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Fatal endocarditis with methicilin-sensible *Staphylococcus aureus* and major complications: rhabdomyolysis, pericarditis, and intracerebral hematoma

A case report and review of the literature

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Abstract

Background: Over the last decades *Staphylococcus aureus* (SA) has become the dominant etiology of native valve infective endocarditis, with the community-acquired methicillin-sensible *Staphylococcus aureus* (CA-MSSA) strains being the prevailing type.

Case: We report here a case of extremely severe CA-MSSA aortic valve acute endocarditis associated with persistent *Staphylococcus aureus* bacteremia (SAB) in a previously healthy man and include a literature review.

The patient developed severe and rare complications (purpura, purulent pericarditis, intracerebral hematoma, and rhabdomyolysis) through systemic embolism; they required drainage of pericardial empyema and cerebral hematoma, the latter eventually caused a fatal outcome. The strains recovered from sequential blood culture sets and pericardial fluid were MSSA negative for genes encoding for staphylococcal toxic shock syndrome toxin (TSST)-1 and Panton–Valentine leukocidin. C, G, and I enterotoxin genes were detected.

Conclusions: This case with unusually severe evolution underlines the limited ability of vancomycin to control some MSSA infections, possibly due to potential involvement of SA virulence factors, hence the importance of clinical vigilance for community SAB cases.

Abbreviations: CA = community-acquired, IE = infectious endocarditis, MSSA = methicillin-sensible *Staphylococcus aureus*, NVIE = native valve infective endocarditis, PBP2a = penicillin binding protein 2a, SA = *Staphylococcus aureus*, SAB = *Staphylococcus aureus* bacteremia, SEC = *Staphylococcus aureus* enterotoxin C, TSS = toxic shock syndrome, TSST = toxic shock syndrome toxin.

Keywords: endocarditis, intracerebral hematoma, methicilin-sensible *Staphylococcus aureus*, pericarditis, rhabdomyolysis

1. Introduction

In the context of an increased global incidence of *Staphylococcus aureus* bacteremia (SAB), there is evidence that it constitutes the main pathogen responsible for native valve infective endocarditis (NVIE) with a prevalence of 22.9% to 34%[1,2]; the methicillin-sensible *Staphylococcus aureus* (MSSA) strains are predominant (72%–85%).[2,3] The aortic localization of infectious endocarditis (IE) with MSSA is cited in 16% to 27% of cases,[2,4] and community acquisition is preponderant (60%–80%).[2,3]

In this article, we are reporting an NVIE with community-acquired MSSA (CA-MSSA), associated with severe sepsis and persistent bacteremia as well as multiple major complications, some of them extremely rare, which lead to fatal evolution; the responsible pathogenic mechanisms are also discussed.

Informed consent was obtained from the relative for publication of this report.

2. Case presentation

A 36-year-old patient, with a history of stage I arterial hypertension and gramineae allergy, is admitted in the 4th day of his disease with malaise, chills, low grade fever, sweating, intense myalgia, and arthralgia, extended purpuric exanthema; the patient reported nausea and vomiting at the onset, which subsided after spasmolytic treatment. On the physical exam, the cardiac frequency was 130 bpm, blood pressure was 130/80 mm Hg, axillary temperature was 36.8 °C, peripheral capillary oxygen saturation was 95%, purpura with partially confluent lesions on the thorax and lower limbs, vasculitic lesions with partial necrotic character, and painless palmoplantar violet lesions; the patient exhibited severe movement impairment due to

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intense myalgia and large joint arthralgia; and a diastolic murmur was present.

Laboratory results after admission showed an inflammatory syndrome, thrombocytopenia, hepatic cytolysis, increase in serum bilirubin, impaired renal function, and marked increase of the creatine phosphokinase level; the echocardiographic examination showed severe aortic insufficiency associated with bicuspid aortic valve (see Fig. 1). Blood cultures were performed and an antibiotic treatment with imipenem (1 g q 8 hours) and vancomycin (1 g q 12 hours) was started due to suspicion of sepsis, no point of entry was evident.

The evolution during the next 36 hours was unfavorable, with plateau fever from day 2, accentuated malaise and obnubilation; the patient remained hemodynamically stable, although vegetations appeared on the aortic valve and pericardial collections developed as well as diffuse cerebral edema with hypodense lesions under the vertex. The diagnosis of acute endocarditis with systemic embolization (cerebral, cutaneous, and pericardial) was established and the treatment was continued with the adjustment of vancomycin dosage to creatinine clearance, pericardiocentesis was delayed.

Subsequently to this deteriorating condition the patient was transferred to the intensive care unit. Since the blood cultures performed on admission (while the patient was afebrile) and during the next 2 days (fever spikes with a maximum value of 38.3 °C) showed the presence of MSSA, oxacillin, and ceftriaxone were considered but the skin testing for allergy was positive.

On day 6 from admission, oligoanuria develops in association with nitrogen retention and therefore continuous veno-venous hemofiltration was instituted.

On day 9, in the context of persistent hyperthermia (39.8 °C) and extended confluent purpura with necrotic vasculitis lesions the patient exhibits altered neurological status then Glasgow coma score 3, increased blood pressure, acute respiratory insufficiency, requiring orotracheal intubation, and mechanic ventilation support; cranial computer tomography scan showed left occipital intraparenchymal hematoma requiring left parietal-occipital craniotomy and drainage using an epidural drain. Echocardiographic reevaluation on the same day showed the expansion of the pericardial collection during the following 24 hours, requiring percutaneous pericardiocentesis under echocardiographic guidance; purulent pericardial fluid was aspirated in large quantities (over 600 mL).

Antibiotic treatment with linezolid (600 mg q 12 hours due to altered renal function) and clindamycin (600 mg q 8 hours) is initiated, but high, continuous fever persists and the blood culture performed on day 10 is still positive with MSSA.

Echocardiographic reevaluations during the next 7 days show aortic vegetation of constant size and the reappearance of a circumferential pericardial collection with a 4.5 to 5 mm thickness that required the placement of negative pressure drainage through which serosanguinous fluid is extracted.

The evolution was severe: the patient developed hepatic dysfunction, profound coma, and acute respiratory distress syndrome; he died on the 19th day after admission.

2.1. Bacteriological and molecular workup

Staphylococcus aureus (SA) was isolated from 6 sets of blood culture and pericardial fluid. Susceptibility to antibiotics was assessed by disk diffusion method and Vitek2 Compact automated system (BioMerieux).

Latex agglutination test (MRSA slidex, BioMérieux) was used to test for the presence of penicillin binding protein 2a (PBP2a).

A triplex polymerase chain reaction was performed for the detection of the following genes: mecA (encoding for PBP2a, the

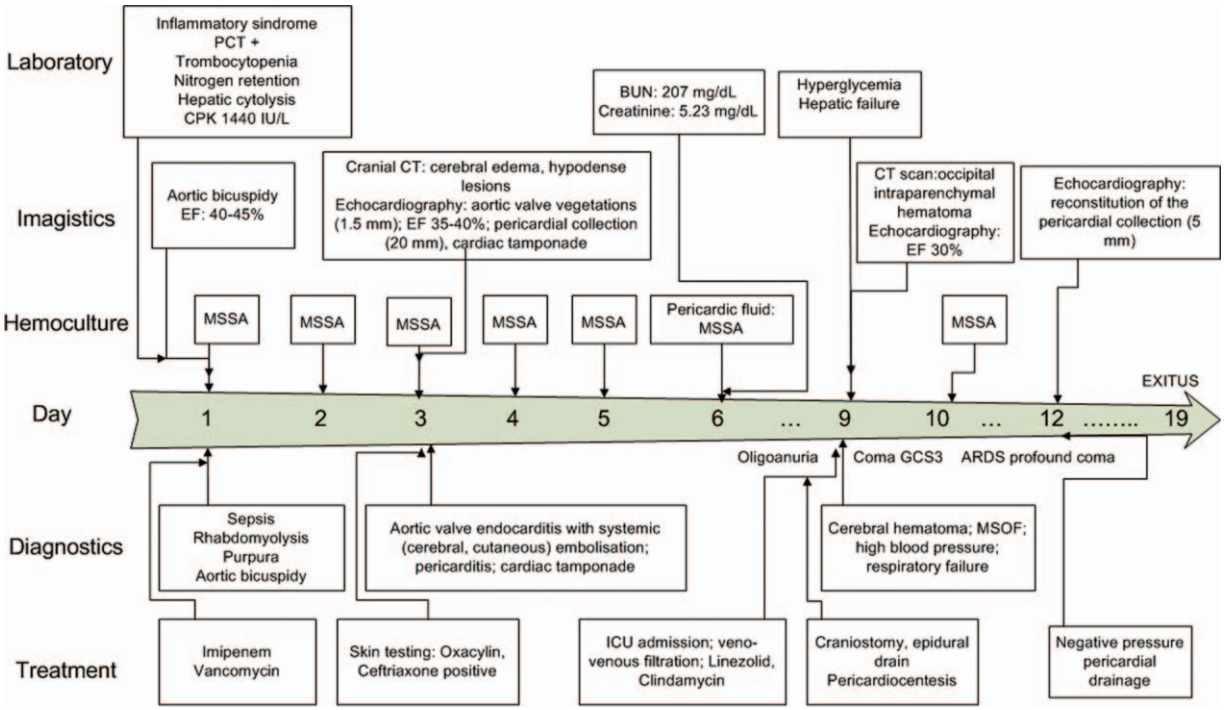

Figure 1. Timeline of clinical course, diagnostics, interventions, and outcome. ARDS = acute respiratory distress syndrome, BUN = blood urea nitrogen, CPK = creatine phosphokinase, EF = ejection fraction, GCS = Glasgow coma score, ICU = intensive care unit, INR = international normalized ratio, MSOF = multisystem organ failure, MSSA = methicilin-sensible *Staphylococcus aureus*, PCT = procalcitonin.

substrate of methicillin resistance), lukS/F-PV (encoding for Panton-Valentine leucocidin), and nuc (encoding for the staphylococcal thermonuclease), as described previously.[5] Additional multiplex polymerase chain reactions were carried out for the detection of genes encoding for staphylococcal enterotoxins A–E and G–I, exfoliative toxins A, B, and staphylococcal toxic shock syndrome toxin (TSST)-1, as described elsewhere.[6] The strain was identified as SA based on conventional phenotypic assays and the presence of the nuc gene. PBP2a and mecA genes were not detected and the strain showed susceptibility to oxacillin, according to these findings it was MSSA. The vancomycin minimum inhibitory concentration determined by the Vitek2C system was 1 mg/L.

Only the staphylococcal enterotoxins C, G, and I genes were detected.

3. Discussion

The occurrence of NVIE in this case was favorized by multiple factors; on one hand, persistent SAB, defined through positive blood cultures for more than 72 hours, constitutes a well-established risk factor for IE, as subsequent NVIE incidence is 10%.[7,8] Over 75% of cases of MSSA endocarditis do not have an identified source of infection;[4,9] acquiring a community SA increases therefore the risk of developing IE.[7] On the other hand, the presence of a congenital bicuspid aortic valve represented a favoring factor for the disease since it was shown as the most common risk factor for aortic NVIE.[10]

Cutaneous lesions were the 1st modifications that suggested septic metastases that represented, together with persistent fever, the other risk factors for the appearance of complications in the course of SA blood stream infections.[7] The presence of Janeway lesions, which are highly specific for IE albeit with reduced prevalence (5%), and, later, of necrotizing vasculitis lesions suggestive for embolization in a febrile context, were highly conducive to our diagnosis.[11] The presence of extended, generalized, confluent purpura raised the possibility of a toxic pathology; previously, *Staphylococcus aureus* enterotoxin C (SEC) was the cause for a series of 3 fatal cases of purpura fulminans associated with SA sepsis.[12]

The rhabdomyolysis diagnosis was based on the presence of intense myalgia and the increase of creatine phosphokinase to over 5 times the normal upper limit. Since there were no classic causal factors of rhabdomyolysis or of other triggering factors, we believe that the muscular damage was caused by the staphylococcal infection in the context of sepsis.[13,14] As far as we know, there are few published cases of rhabdomyolysis in patients with SA endocarditis and some of them presented similitudes with this case; in 2 cases, a child with severe myositis in a septic context and an adult with dermatomyositis-like syndrome, rhabdomyolysis (associated with cutaneous manifestations in the adult) constituted the inaugural symptom that preceded the apparition of endocardial vegetation.[15–17]

Sepsis is not a frequent cause of rhabdomyolysis: only few cases of staphylococcal sepsis associated with rhabdomyolysis have been reported in the literature.[18] The pathogenesis of staphylococcal role in rhabdomyolysis is complex. The invasive mechanism, with subsequent inducement of diffuse pyomyositis through direct muscular invasion, has been demonstrated through the isolation of the pathogen in the muscle tissue;[18] perimyositis can also be the initiating factor for rhabdomyolysis.[17] The toxemic mechanism through the implication of TSST during the toxic shock syndrome (TSS) is accepted, but was excluded in this case; there are reports that suggest the possibility of another nonsupurative toxemic mechanism, not mediated by TSST-1; a previous case of SEC-secreting MSSA sepsis associated rhabdomyolysis was reported in which, similarly, the patient presented purpura and embolic cerebral complications but without of endocardial determination.[12] In the absence of muscle biopsy, we consider pyomyositis as most likely, but we cannot fully exclude the involvement of one or more enterotoxins.

Concomitant diagnosis of purulent pericarditis with signs of cardiac tamponade with aortic endocarditis at only 48 hours after the negative initial echocardiographic evaluation was a particularity of this case.

SA pericarditis sometimes accompanies fulminant cases of fatal IE but is rarely the inaugural symptom. SA was the most frequently isolated pathogen in blood cultures and pericardial fluid in a group of 21 patients in which pericarditis was the revealing symptom of endocarditis; the aortic valve was mainly affected and 47% of the cases exhibited cardiac tamponade, similarly to the presented case.[19] Autopsies show a prevalence of 22% of purulent pericarditis in IE, superior to intravitam diagnosis and they also confirm the predominant involvement of the aortic valve;[20] forms of the disease with voluminous collections, similar to the present case, appear less frequently (2%) and they increase the risk of cardiac tamponade as the first symptom.[21]

The diagnosis of purulent staphylococcal pericarditis was based on the isolation of SA in purulent pericardial fluid. Theoretically, it could be caused by local propagation from the endocardial source or even caused by blood spread. The concomitant endocardial and pericardial determination, the small size of the vegetation, and the involvement of a native valve make the first mechanism unlikely; even in the absence of risk factors for SAB complications development (diabetes, human immunodeficiency virus infection or immunosuppressed conditions, renal insufficiency, alcoholism, and thoracic surgery), the context of persistent staphylococcal bacteremia, the presence of embolic manifestations, and voluminous pericardial collections suggest a blood-borne infection, as the risk factors in this case were the absence of a known infectious origin and community acquisition.[21–23]

On the other hand, the onset of pericardial empyema in the course of SAB in adults is rare in the absence of endocardial determination; only few cases have been reported, although SA became the prevailing etiological isolated agent of purulent pericarditis (36% of the total number of cases) during the postantibiotic era, and blood-borne dissemination is still a major pathogenic pathway.[23] Cardiac tamponade is extremely rarely diagnosed in the context of bacterial infections; in a series of 136 consecutive cases, only 5 patients had positive cultures out of which 2 were with SA and other 3 were diagnosed with infective endocarditis.[24]

Neurological complications appear in over 35% of patients with left valve SA-NVIE.[1] However, primary intracerebral hemorrhage is cited in only 1.8% to 2.4% of the total number of IE cases;[25,26] the occurrence of a hematoma is very rare as a consequence of IE or mycotic aneurysm rupture.[27]

We believe that in this patient the uncontrolled character of the infection, characterized by persistent fever and the coexistence of other septic complications (pericarditis, cutaneous lesions), represents, together with the acute, rapidly evolving cerebral hemorrhage arguments for its appearance as a result of septic embolization, followed by the rupture of the arterial wall; the

latter might be due to erosive arteritis,[28] as a consequence of the high incidence of systemic embolic events in SA-NVIE (54.9%).[1] It is worth noting the aspect described on the 1st computer tomography scan, in which disseminated hypodense lesions were suggestive for embolic infarcts.

In IE, the drastic decrease in the incidence of cerebral vascular complications after therapy evolves in parallel with the decrease in embolic events;[28] a cerebral hematoma that occurs after 9 days of treatment is unusual; and a stroke occurs before the endocarditis diagnosis in 72% to 85% of the cases uncontrolled infection could again explain the evolution in this case.[26,27,29]

The embolic mechanism frequently constitutes the cause of neurological complications in IE; furthermore, SA, especially MSSA strains, known for its virulent character, is an independent embolic risk factor.[30,31] In left-valve IE, SA is correlated with symptomatic cerebral embolic complications; the prevalence of central nervous system complications when the native valves were involved is 20% to 29%.[2,27]

The severity of this case was extreme; the fatal evolution is consistent with the reported lethality rate of 25.3% to 28.5% in SA-NVIE and 30% in MSSA IE.[1,2,4] The SA etiology increases the risk and/or severity of IE; the involvement of the aortic valve as well as persistent bacteremia were, together with systemic embolization and stroke, major mortality risk factors.[25,31] On the other hand, the succession of clinical events, the appearance of vegetation during preexistent sepsis and its stagnation at its small, initial dimensions, support SAB-associated sepsis as a determining factor of death; mortality through SAB sepsis increases significantly to 15% if it's associated with SA-IE, while sepsis per se is also a risk factor associated with hospital mortality in SA-NVIE.[1,32] Pericardial empyema, complicated by pericardial tamponade, is a factor that carries its own increased, independent, mortality risk; although statistical evidence is missing due to the rarity of the pathology, the mortality risk in purulent pericarditis is 40%, even in treated forms, and cardiac tamponade in itself is a life-threatening condition.[23] Although pericardiocentesis was not considered initially mandatory, and it was delayed as the patient was hemodynamically stable, we believe that performing it earlier could have benefited the treatment and the evolution of this complication.[33]

A possible reason for the lack of success in controlling the infection in this case is the use of vancomycin, which has been associated with a risk of failure in MSSA infections of 30% and with an increased mortality in MSSAB.[34,35] The susceptibility to vancomycin of the isolated strain does not explain the lack of infection control, since the tested minimum inhibitory concentration was inferior to the 1.5 mg/L threshold associated with MSSAB;[36] a recent meta-analysis has however revealed the limited influence this parameter has on the risk of death in SAB.[37] Its inclusion in the initial treatment was due to the relatively increased prevalence of MRSA infections in Romania, including CA strains.[38] The beta-lactam allergy and the development of renal failure lead to alternative antibiotic treatments (linezolid); the association of clindamycin to linezolid in the therapeutic regimen was considered an alternative option for treating the IE with MSSA, knowing that the strain was sensible and without inducible resistance (sensibility to erythromycin); although both of them are bacteriostatic, there is evidence of a potential antagonism when associated in SAB.[39] We still had to use them in the absence of a better option: injectable cotrimoxazole recommended in association with clindamycin was not available. The patient might have theoretically benefitted of betalactamine (oxacylin) desensitizing procedure; however, the clinical status deteriorated very rapidly and we considered the procedure to be too risky at the time when the etiologic diagnostic was established.[40]

A significant role of enterotoxins in the uncontrolled evolution of this sepsis is unlikely (with the possible exception of SEC involvement in cutaneous, muscular, and endocardial manifestations, due to the capacity to rapidly cause tissue destruction and abscesses).[12,41] Besides, published studies showed no statistically significant differences in the distribution of toxin encoding genes between community-SA strains involved in IE, and strains that determined uncomplicated SAB, and no association with IE mortality.[42,43] The dramatic evolution of this case prompts to the need of surveillance for high virulence MSSA strains that appear to combine extracellular toxins and/or virulence factors with a synergic effect, augmenting the pathogeny of the strains through an increase in adhesion, cellular invasion, and immune response avoidance capabilities.

We conclude that CA SAB remains a life-threatening condition and must be regarded as a medical emergency. Methicillin-susceptible strains may lead to fatal outcomes due to their high embolic risk. Lack of a known source for infection warrants increased vigilance.

Persistent fever during staphylococcal bacteremia is suggestive of septic complications and calls for a systematic echocardiographic screening.

The present case confirms the limited effectiveness of vancomycin in MSSA infections. The use of vancomycin in the empirical treatment of CA sepsis as a consequence of the increasing prevalence of MRSA strains may favor the risk of MSSA blood infections therapy failure. It is highly recommended to include an antistaphylococcal beta-lactam in the empirical treatment of both CA sepsis and MSSA bloodstream infections.

References

[1] Abdallah L, Remadi JP, Habib G, et al. Long-term prognosis of left-sided native-valve Staphylococcus aureus endocarditis. Arch Cardiovasc Dis 2016;109:260–7.

[2] Miro JM, Anguera I, Cabell CH, et al. Staphylococcus aureus native valve infective endocarditis: report of 566 episodes from the International Collaboration on Endocarditis Merged Database. Clin Infect Dis 2005;41:507–14.

[3] Campanile F, Bongiorno D, Falcone M, et al. Changing Italian nosocomial-community trends and heteroresistance in Staphylococcus aureus from bacteremia and endocarditis. Eur J Clin Microbiol Infect Dis 2012;31:739–45.

[4] Hill EE, Peetermans WE, Vanderschueren S, et al. Methicillin-resistant versus methicillin-sensitive Staphylococcus aureus infective endocarditis. Eur J Clin Microbiol Infect Dis 2008;27:445–50.

[5] Székely E, Man A, Mare A, et al. Molecular epidemiology and virulence factors of methicillin-resistant Staphylococcus aureus strains in a Romanian university hospital. Rev Romana Med Lab 2012;20:371–82.

[6] Jarraud S, Mougel C, Thioulouse J, et al. Relationship between Staphylococcus aureus genetic background, virulence factors, agr groups (alleles) and human disease. Infect Immun 2002;70:631–41.

[7] Fowler VGJr, Olsen MK, Corey GR, et al. Clinical identifiers of complicated Staphylococcus aureus bacteremia. Arch Intern Med 2003;163:2066–72.

[8] Hill EE, Vanderschueren S, Verhaegen J, et al. Risk factors for infective endocarditis and outcome of patients with Staphylococcus aureus bacteremia. Mayo Clin Proc 2007;82:1165–9.

[9] Kaech C, Elzi L, Sendi P, et al. Course and outcome of Staphylococcus aureus bacteraemia: a retrospective analysis of 308 episodes in a Swiss tertiary-care centre. Clin Microbiol Infect 2006;12:345–52.

[10] Castonguay MC, Burner KD, Edwards WD, et al. Surgical pathology of native valve endocarditis in 310 specimens from 287 patients (1985–2004). Cardiovasc Pathol 2013;22:19–27.

[11] Murdoch DR, Corey GR, Hoen B, et al. Clinical presentation, etiology, and outcome of infective endocarditis in the 21st century:

the International Collaboration on Endocarditis-Prospective Cohort Study. Arch Intern Med 2009;169:463–73.
[12] Kravitz GR, Dries DJ, Peterson ML, et al. Purpura fulminans due to Staphylococcus aureus. Clin Infect Dis 2005;40:941–7.
[13] Singer M, Deutschman CS, Seymour CW, et al. The third international consensus definitions for sepsis and septic shock (Sepsis-3). JAMA 2016;315:801–10.
[14] Copotoiu SM, Copotoiu R. Much ado about the new definitions of sepsis. J Crit Care Med 2016;2:67–72.
[15] Ravry C, Fedou AL, Dubos M, et al. Severe rhabdomyolysis associated with Staphylococcus aureus acute endocarditis requiring surgery. Surg Infect (Larchmt) 2015;16:840–2.
[16] Bandi S, Chikermane A. Rhabdomyolysis in a child secondary to staphylococcus aureus endocarditis. J Glob Infect Dis 2009;1:146–8.
[17] Ojeda J, López-López L, González A, et al. Infective endocarditis initially presenting with a dermatomyositis-like syndrome. BMJ Case Rep 2014; pii: bcr2013200865. doi: 10.1136/bcr-2013-200865.
[18] Lannigam R, Austin TW, Vestrup J. Myositis and rhabdomyolysis due to Staphylococcus aureus septicemia. J Infect Dis 1984;150:784.
[19] Katz LH, Pitlik S, Porat E, et al. Pericarditis as a presenting sign of infective endocarditis: two case reports and review of the literature. Scand J Infect Dis 2008;40:785–91.
[20] Fernández Guerrero ML, Álvarez B, Manzarbeitia F, et al. Infective endocarditis at autopsy: a review of pathologic manifestations and clinical correlates. Medicine (Baltimore) 2012;91:152–64.
[21] Regueiro A, Falces C, Cervera C, et al. Risk factors for pericardial effusion in native valve infective endocarditis and its influence on outcome. Am J Cardiol 2013;112:1646–51.
[22] Fortuin-de Smidt MC, Singh-Moodley A, Badat R, et al. Staphylococcus aureus bacteraemia in Gauteng academic hospitals, South Africa. Int J Infect Dis 2015;30:41–8.
[23] Parikh SV, Memon N, Echols M, et al. Purulent pericarditis: report of 2 cases and review of the literature. Medicine (Baltimore) 2009;88:52–65.
[24] Sánchez-Enrique C, Nuñez-Gil IJ, Viana-Tejedor A, et al. Cause and long-term outcome of cardiac tamponade. Am J Cardiol 2016;117: 664–9.
[25] González-Melchor L, Kimura-Hayama E, Díaz-Zamudio M, et al. In-hospital mortality risk factors for patients with cerebral vascular events in infectious endocarditis. A correlative study of clinical, echocardiographic, microbiologic and neuroimaging findings. Arch Cardiol Mex 2015;85:195–200.
[26] Thuny F, Avierinos JF, Tribouilloy C, et al. Impact of cerebrovascular complications on mortality and neurologic outcome during infective endocarditis: a prospective multicentre study. Eur Heart J 2007;28: 1155–61.
[27] Snygg-Martin U, Gustafsson L, Rosengren L, et al. Cerebrovascular complications in patients with left-sided infective endocarditis are common: a prospective study using magnetic resonance imaging and neurochemical brain damage markers. Clin Infect Dis 2008;47:23–30.
[28] Aziz F, Perwaiz S, Penupolu S, et al. Intracranial hemorrhage in infective endocarditis: a case report. J Thorac Dis 2011;3:134–7.
[29] Goulenok T, Klein I, Mazighi M, et al. Infective endocarditis with symptomatic cerebral complications: contribution of cerebral magnetic resonance imaging. Cerebrovasc Dis 2013;35:327–36.
[30] Thuny F, Di Salvo G, Belliard O, et al. Risk of embolism and death in infective endocarditis: prognostic value of echocardiography: a prospective multicenter study. Circulation 2005;112:69–75.
[31] Fowler VGJr, Miro JM, Hoen B, et al. Staphylococcus aureus endocarditis: a consequence of medical progress. JAMA 2005;293: 3012–21.
[32] Fowler VGJr, Li J, Corey GR, et al. Role of echocardiography in evaluation of patients with Staphylococcus aureus bacteremia: experience in 103 patients. J Am Coll Cardiol 1997;30:1072–8.
[33] Charron P, Adler Y. 'Ten Commandments' of 2015 ESC Guidelines for diagnosis and management of pericardial diseases. Eur Heart J 2015;36: 2874.
[34] Murray RJ. Staphylococcus aureus infective endocarditis: diagnosis and management guidelines. Intern Med J 2005;35(Suppl 2):S25–44.
[35] Kim SH, Kim KH, Kim HB, et al. Outcome of vancomycin treatment in patients with methicillin-susceptible Staphylococcus aureus bacteremia. Antimicrob Agents Chemother 2008;52:192–7.
[36] Holmes NE, Turnidge JD, Munckhof WJ, et al. Antibiotic choice may not explain poorer outcomes in patients with Staphylococcus aureus bacteremia and high vancomycin minimum inhibitory concentrations. J Infect Dis 2011;204:340–7.
[37] Kalil AC, Van Schooneveld TC, Fey PD, et al. Association between vancomycin minimum inhibitory concentration and mortality among patients with Staphylococcus aureus bloodstream infections: a systematic review and meta-analysis. JAMA 2014;312:1552–64.
[38] European Centre for Diseases Prevention and Control. Antimicrobial resistance surveillance in Europe 2014. Stockholm ECDC 2015; doi 10.2900/23549.
[39] Soriano A, Jurado A, Marco F, et al. In vitro activity of linezolid, moxifloxacin, levofloxacin, clindamycin and rifampin, alone and in combination, against Staphylococcus aureus and Staphylococcus epidermidis. Rev Esp Quimioter 2005;18:168–72.
[40] Habib G, Lancellotti P, Antunes MJ, et al. 2015 ESC Guidelines for the management of infective endocarditis: The Task Force for the Management of Infective Endocarditis of the European Society of Cardiology (ESC). Endorsed by: European Association for Cardio-Thoracic Surgery (EACTS), the European Association of Nuclear Medicine (EANM). Eur Heart J 2015;36:3075–128.
[41] Salgado-Pabón W, Breshears L, Spaulding AR, et al. Superantigens are critical for Staphylococcus aureus Infective endocarditis, sepsis, and acute kidney injury. MBio 2013;4: pii: e00494-13. doi: 10.1128/mBio. 00494-13.
[42] Chi CY, Wang SM, Lin CC, et al. Microbiological characteristics of community-associated Staphylococcus aureus causing uncomplicated bacteremia and infective endocarditis. J Clin Microbiol 2010;48:292–4.
[43] Chung JW, Karau MJ, Greenwood-Quaintance KE, et al. Superantigen profiling of Staphylococcus aureus infective endocarditis isolates. Diagn Microbiol Infect Dis 2014;79:119–24.