB treatment
11	16/F [16]	Th + Ab AA						EVAR	Favourable	History of TB Anti-TB treatment
12	31/M [17]	Th AA					Anti-TB	EVAR	Favourable	
13	59/M [18]	Th + Ab AA	Peritoneum TB			Anti-TB	Anti-TB (9M)	S	Favourable	
14	54/F [19]	Th AA	Miliary TB			Anti-TB (6M)	Anti-TB (3M)	EVAR	Favourable	
15	49/F [20]	Th AA	Miliary TB	+			Anti-TB (3M)	EVAR	Favourable	
16	37/F [21]	Th AA	Miliary TB	+	+	Anti-TB	Anti-TB	S	Favourable	
17	30/M [22]	Th AA					4D Anti-TB	S	Favourable	History of TB
18	21/F [23]	Th AA	Miliary TB TB pleural effusion		+	Anti-TB		S	Death	
19	32/F [24]	Ab AA	Miliary TB		+	Anti-TB		S	Favourable	
20	72/M [25]	aorto-iliac		+	+		Anti-TB (12M)	S-EVAR	Favourable	History of TB
21	40/F [26]	Th AA					4D Anti-TB (10M)	S	Favourable	
22	44/M [27]	Ab AA	vertebral - kidney	+	+	4D Anti-TB (6M)	4D Anti-TB (12M)	EVAR (LEAKS)	Favourable	
23	51/M [28]	Th AA	Miliary TB		+	3D Anti-TB	3D Anti-TB (6M)	S	Favourable	
24	16/F [29]	Th AA	axilla & necks lymph nodes	clots	+	4D Anti-TB			Death	
25	19/F [30]	Th + Ab AA	celio-mesenteric lymph nodes		+	4D Anti-TB	4D Anti-TB (9M)	S	Favourable	
26	38/F [31]	Ab AA			+	4D Anti-TB	4D Anti-TB	EVAR	Favourable	History of TB
27	38/M [32]	iliac	lymph nodes		+		4D Anti-TB (6M)	S	Favourable	
28	40/M [33]	Th AA	Miliary TB		+	4D Anti-TB	4D Anti-TB	S	Favourable	

Th AA: Thoracic Aortic Artery, Ab AA: Abdominal Aortic Artery, TB: Tuberculosis, D: Drugs, S: Surgical, EVAR: Endovascular Aortic Repair, Ps: Pseudoaneurysm.

pseudoaneurysms. The aorta is the most common site of tuberculous aneurysms, and an approximately equal incidence rate is reported in the thorax and the abdomen, while localizations in other arteries have also been reported [5]. Our literature review reports 15 (53%) cases of thoracic aortic aneurysm, 7 (25%) cases of abdominal aortic aneurysms and 4 (14%) cases in which aneurysms were detected in both the thoracic and abdominal aorta. The review reports 1 case of aortoiliac aneurysm and 1 iliac artery aneurysm.

Diagnosis of tuberculous aneurysms may be challenging. In the present review of the literature diagnosis was based on histological and microbiological results from the aneurysm in 10 out of the 28 cases whereas only histological and only microbiological results confirmed the diagnosis in another 5 and 2 cases respectively. Tuberculosis was confirmed from other sites in 7 of the remaining 11 cases. Treatment was initiated empirically in 4 patients. Blood cultures for *M. tuberculosis* were sent in 4 patients and were all negative. Interestingly molecular testing was not performed in any of the cases.

Miliary tuberculosis, in contrast to what was previously thought, is not a purely pediatric disease, as it accounts for 2% of tuberculosis cases in immunocompetent adults [36–38], and occurs most often in adolescents and elderly patients [36–38]. The coexistence of miliary tuberculosis with tuberculous aortic aneurysm, as in the case described here, is not rare. Typically, miliary tuberculosis was reported in 46% of patients in the review by Long [1], a percentage significantly higher than expected [39]. In this literature review, miliary tuberculosis occurred in 9 (32%) cases. The causal relationship of those two diseases is not clear, because theoretically miliary tuberculosis could affect the vascular wall, through a hematogenous spread, but on the other hand vascular wall infection could also cause hematogenous spread. In the case presented here, it may be assumed that the miliary spread was the effect and not the cause of the tuberculous aneurysm due to the occurrence of miliary tuberculosis months following the detection of the aneurysm, a fact also mentioned in the literature [40]. The possibility that placement of the intraluminal aortic stent may have aggravated or even be the sole cause of military spread cannot be excluded. In fact, miliary spread after angiography in a tuberculous aneurysm has already been reported in the literature [41]. Therefore, in this case, the patient, who may have been infected by tuberculosis in childhood, before the release of anti-TB drugs, showed resurgence in the form of paravertebral abscess that

affected also the adjacent aorta and resulted in the hematogenous occurrence of miliary tuberculosis, after placement of intraluminal stent.

The tuberculous aortic aneurysm is fatal if not diagnosed and treated properly [1]. The treatment includes a combination of antituberculosis treatment and surgical management. Cortisone is not indicated by recent guidelines [42] for miliary tuberculosis and was not used in any of the cases reviewed here. In the review of Log et al., all 20 patients who received medication alone, or only underwent surgery or no treatment at all, died. On the contrary, only 3 (12.5%) died out of the 24 patients who received combination therapy. It is interesting that half of these patients had not received antituberculosis therapy for more than one month before the restoration of the aorta, like in this patient's case. In this review 25 (90%) patients received both medication and surgical treatment and 2 (8%) died. One of the remaining 3 patients received only antituberculosis treatment and died before the aneurysm repair, while the other two did not receive any anti-tuberculosis medication, since only an endovascular repair was performed. Both of them had a history of tuberculosis and received anti-tuberculosis medication in the past. In one of these two cases the aneurysm was not considered as a relapse of tuberculosis since imaging findings had been stable in a 4-year period [15]. No explanation why antituberculosis treatment was withheld is given for the other case [16]. As a principal in our center we would be very skeptical about not initiating anti-tuberculosis drugs for tuberculous aneurysms. It is worth noting that only 12 (42%) patients were treated with antituberculosis treatment before any invasive method was performed. In our center we prefer initiation of anti-tuberculosis drugs 1–2 weeks prior to surgery, although this issue has not been officially addressed. Interestingly 2 out of the 3 patients who died suffered from miliary tuberculosis, which leads to a mortality of 22.2% in the case of military tuberculosis versus 5.2% in the rest of the cases. Seven out of 9 patients with miliary tuberculosis had a favourable outcome.

The type of surgical treatment of the tuberculous aortic aneurysm remains uncertain. The classical surgery, consisting of an open surgical repair of the vessel, ensures the extensive excision and lavage of the “contaminated” tissue [5,17]. On the other hand, the placement of intravascular prosthesis described in 2000 by Liu et al. [35] shortens the duration of hospitalization, while avoiding the morbidity and mortality of open surgery. However, the placement of intravascular prosthesis may be associated with a high risk of relapse of the infection resulting in bleeding, as reported in the literature [5,43]. In the case presented here, the placement of intravascular prosthesis preceded the verification of the aneurysm's cause, while the patient's old age was taken into account for the selection of surgical management. 42% (12 cases) of this review's patients were treated with endovascular repair and stent placement without any complication, since only one (1) case reported a minor leak from the stent area. Half of the cases (14) were treated with open surgical repair of the vessel while both surgeries were performed in one (1) patient. One patient died before any invasive method was performed.

In conclusion, based on the present case and the literature review of the last 8 years, tuberculosis, as a cause of mycotic aneurysm, remains a reality. Increased awareness and pursue of histological and microbiological confirmation as well as combination therapy with anti-tuberculosis treatment and invasive management of the aneurysm lead to relatively good results. Despite our patient's advanced age which was significantly higher that the mean age of the patients included in the review and the presence of miliary tuberculosis, his excellent response to treatment verify that elderly people can also benefit from “aggressive” diagnostic and therapeutic approach of mycotic aneurysms.

Conflicts of interest

None.

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