

Infective endocarditis: a consumptive disease among the elderly

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ABSTRACT

The clinical presentation of infective endocarditis varies according to the etiologic agent and the host. In elderly individuals, infective endocarditis can be difficult to diagnose and poses a challenge for the physician. The course of subacute infective endocarditis is indolent, and the onset of cardiac structural lesion is slow and gradual. In elderly patients, anemia and weight loss are occasionally the only or the most striking symptoms. In such cases, the clinical reasoning process leads to a hypothesis of wasting syndrome or neoplastic disease, especially when there is no fever. We report the case of an elderly patient who had mitral insufficiency due to degenerative valve disease and presented with bacterial endocarditis due to *Streptococcus mitis*. The patient was not treated, because the diagnosis was not established in a timely manner. It is of note that the patient presented with marked weight loss and no fever. The autopsy revealed impairment of the mitral valve and left atrium due to endocarditis, as well as lung involvement due to chronic inhalation of smoke from biomass burning, such as that produced by wood-burning stoves.

Keywords: Endocarditis bacterial; Mitral valve; Weight loss; Biomass.

CASE REPORT

A 73-year-old female patient, from the northeast of Brazil (the state of Bahia), was brought to our emergency room because of sudden-onset chest and neck pain accompanied by a drop in the level of consciousness. The patient had been diagnosed with systemic arterial hypertension, mitral insufficiency, and congestive heart failure. In addition, she reported a history of anorexia and weight loss, having lost 15 kg in 6 months. Transthoracic Doppler echocardiography performed 5 months prior showed severe mitral insufficiency, normal left ventricular systolic function, and pulmonary artery systolic pressure of 60 mmHg. The patient had a personal history of smoking and

exposure to smoke from wood-burning stoves. She had recently been hospitalized for acute pulmonary edema. The patient had been under treatment with furosemide, carvedilol, losartan, aspirin, hydralazine, isosorbide mononitrate, and simvastatin. She reported no fever. Physical examination revealed the following: torpor (Glasgow coma scale score, 9); dyspnea; pallor; blood pressure, 60/40 mmHg; heart rate, 130 bpm; respiratory rate, 28 breaths/minutes; delayed capillary refill; systolic thrill and systolic murmur in the mitral area. Pulmonary auscultation revealed rhonchi and wheezing. Neurological examination revealed no motor deficits. Examination of the abdomen and

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extremities was unremarkable. Laboratory test results are shown in Table 1.

Urinalysis revealed the following: leukocytes, 220,000/mm³; red blood cells > 1 million/mm³; proteinuria; and the absence of casts and crystals.

Table 1 – Results of the laboratory tests performed at admission

Variable	At admission	Reference value
Hb (g.dL ⁻¹)/Ht (%)	7.7/23	12.3-15.3/36.0-45.0
Leukocytes (×10 ³ .mm ⁻³)	6,700	4.4-11.3
Band neutrophils (%)	3	1-5
Segmented neutrophils (%)	86	45-70
Eosinophils (%)	0	1-4
Basophils (%)	0	0-2.5
Lymphocytes (%)	9	18-40
Monocytes (%)	2	2-9
Platelets (×10 ³ .mm ⁻³)	96,000	150-400
Urea/Creatinine (mg.dL ⁻¹)	60/1.2	10-50/0.4-1.3
Na/K (mEq.L ⁻¹)	134/3.8	135-146/3.5-5.0
Ionized calcium (mmol.L ⁻¹)	1.1	1.1-1.4
Lactate (mEq.L ⁻¹)	18.2	136-146
Troponin I (ng.mL ⁻¹)	0.21	<0.06
CK-MB (ng.mL ⁻¹)	0.18	<5.0
Total proteins (g.dL ⁻¹)	5.7	6.0-8.0
Albumin (g.dL ⁻¹)	2.2	3.0-5.0
Globulins (g.dL ⁻¹)	3.5	1.5-3.5
CRP (mg.L ⁻¹)	131	<5

Hb/Ht, hemoglobin/hematocrit; Na, sodium; K, potassium; CK-MB, creatine kinase MB isoenzyme; CRP, C-reactive protein.

A chest X-ray revealed a normal cardiac silhouette, signs of pulmonary congestion, and a possible focus of pulmonary infection. An electrocardiogram showed sinus rhythm, left atrial overload, QRS axis of 0°, and ST-segment depression, as well as T-wave inversion in leads V4–V6, D1, and aVL.

After having performed the initial ancillary tests, ceftriaxone and clarithromycin were prescribed because of the possibility of pulmonary infection. However, the patient developed shock that did not respond to saline overload or noradrenaline (at the usual dose or at progressively higher doses) and died on postadmission day 1.

The culture of blood samples collected at admission revealed, after 12 hours, growth of *Streptococcus mitis*, which was found to be resistant to penicillin G and ceftriaxone but sensitive to clindamycin, chloramphenicol, erythromycin, and vancomycin.

An autopsy was performed, and the findings included changes that were consistent with septic shock, the primary focus of infection being located near the mitral valve.

The heart weighed 355 g (mean reference value, 243 g; range, 166-356 g) and showed left atrial enlargement secondary to the severe mitral valve prolapse. We found some brownish mitral valve vegetations measuring up to 1.2 cm, as well as smaller vegetations, with similar characteristics, close to the atrial endocardium (Figure 1).



Figure 1 – A – Panoramic view of the left heart; B – Multiple vegetations in the left atrium and mitral valve.

The histological study revealed infective endocarditis, with areas of abscess formation, accompanied by granulation tissue,¹ which was suggestive of subacute endocarditis (Figure 2). The Brown-Hopps method revealed no bacteria,

and the Grocott-Gomori methenamine-silver stain technique revealed no fungi. Mitral valve prolapse-related changes, such as myxomatous degeneration, fibrosis, and dystrophic calcification, were found (Figure 3).

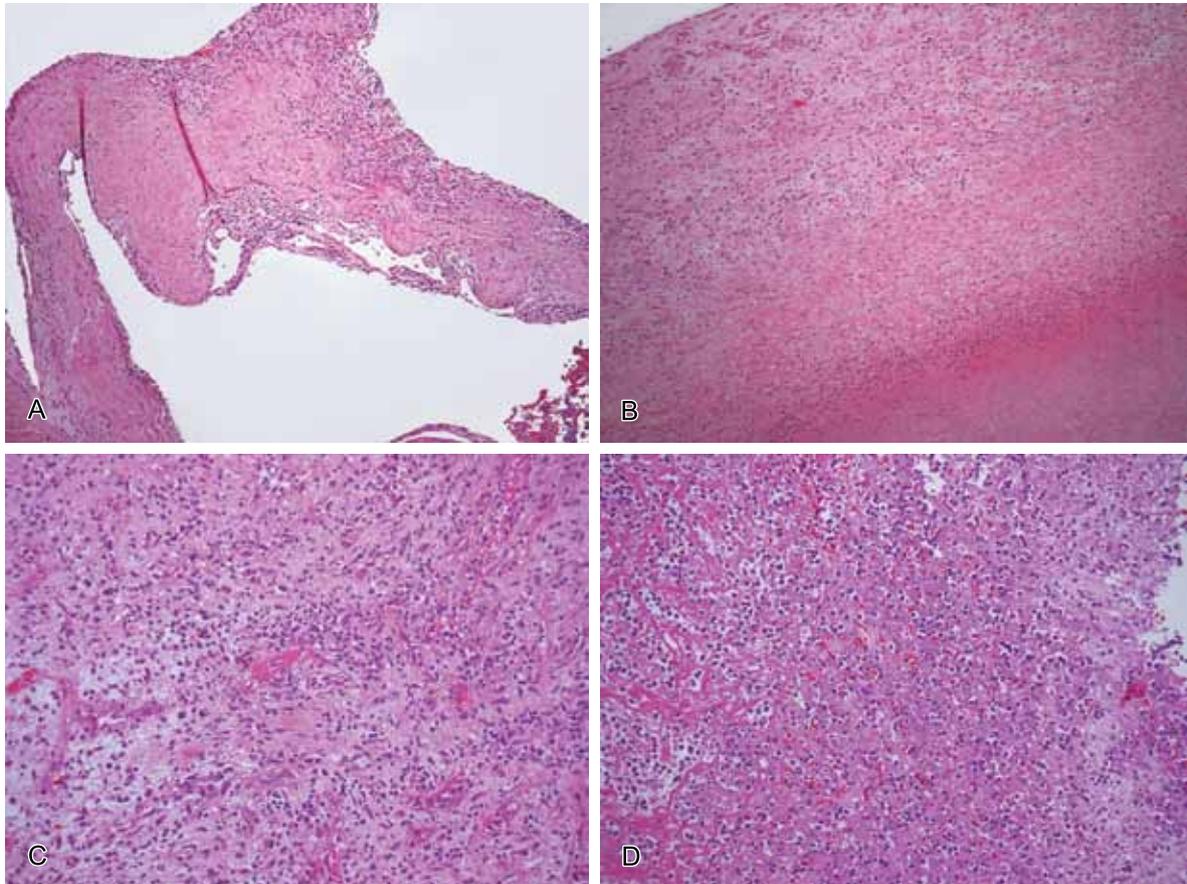


Figure 2 – A – Vegetation on the mitral valve (hematoxylin and eosin; magnification, 100X); **B –** Transition between the granulation tissue and the area of abscess formation of endocarditis (hematoxylin and eosin; magnification, 200X); **C –** Mixed inflammation and neovascularization in the granulation tissue (hematoxylin and eosin; magnification, 400X); **D –** Neutrophilic exudate with pus cells and fibrin in the area of abscess formation of endocarditis (hematoxylin and eosin; magnification, 400X).

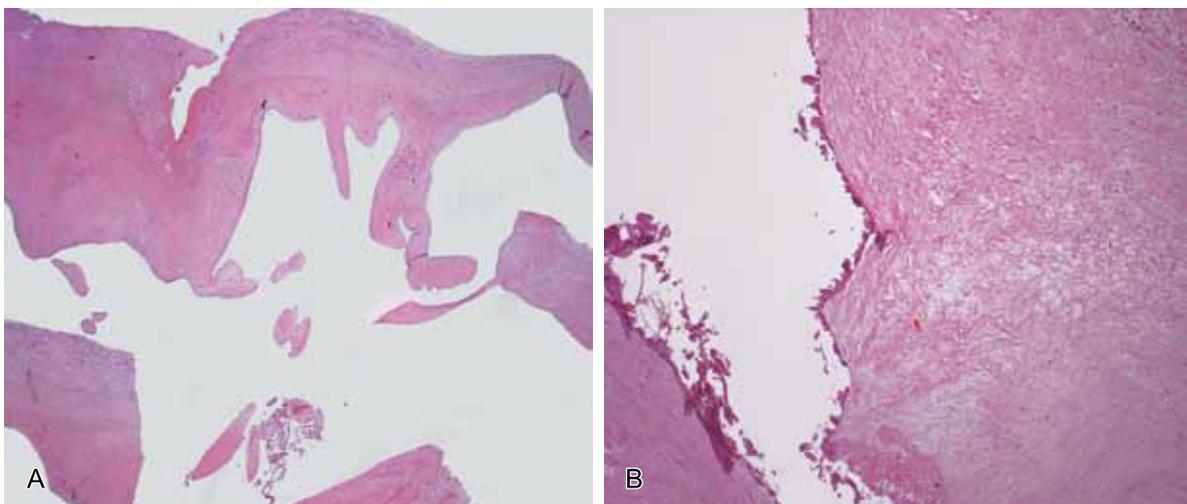


Figure 3 – A and B – Mitral valve prolapse with myxomatous degeneration and a focus of dystrophic calcification (hematoxylin and eosin; magnification, in A 25X and in B 400X).

The macroscopic appearance of the lungs and adjacent lymph nodes was also remarkable. The right lung weighed 410 g (mean reference value, 450 g; range, 360-570 g), and the left lung weighed 390 g (mean reference value, 375 g; range, 325-480 g). We also found small, citrine, bilateral pleural effusion. Paratracheal lymph node enlargement was found in the carinal and peribronchial regions (the lymph nodes in the former measuring up to 5.0 cm), and there were nodules, measuring up to 1,5 cm, in the adjacent connective tissue surrounding the main and segmental bronchi, although only superficially in the peribronchial lung tissue (Figures 4A and 4B).

There was no diffuse distribution of nodules in the lung parenchyma. Macroscopic examination revealed that the lesions were dark and, for the most part, firm, some being hard (Figures 4C and 4D). Microscopic examination revealed multiple, sometimes coalescent, oval-shaped nodules, some of which had spiculated margins; the nodules were characterized by severe fibrosis exhibiting thick collagen bands and numerous black-pigmented macrophages (Figures 5 and 6A).

Some areas showed amorphous necrotic material and cholesterol crystal clefts, accompanied by foreign body giant cell reaction and groups of xanthomatous macrophages (Figure 6B).

The Ziehl-Neelsen method and the Grocott-Gomori methenamine-silver stain technique were consecutively used in order to screen for acid-fast bacilli and fungi, and the results were negative. Some foci of osseous metaplasia were seen. Under polarized light, we found no birefringent particles in the lesions. The findings of abundant black pigment, severe fibrosis, and spiculated nodules were suggestive of mixed-dust pneumoconiosis.²

Many hemosiderine-laden macrophages (“heart-failure” cells) were found in intra-alveolar spaces. This finding is probably related to previous episodes of pulmonary edema in a patient with left-sided heart failure.

Adicionally, there were inhaled carbon pigment engulfed by alveolar and interstitial macrophages (pulmonary anthracosis).

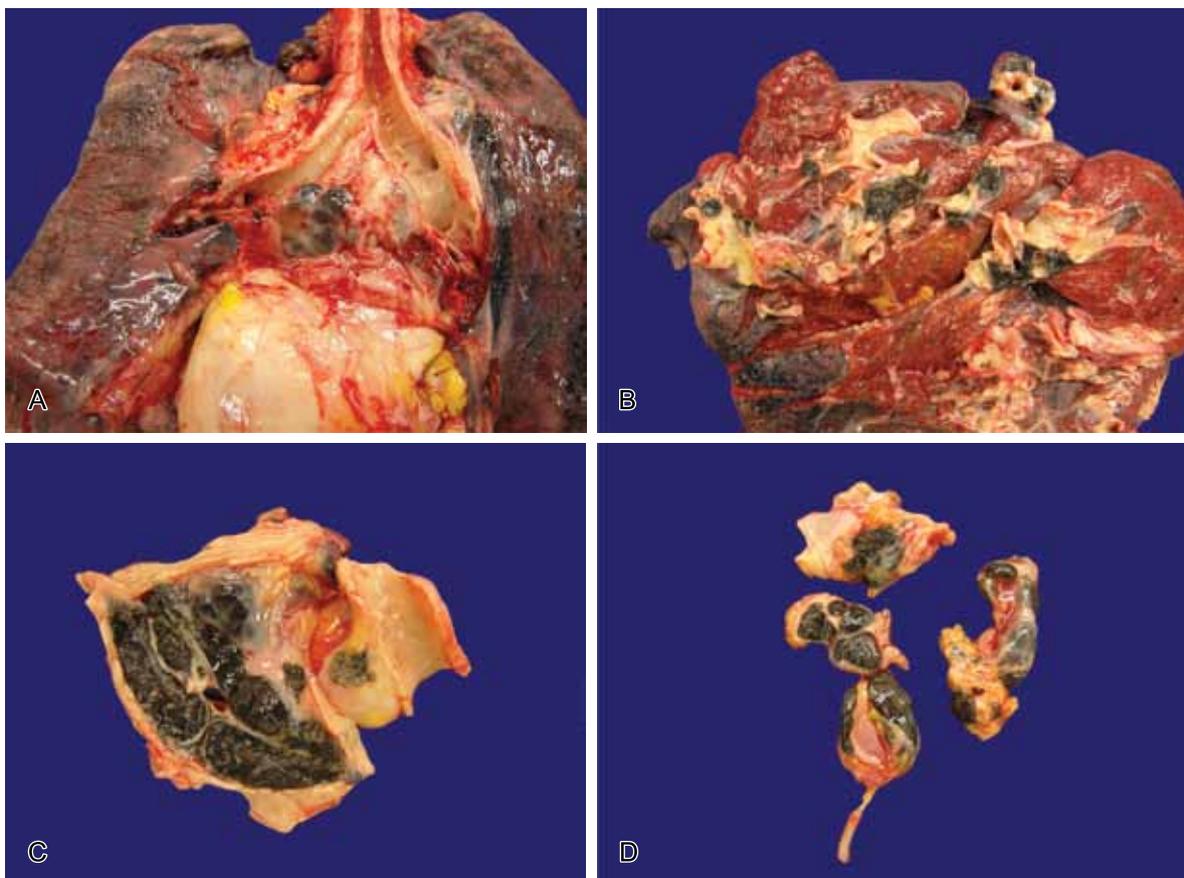


Figure 4 – A – Panoramic view of the mediastinum with paratracheal and infracarinal lymph node enlargement; **B –** Partial cross sections of the lung showing dark nodules surrounding bronchovascular structures. The lung parenchyma is slightly red and has small foci of anthracosis; **C –** Cross section of a black, firm paratracheal lymph node mass; **D –** Intrathoracic lymph node enlargement.

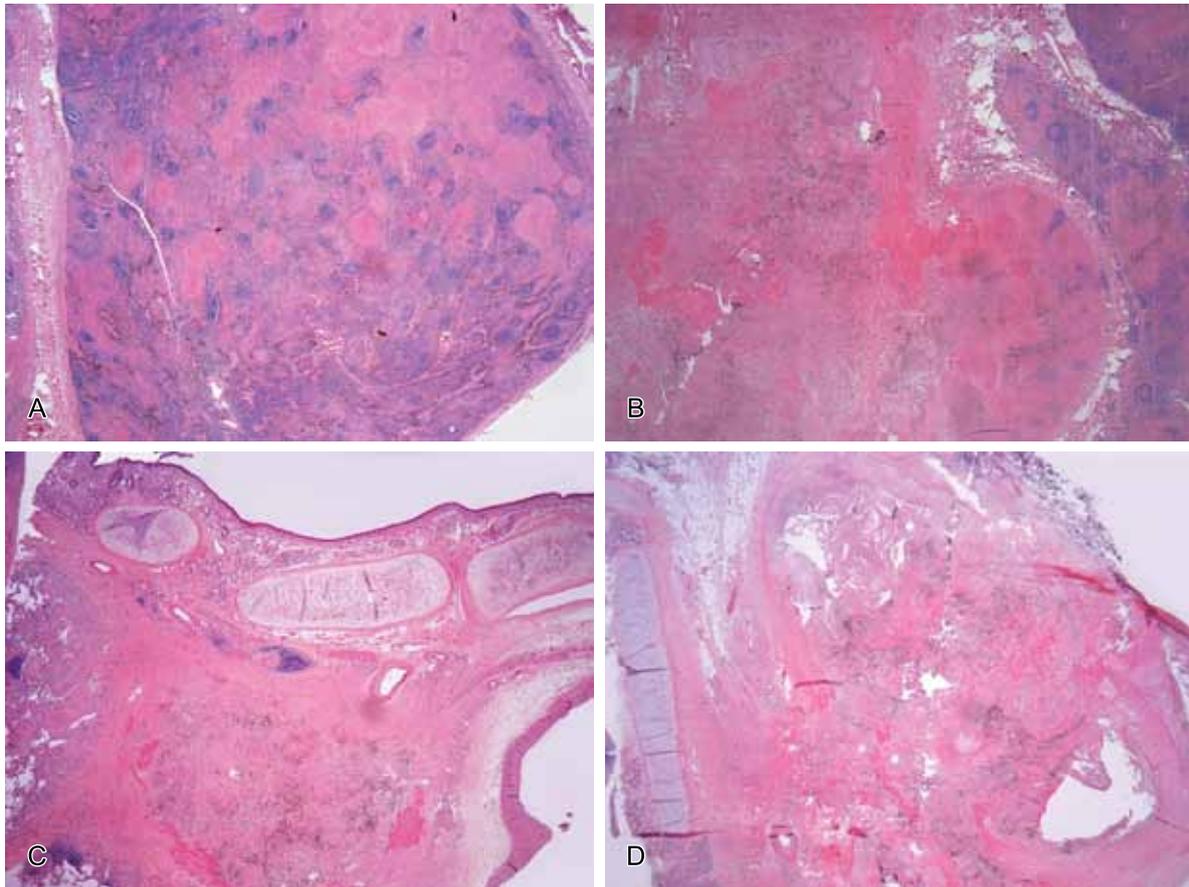


Figure 5 – Lymph nodes (in **A** and **B**) and peribronchial lung tissue (**C** and **D**) surrounded by oval or irregular nodules with severe fibrosis, dark pigmentation, and rare foci of amorphous material (hematoxylin and eosin; magnification, 25X).

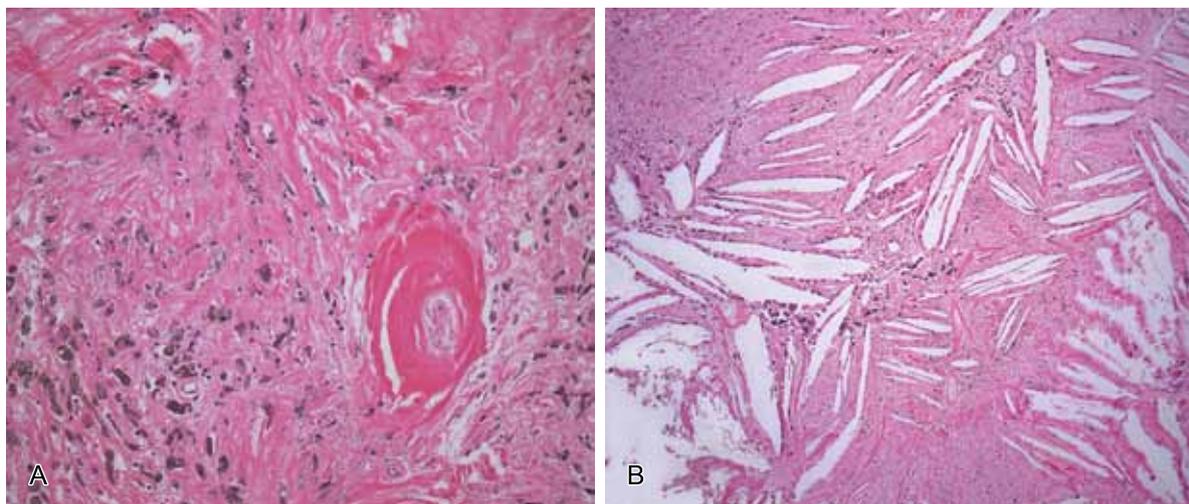


Figure 6 – **A** – Note that the most common appearance of the nodules consisted of severe fibrosis and numerous macrophages containing black pigment (hematoxylin and eosin; magnification, 400X); **B** – Note that there were very few areas of amorphous necrotic material accompanied by cholesterol crystal clefts (hematoxylin and eosin; magnification, 200X).

The spleen weighed 221 g (mean reference value, 145 g; range, 75-245 g). Macroscopic examination of the spleen revealed that the red

pulp was extremely soft. The histological findings were consistent with acute splenitis secondary to sepsis.

We found shrunken ischemic neurons, which were probably evidence of the cerebral hypoperfusion caused by the shock.

There was severe atherosclerosis in the aorta, with calcifications and ulcerations. Atheromatous plaques were detected in the left renal and splenic arteries. The coronary arteries were rigid, and there were areas of fibrosis in the ventricles. Signs of cardiogenic shock or pulmonary hypertension were not detected on autopsy.

DISCUSSION

Although the patient had a 6-month history of weight loss and anorexia, she sought emergency room treatment because of an acute profile, which was characterized by arterial hypotension associated with signs of tissue hypoperfusion (decreased level of consciousness, tachycardia, decreased capillary refill, oliguria, and respiratory distress). The congestive heart failure caused by hypertensive cardiomyopathy and the mitral valve disease can partially explain the weight loss in our patient. The acute profile was attributed to cardiogenic and septic shock. Because there was no recent ischemic electrocardiographic changes and because the markers of myocardial necrosis were not significantly increased, acute coronary syndrome was ruled out as the cause of cardiogenic shock. The initial hypothesis to explain the sepsis in this patient was pulmonary infection, for which she received antibiotic therapy. However, we should also have considered the possibility of bacterial endocarditis, given that our patient was an elderly individual with mitral valve disease and was therefore at a higher risk of developing that infection. The risk groups for infective endocarditis include individuals with rheumatic mitral valve disease, intravenous drug users, patients with heart valve prostheses, hemodialysis patients, individuals with intravenous catheters, and elderly individuals with degenerative valve lesions.³⁻⁵

The clinical presentation of infective endocarditis can be nonspecific and difficult to diagnose. When patients with valvular lesions and those in the risk groups for infective endocarditis present with fever and other nonspecific symptoms, such as weight loss, a diagnosis of infective endocarditis should always be considered.

Nonbacterial thrombotic endocarditis is characterized by lesions ranging in size from 0.1 to

0.5 cm, corresponding to non-invasive vegetation and without inflammatory reaction, weakly attached to the valve. The Libman-Sachs disease, found in systemic lupus erythematosus, is constituted by multiple vegetations measuring generally from 0.1 to 0.4 cm. These lesions show fibrinous eosinophilic material, hematoxylinic bodies; fibrinoid necrosis is observed when intense vasculitis is present.¹ In the case presented here, the vegetations were bigger and a liquefactive necrosis of abscess was observed within the vegetations confirming the diagnosis of infective endocarditis, despite the lack of etiologic agent demonstration on histology.

Although fever occurs in 80-90% of patients with infective endocarditis, it might be absent in severely debilitated patients, in patients with severe heart failure, in elderly patients, and in patients with renal failure. That frequency is lower in cases of subacute infective endocarditis than in those of acute infective endocarditis.^{5,6}

The principal factor that determines the type of presentation is the etiologic agent. Acute endocarditis is generally caused by beta-hemolytic streptococci, *S. aureus*, and *S. pneumoniae*, whereas subacute endocarditis is caused by viridans group streptococci, enterococci, coagulase-negative staphylococci, and the HACEK group, which comprises *Haemophilus* spp., *Aggregatibacter actinomycetemcomitans*, *Cardiobacterium hominis*, *Eikenella corrodens*, and *Kingella kingae*.

For the detection of valvular vegetations, transesophageal echocardiography has a sensitivity of 90-100%, whereas transthoracic echocardiography has a sensitivity of 40-63%. The modified Duke criteria^{3,5,7} assist in the diagnosis of infective endocarditis and underscore the importance of those ancillary tests.

The treatment of infective endocarditis is based on bacterial eradication by antibiotic therapy in isolation or in combination with surgery. High serum concentrations of antibiotics are desirable in order to allow the drug to enter the vegetation. Prolonged treatment (4-6 weeks) is needed in order to eliminate the bacteria from the focus of infection. Surgery is required in up to 50% of cases, the principal indications being heart failure (generally related to valvular dysfunction), uncontrolled infection (associated with perivalvular extension accompanied by atrioventricular conduction defects), and prevention of systemic embolism.^{3,8}

Critically ill patients who present with an acute clinical profile (as was the case for our patient) should receive empirical treatment as soon as possible (i.e., after blood sample collection for blood culture). The empirical treatment should cover the principal causative agents: staphylococci (20-35%); streptococci (*Streptococcus viridans*, 30-40%; other streptococci, 15-25%); and enterococci (5-18%). It has been suggested that patients should be started on penicillin, oxacillin, and gentamicin.⁹ The alternative choice for the initial treatment is the use of vancomycin.^{8,9}

Although the number of viridans group streptococci that are partially or completely resistant to penicillin has increased worldwide, only a limited number of penicillin-resistant *Streptococcus viridans* strains have been reported to cause bacterial endocarditis.^{3,8,10}

It is important to establish an accurate diagnosis of subacute bacterial endocarditis in order to administer the appropriate treatment. When this does not happen, the disease inexorably progresses to death. In the case reported here, it was impossible to treat the patient because she was admitted with septic shock and died less than 1 day after hospitalization. Although the patient had no fever, she had a 6-month history of constitutional symptoms, such as weight loss, asthenia, and anorexia, which were suggestive of a subacute profile. However, the diagnostic investigation was not conducted in a timely manner. The autopsy confirmed the diagnosis of infective endocarditis, and the absence of other diseases shows that the course of infective endocarditis can be similar to that of wasting syndrome.

Another interesting aspect revealed by the autopsy was the presence of major lymph node enlargement (paratracheal and peribronchial lymph node enlargement) and nodules in the connective tissue surrounding pulmonary hilar structures, as well as in the adjacent superficial lung tissue. Those changes were suggestive of mixed-dust pneumoconiosis: anthracotic pigment (such as that caused by inhalation of coal dust) accompanied by other fibrogenic particles (e.g., silica). However, because the patient presented with significant weight loss, those changes could also have been interpreted as being suggestive of neoplasia. In the case of pneumoconiosis, the lesions are generally more diffusely distributed in the lung parenchyma, whereas in the case reported here the nodules were located more centrally.

The patient not only inhaled pollutants derived from biomass burning (a wood-burning stove) but also had a history of chronic smoking, both of which can explain the histopathological findings.

Worldwide, approximately 50% of all households and 90% of all households in rural areas use solid fuels (charcoal or biomass) as the principal source of energy, both for cooking and for indoor heating.^{11,12} Therefore, approximately half of the world population (i.e., nearly three billion people) is subject to the deleterious effects of combustion products. In the rural areas of Latin America, 30-75% of all households use biomass as fuel for cooking. In Brazil, wood-burning stoves are still used in many households (in 40.9% of all households in rural areas and in 2.6% of those in urban areas). In 2003, the Brazilian Institute of Geography and Statistics estimated that 8.6% of all households used wood as the primary fuel.¹³

Various biomass burning products are toxic or irritating to the respiratory system, including respirable particulate matter, which is the product that is most deleterious to the respiratory system.^{13,14} Larger particles are filtered in the nose and throat, whereas those smaller than 10 µm in diameter can settle in the respiratory tract. Fine particles (those smaller than 2.5 µm in diameter) can penetrate the alveoli, whereas ultrafine particles (those smaller than 0.1 µm in diameter) can pass through the alveoli and spread to other organs.¹³ Fine and ultrafine particles can reach the most distal parts of the respiratory system and are responsible for triggering the inflammatory process.¹³

Various studies have shown that long-term exposure to smoke from indoor biomass burning is associated with respiratory diseases. Systematic reviews and meta-analyses^{11,15-17} have shown that children who are under five years of age and are exposed to smoke from biomass burning are at a higher risk of developing pneumonia and other lower airway infections. Smoke inhalation affects various pulmonary defense mechanisms, including mucociliary transport and macrophage function. The risk of developing chronic obstructive pulmonary disease and chronic bronchitis more than doubles in adults exposed to smoke from biomass burning. The principal population at risk comprises women who use solid fuels for cooking, who can present with respiratory complaints such as chronic cough, increased pulmonary secretions, dyspnea, wheezing, and subsequent development of cor pulmonale.^{11,18,19} The smoke from the burning of coal is currently

considered a carcinogen, whereas that from biomass burning is considered a probable carcinogen.^{11,20} The smoke from biomass burning has substantial concentrations of known carcinogens, such as polycyclic aromatic hydrocarbons (benzopyrene, and benzene) and formaldehyde.

Other, previously described, health effects of biomass burning include asthma, pneumoconiosis, cataracts, blindness, tuberculosis, neoplasia, and adverse effects during pregnancy.^{11,15-17} Although such associations have been described, the results are still considered inconclusive.

We conclude that infective endocarditis should be included in the differential diagnosis of consumptive syndrome in elderly patients who are at risk for developing infective endocarditis. Another important finding of our autopsy was major paratracheal and pulmonary hilar lymph node enlargement due to the inhalation of smoke from biomass burning. That finding could have been clinically interpreted as being suggestive of neoplastic disease.

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