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Graft infection after a Bentall procedure: A case series and systematic review of the literature

I. Machelart [a], C. Greib [a], G. Wirth [b], F. Camou [c], N. Issa [c], J.F. Viallard [a], J.L. Pellegrin [a], E. Lazaro [a]

[a] Department of Internal Medicine and Infectious Diseases, Haut-Lévêque Hospital, Pessac, France
[b] Department of Infectious Diseases, Pellegrin Hospital, Bordeaux, France
[c] Medical Intensive Care Unit, Saint André Hospital, Bordeaux, France

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ABSTRACT

Introduction: The Bentall procedure is a cardiac surgery involving graft replacement of the aortic valve, aortic root and ascending aorta. Graft infection after Bentall's procedure (BGI) is infrequent but severe, and often difficult to diagnose and treat.
Patients and Methods: A retrospective cohort study was performed using the Bordeaux endocarditis database of adult patients admitted to the Bordeaux University Medical Hospital for BGI between 2008 and 2014. Published case reports were identified in the literature.
Results: We identified 10 BGI patients in the database and 13 in the literature. The majority of infections were late-onset (20/23) and occurred as a result of gram positive cocci bacterial infection (16/22). Detailed diagnoses of the described BGI were determined using echocardiography, computed tomography (CT) and positron emission tomography/CT (PET/CT). Labeled-leukocyte scintigraphy was not reported in any case. Prolonged antibiotic therapy and surgery were found to be the treatment of choice for BGI; however it was not always possible to perform a surgical intervention. Clinical relapses occurred even with a negative PET/CT, while PET/CT consistently positive for BGI occurred in the absence of clinical relapse. This suggests that the use of PET/CT for follow-up is questionable.
Conclusion: Diagnosis of BGI is difficult, due to the combination of clinical, biological, and radiological observations obtained through transesophageal echocardiography and CT. PET/CT is an alternative method to diagnosis BGI, but its impact on clinical management remains unclear. Current data suggests that if surgical replacement of the prosthesis is not possible, patients should be treated with prolonged antibiotic therapy.

1. Introduction

A Bentall procedure is a cardiac surgery involving composite graft replacement of the aortic valve, aortic root and ascending aorta, and a reimplantation of the coronary arteries into the graft (Bentall and De Bono, 1968). This surgery is indicated for a large spectrum of pathological conditions involving aortic regurgitation, Marfan's syndrome, aortic dissection, and aortic aneurysm. This procedure is complicated by infection in 1.4% of cases (Joo et al., 2012).

Data are lacking regarding the diagnostic strategy and treatment of graft infection after a Bentall procedure (BGI). In this article, we consider 23 cases including a case series of 10 patients managed in our institution and 13 published cases, to determine an improved process of diagnosis and treatment for BGI.

2. Methods

2.1. Patients

A retrospective study was performed using all adult patients admitted to the Bordeaux University Medical Hospital for BGI between 2008 and 2014 as recorded in the Bordeaux endocarditis database accredited by the French national data protection commission (CNIL number: 2,009,020). Epidemiological, and clinical characteristics, as well as outcomes, were recorded for each patient.

2.2. Literature analysis

Published case reports were identified in a Medline search of literature reported in the English-language from the years 1968–2016. The following keywords were used: vascular graft infection (VGI), Bentall procedure, and endocarditis.

2.3. Definitions

BGI was defined by VGI and/or aortic endocarditis, according to specific criteria proposed by Fitzgerald et al. (FitzGerald et al., 2005). VGI was diagnosed in a patient if at least 2 of the 3 following criteria were present: (i) clinical signs of infection (fever, chills, septic shock); (ii) positive bacterial culture or bacterial polymerase chain reaction (PCR) of intraoperative specimens or blood samples; (iii) biological signs of infection (C-reactive protein >10 mg/L, white blood count >10 G/L) or

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other radiological signs of infection diagnosed by computed tomography (CT), echocardiography or positron emission tomography/CT (PET/CT). A diagnosis of associated endocarditis was made according to the modified Duke criteria that include the confirmation of the presence of microorganisms and specific echocardiographic observations, as previously described (Durack et al., 1994). Each case of VGI was classified either as early-onset infection (occurring within 4 months after surgery) or late-onset infection (occurring more than 4 months after surgery). As 4 months is considered the gold standard for onset of VGI, and corresponds to the timeframe during which both VGI and IE are classified as early-onset, it was selected as the threshold between early and late infection.

3. Results

3.1. Characteristics of BGI cases

Ten patients with BGI were identified over a 7-year period from our institutional database and included both early ($n = 1$) and late-onset ($n = 9$) cases with a median follow-up time from diagnosis of 30.5 months [interquartile range (IQR) 18–46 months]. The main clinical and biological characteristics are described in Table 1.

The median age at diagnosis of BGI was 74 years (IQR 69–76.5 years) and 90% were male. The valvular prosthesis was a bioprosthesis in 7 cases. Half of the patients had risk factors for infection: diabetes mellitus ($n = 2$), neutropenia ($n = 1$), immunodepression defined by steroid therapy >7.5 mg/day and/or immunosuppressive treatments ($n = 2$). Most of the patients had numerous comorbidities: medical history of cardiovascular disease independent from the Bentall intervention ($n = 5$), at least 2 risk factors for cardiovascular disease ($n = 3$), and medical history of cancer ($n = 2$). The mean values of white blood cell count and C-reactive protein were 8.9 ± 3.3 G/L and 88.6 ± 70.2 mg/L, respectively.

At admission, clinical signs suggesting an infectious process involving the prosthetic vascular graft were fever >38 °C ($n = 10$) and general deterioration ($n = 4$). Presentation of clinical complications was frequent: septic emboli (splenic ($n = 2$), cerebral ($n = 1$)), spondylodiscitis ($n = 2$), abscess ($n = 2$), left ventricular fistulae ($n = 2$), rupture of a cerebral mycotic aneurysm ($n = 1$), and transient ischemic attack ($n = 1$). These complications were present at admission with the exception of one patient who presented spondylodiscitis and rupture of a cerebral mycotic aneurysm during follow-up.

3.2. Relationship between radiological imaging and BGI diagnosis

Of 10 patients, 9 underwent both transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE). TTE was normal in all cases with the exception of 2, in which a potential abscess was visualized. TEE was abnormal in 7 cases, with isolated signs of aortic endocarditis in 5 cases. The specific details included vegetations ($n = 3$), abscesses on the valvular prosthesis ($n = 2$) and both signs of endocarditis and vascular prosthesis infection ($n = 2$). Of the 8 cases that used CT, only 3 showed radiological signs of infection. PET combined with CT (PET/CT) was performed in 7 cases and showed signs for BGI in each patient. Presentation of endocarditis in these 7 patients was the following: only endocarditis ($n = 2$) or endocarditis and VGI ($n = 5$). From the same 7 cases, results of TEE or CT suggested BGI except for one patient. PET/CT showed an abnormal uptake on the valvular prosthesis and/or on the vascular prosthesis with a mean standardized uptake value (SUV) maximum of 4.5 (IQR 4–6.6). Labeled-leukocyte scintigraphy was not performed in any of the patients. Taken together, TTE, TEE, CT and/or PET/CT are able to diagnose BGI to varying degrees, since analysis of the scans showed positive signs of endocarditis ($n = 2$), VGI ($n = 1$), or both endocarditis and VGI ($n = 7$) (Table 2).

3.3. Analysis of microbiological data, treatment, and outcomes

As summarized in Table 3, microbiological data was obtained for 9 patients, and a total of 12 causative microorganisms were isolated from blood culture ($n = 7$) or by PCR ($n = 2$): *Methicillin-resistant Staphylococcus epidermidis* (MRSE, $n = 2$), *Methicillin-sensitive Staphylococcus epidermidis* (MSSE, $n = 2$), *Streptococcus agalactiae* ($n = 1$), *Enterococcus faecalis* ($n = 1$), *Streptococcus sanguinis* ($n = 1$), *Candida parapsilosis* ($n = 1$), *Achromobacter species* ($n = 1$), *Serratia marcescens* ($n = 1$), *Bartonella quintana* ($n = 1$) and *Coxiella burnetii* ($n = 1$). Seven patients had concomitant bacteremia, while one patient had a polymicrobial infection involving MRSE, *Candida parapsilosis, Achromobacter species,* and *Serratia marcescens*. In 3 cases, the bacterial port-of-entry was identified: the *Streptococcus agalactiae* infection was of dental origin; the polymicrobial infection occurred at the surgical site; and the *Enterococcus faecalis* infection was of digestive origin.

All patients were treated with antibiotics, according to the causative organism and antibiotic sensitivity. The median duration of treatment was 7 months (IQR 5–13.5 months), including a median intravenous therapy duration of 2 weeks (IQR 0.7–7 weeks). Two patients underwent surgery 2 days and 28 days after BGI diagnosis to complete the Bentall procedure and valvular bioprosthesis replacement, and drainage of an abscess, respectively. Among the 6 patients who received complete antibiotic therapy, the mean duration was 10.5 months. Over the course of the entire follow-up period, 2 patients died. One death was a result of hemorrhagic stroke after 6 weeks of treatment while magnetic resonance angiography did not show evidence of mycotic aneurysm. The other death was a result of an uncontrolled systemic polymicrobial infection with septic emboli and mycotic aneurysms after 18 months of antibiotic treatment. Neither patient underwent surgical intervention. Contact with one patient who started antibiotic treatment was lost during follow-up. One patient has received antibiotic treatment for 6 months for *Coxiella burnetii* BGI, and continues to receive treatment. Of the 6 patients with a mean post-treatment follow up >2 years, remission of infection was observed in 4 patients. This occurred after a median duration of antibiotic treatment of 7 (5.4–8.6) months, during which time one patient underwent surgery. The patients that went into

Table 1
Clinical characteristics of the BGI patients.

	Age	Gender	Type of valvular prosthesis	Definite VGI	Definite endocarditis	White blood cell count (G/L)	CRP (mg/L)	Time to infection	Follow-up (months)
Patient 1	79	F	Bioprothesis	Yes	Yes	13.1	204	3 years	48
Patient 2	59	M	Mechanical	Yes	Yes	2.2	11	6 years	30.5
Patient 3	57	M	Mechanical	Yes	No	8.46	13	5 days	18
Patient 4	74	M	Bioprothesis	Yes	Yes	5.03	29	2 years	1.5
Patient 5	72	M	Mechanical	Yes	Yes	9.8	130	9 years	46
Patient 6	74	M	Bioprothesis	No	Yes	9.35	167	3 years	Lost
Patient 7	68	M	Bioprothesis	Yes	Yes	7.9	110	1 years	39
Patient 8	80	M	Bioprothesis	Yes	Yes	11.2	80	3 years	68
Patient 9	77	M	Bioprothesis	Yes	Yes	12.31	129	8 years	22
Patient 10	75	M	Bioprothesis	No	Yes	9.84	13	2 years	4

F = Female; M = Male; G/L = Giga/Liter; CRP = C-reactive-protein; mg/mL = milligram/milliliter.