

1 Urothelial Carcinoma Associated with Infective Endocarditis Due 2 to a *Leuconostoc* Species: A Rare Presentation

3 A.Drighil M.D

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6 Abstract

7 Introduction-Infective endocarditis (IE) is commonly caused by the hematogenous spread of
8 various microorganisms that target the endocardium with staphylococci and streptococci
9 accounting for the majority of cases. Due to the multitude of bacterial and even fungal
10 pathogens, treatment options should be targeted specifically against microorganisms that are
11 isolated in blood cultures. If an empiric antibiotic therapy is warranted, first-line treatment
12 usually targets methicillin susceptible and resistant staphylococci, streptococci, and
13 enterococci. Although there is an important caveat, clinicians must consider when using
14 vancomycin antibiotic therapy. *Leuconostoc* is a genus of gram-positive bacteria, placed within
15 the family of Lactobacillaceae, this type of bacteria, which can be found in green vegetables
16 and are used in wine, cheese, and sugar production, is an uncommon cause of disease in human
17 beings(1); these microorganisms have only recently been recognized as a potential cause of
18 infection in a variety of patient populations(2) GJMR-I Classification: NLMC Code: WP 460

20 *Index terms—*

21 1 Introduction

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24 of bacterial and even fungal pathogens, treatment options should be targeted specifically against microorganisms
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28 *Leuconostoc* is a genus of gram-positive bacteria, placed within the family of Lacto-bacillaceae, this type of
29 bacteria, which can be found in green vegetables and are used in wine, cheese, and sugar production, is an
30 uncommon cause of disease in human beings(1); these microorganisms have only recently been recognized as a
31 potential cause of infection in a variety of patient populations(2) II.

32 2 Case Report

33 We report the case of a 60 years old male, with a medical history of nasopharyngeal carcinoma 26 years ago
34 treated by chemotherapy and radiotherapy complicated with hypothyroidism under levothyroxine, our patient
35 was diagnosed with a right renal urothelial carcinoma (UC) 2 years ago that was treated with surgery, an end
36 stage kidney failure undergoing dialysis twice a week using a tunneled central venous catheter that was placed 3
37 years ago and a deafness caused by an operated cholesteatoma.

38 Author ? : e-mail: saraabouradi17@gmail.com

39 The patient was admitted in the cardiology department for significant weight loss associated to nausea,
40 vomiting, dyspnea, total hematuria and episodic fever (39°C) for the last 2 months. The medical examination
41 revealed a conscious patient with a blood pressure of 100/64 mmHg, heart rate of 113bpm, temperature of 38.5
42 C, respiratory rate of 18cpm, and oxygen saturation of 97% on room air. The cardiovascular examination found
43 a grade IV/VI systolic and diastolic murmurs, no Janeway lesions or Osler nodes were found.

4 DISCUSSION

44 Complete blood count found an anemia with a hemoglobin rate at 5g/dl, white blood cell count (WBC) at
45 18,000/ ml, C-reactive protein (CRP) elevated at 104 mg/dl, Procalcitonin at 1, erythrocyte sedimentation rate
46 (ESR) was 48 mm, creatinine (Cr) 40.6 mg/dl, with a GFR of 15 ml / min / m²; a positive rheumatoid factor,
47 hypothyroidism with a pituitary thyroid stimulating hormone at 100mUI/l.

48 The EKG showed an incomplete left bundle branch block with no anginal symptoms, transthoracic echocar-
49 diography (TTE) showed a mitral valve with calcified leaflets, moderate mitral regurgitation (Fig. ??), severe
50 mitral stenosis with a valve area of 1.5cm², and a mobile vegetation measuring 14x6 mm on A2 part of the
51 anterior mitral valve (Fig 2 and 3). We also observed a tricuspid aortic valve with calcified leaflets and reduced
52 cusp separation, moderate aortic regurgitation, moderate aortic stenosis with a valve area of 1.2 cm². The left
53 ventricular size was within normal limits and the left ventricular ejection fraction was 63%. Transoesophageal
54 echocardiography (TEE) showed a 16x8 mm mitral vegetation. An empirical antibiotic therapy was initiated
55 after the collection of recipient blood samples for culturing.

56 *Leuconostoc* species grew in 2 out of 2 blood cultures. Antibiotic treatment was adapted to the antibiogram
57 with ceftriaxone and gentamicin. A cranial and Thoracoabdomino pelvic scan were realized and revealed an
58 occipital ischemic injury, bilateral mild pleural effusion, metastatic damage to the liver, bladder tumor occupying
59 all the lumen measuring 59x56x49mm and a mild peritoneal effusion.

60 Considering the results of imaging studies, clinical findings and blood tests, a diagnosis of infective endocarditis
61 due to *Leuconostoc* spp was established. When dealing with IE caused by *Leuconostoc*, vancomycin is not a suitable
62 option for treatment. *Leuconostoc* is catalase-negative, produces lactic acid, and is characterized by its intrinsic
63 and chromosomal resistance to vancomycin. (2,3,4). It was previously believed that this bacterial species was non-
64 pathogenic in nature until recently published reports revealed the infectious potential of the *Leuconostoc* species
65 in many patient populations (5,6).

66 The patient received intravenous antibiotic therapy consisting of ceftriaxone 2g and gentamicin adapted to
67 renal function.

68 The Nephrology team was consulted to assist in the management of the patient's chronic kidney disease.
69 Throughout the patient's hospitalization, his tunneled central venous catheter was removed and the patient
70 received a transfusion of 4 blood bags per dialysis because of his severe anemia with a control of hemoglobin at
71 9.5g/dl.

72 During his hospitalization, the patient had a transurethral endoscopic bladder resection of his mass that
73 revealed a secondary extension of his primary renal cancer.

74 Other departments took part in the management of our patient, endocrinology with the adaptation of doses
75 of L-thyroxin and Oncology team who pronounced that his cancer is in a late stage and decided for a palliative
76 chemotherapy after treatment of his actual endocarditis.

77 2 months after his discharge from cardiology department, a palliative chemotherapy was decided by oncologists
78 but the patient died from a severe hematuria before starting his chemotherapy.

3 III.

4 Discussion

81 This case reports a story of a cancer patient afflicted by a complicated course of infective endocarditis with
82 an uncommon organism: *Leuconostoc* spp. What had initially been described as a nagging headache, quickly
83 developed into what we now know to be *Leuconostoc* species bacteremia from seeded aortic valves. In evaluating
84 what may have led to this patient's eventual clinical course, it is imperative to note all predisposing factors. Our
85 patient had a history of nasopharyngeal cancer, a renal carcinoma and a chronic renal failure undergoing dialysis
86 with a persistent central venous catheter that was never changed and kept over 3 years, all of those factors had
87 placed our patient at an extremely elevated risk for infective endocarditis. This case is interesting because the
88 pathogenic bacterial species for IE are typically staphylococci and streptococci, not *Leuconostoc* species. (1) Until
89 1985, *Leuconostoc* were known as "nonpathogenic to plants and animals". However, due to continued reports
90 of different infections, they are currently recognized as opportunistic pathogens affecting patients with a wide
91 spectrum of underlying diseases; Still the portal of entry remains uncertain. One possibility is their introduction
92 into the blood stream during catheter implantation, which could explain the case of our patient, another portal
93 of entry is the gastrointestinal tract due to the natural habitat of *Leuconostoc* in food, which would explain the
94 association with underlying gastrointestinal disease and frequent gastrointestinal symptoms. (7) *Leuconostoc* is
95 a genus of Gram-positive, catalase and oxidase negative, chain forming ovoid cocci placed within the family of
96 *Leuconostocaceae* (1,5,8). This bacterial species was thought to be nonpathogenic until recently published reports
97 have revealed their infectious potential in immunocompromised and severely ill patients. IE with *Leuconostoc*
98 species can be troubling considering they are hetero-fermentative and potentially "slime" (dextran and sucrose
99 producing) forming. (9,10).

100 High-level resistance to vancomycin is nearly a constant in *Leuconostoc* species. Reports suggest the
101 involvement of a chromosomal factor, which leads to a change in the end of a pentapeptide in the cell wall. This
102 vancomycin binding site usually ends in alanine-alanine, but in *Leuconostoc* species it ends in alanine-lactate.
103 Another possibility, as in *Enterococci*, is the production of a new membrane protein codified by plasmids (11).

104 Concerning treatment, multiple studies showed that the complete elimination of most bacterial pathogens of

105 endocarditis needs two to four weeks of monotherapy, so we opted to treat our patient for six weeks following the
106 American Heart Association (AHA) guidelines for treatment of penicillin-resistant bacteria in a high-risk patient
107 (12,15). Additionally, the AHA advises that daptomycin alone is not effective against multidrug resistant IE
108 and should be used in combination with other agents (12). Upon further review of the available literature
109 on *Leuconostoc* species infection, several studies listed daptomycin as an effective treatment for *Leuconostoc*-
110 associated bacteremia (13). Considering our patient had an uncommon bacteria and an aortic valve vegetation, we
111 pursued a full six-week course of an intravenous antibiotic therapy. As published reports do show effective therapy
112 of penicillin-resistant group viridians streptococci with combination therapy, typically ceftriaxone or penicillin
113 with gentamycin (14,15), our team opted for empiric treatment with ceftriaxone associated to gentamycine.

114 5 IV.

115 6 Conclusion

116 Infective endocarditis can prove to be a threatening disease when left untreated also if caused by a new organism.
117 It is critical for clinicians to be aware of the many pathogenic organisms, including *Leuconostoc* species, and
118 appropriate management strategies in order to avoid different complications that may ensue. It is also clear that
119 a higher index of suspicion must be maintained in patients with multiple predisposing factors such as the patient
in the case presented. ¹

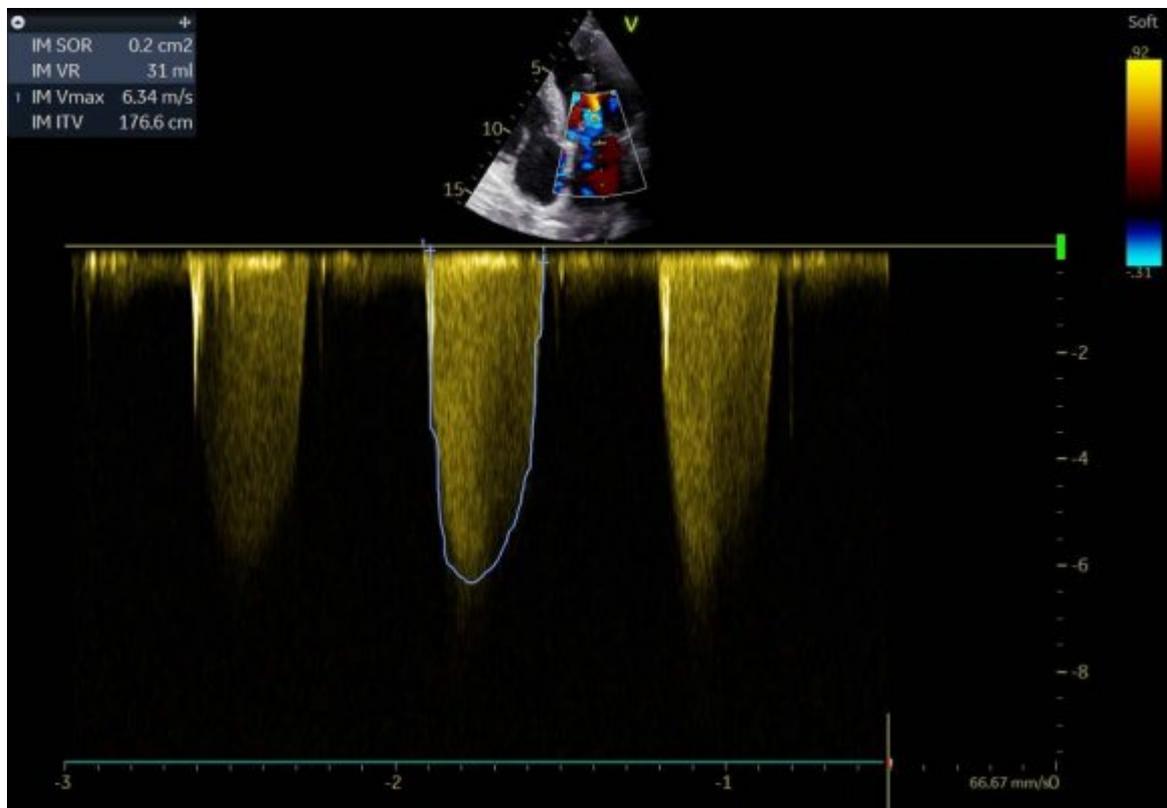


Figure 1: I

120



Figure 2: Figure 1 :Figure 2 :I



Figure 3: Figure 3 :I

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