Echocardiographic findings in patent ductus arteriosus-associated infective endarteritis

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Abstract

Objective: Infectious endarteritis associated with patent ductus arteriosus (PDA-IE) is an uncommon complication in the era of antibiotics. However, it implies a clinical challenge in patients with a fever of undetermined origin. Two-dimensional transthoracic echocardiography (TTE) plays a fundamental role in diagnosis and follow-up.

Methods: A retrospective analysis of the data of all patients admitted to our center with PDA-IE within 15 years was conducted, and a review of the literature regarding diagnosis, TTE findings, and treatment was performed.

Results: A total of 17 patients were identified with a mean age of 17.8 years. TTE done in all patients confirmed the diagnosis of PDA and pulmonary artery vegetation. In five patients, one vegetation was present; in three patients, two vegetations were found; and in the nine remaining patients, three or more vegetations were observed. In two-thirds of the patients, the size of the vegetation was three to 28 mm, and the principal morphology was filiform. In all patients, at least one vegetation developed on the lateral wall of the ductus arteriosus. Pulmonary valve was affected in 41% of the patients and caused low to moderate valvular regurgitation. Pulmonary embolism was present in seven patients and pulmonary aneurysm in one patient.

Conclusion: The incidence of PDA-IE has decreased in the recent years with early antibiotic therapy. However, today, this complication carries a significant risk of valve damage and other cardiac structures' involvement.

Keywords: patent ductus arteriosus, endarteritis, echocardiography, congenital heart disease

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Introduction

The first patent ductus arteriosus (PDA) cases with infective endarteritis (IE) were described by Chevers in 1945 (1). This malformation is the consequence of a lack of closure of the ductus arteriosus (DA) after birth and is characterized by a tubular structure that connects the proximal part of the left pulmonary artery to the descending aorta. The incidence of term newborn infants having PDA is 1/2,000. IE of the DA is a complication of PDA; furthermore, there is a risk of other complications such as septic pulmonary embolisms (PEm) and mycotic aneurysms in pulmonary arteries (PAn). The advent of echocardiography allowed for timely diagnosis through a noninvasive register. In 1985, Vargas-Barron et al. (2) reported the echocardiographic diagnosis of patent ductus arteriosus-associated infective endarteritis (PDA-IE) for the first time. Although antibiotics early, prophylaxis, and less delay in the diagnosis have caused a decrease in PDA-IE, the diagnosis and treatment are still challenging. This study aimed to show the echocardiographic characteristics, clinical association, diagnostic methods, clinical evolution, and complications in patients with PDA-IE and the literature review.

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HIGHLIGHTS

- Infectious endarteritis associated with patent ductus arteriosus is an uncommon complication in the era of antibiotics.
- In the majority of patients, the vegetation developed on the lateral wall of the ductus arteriosus.
- The pulmonary valve was affected in 41% of the patients and caused low to moderate valvular regurgitation.

Methods

The clinical records of 17 patients of various ages and sex diagnosed with PDA-IE with or without associated valvular malformations between January 2005 and December 2020 were retrospectively analyzed. Patients with other associated congenital heart diseases were excluded.

The images recorded from the two-dimensional (2D) transthoracic echocardiogram (TTE) or three-dimensional (3D) transesophageal echocardiogram (TEE) were reviewed upon the admission of the patient; the echocardiograms were performed with a Phillips IE-33, with PureWave cardiac transducer sector S5-1 (1–5 MHz) and transesophageal probe in 4D X7-2t (2–7 MHz) or pediatric transesophageal probe TEE S7-3t (3–7 MHz). A bibliographic search was carried out on diagnosis, echocardiographic findings, and treatment in patients with PDA-IE.

Results

The patients included 12 women and five men aged between 9 and 38 (mean 17.8) years. All admitted patients presented with fever, two presented with dyspnea, and one patient presented with heart failure. On physical examination, a continuous systolic murmur in the second left intercostal space was found in all patients (none with silent PDA). Four patients had cardiovascular defects, three patients had subaortic stenosis, and one patient had aortic coarctation. TTE was performed in all patients; in six, it was complemented with a TEE. In nine patients, cardiac computed tomography (CT) was done, and two cardiac magnetic resonance (MRI) images were used. The blood culture outcomes and the presence of complications are described in Table 1.

TTE done in 17 patients confirmed the diagnosis of PDA and PA vegetation (Videos 1–4); the median PDA diameter in all patients was 1.7 mm (0.9–4.0 mm). In five patients, one vegetation was present; in three patients, two vegetations were found; and in the remaining nine patients, three or more vegetations were observed (Fig. 1, Table 1). In two-thirds of the patients, the

Table 1. Clinical characteristics of patients with PDA-IE at National Institute of Cardiology from 2005 to 2020

#	Sex	Age (years)	PA Veg	Associated Defects	Diagnostic Method	Valvular endocarditis	PAn	PEm	Blood culture	Treatment	Evolution
1	M	9	1		TTE	–	–	–	*Diphtheroids sp.*	Ligature	U/E
2	F	10	1	–	TTE	–	–	–	–	Ligature	U/E
3	F	16	1	–	TTE	–	–	Yes	–	Ligature	U/E
4	M	11	Several	AoCo	TTE	–	Yes	No	*S. aureus*	OHS	U/E
5	F	9	2	SubAoS	TTE/TEE	AoV	No	No	–	OHS	U/E
6	F	14	2	–	TTE/TEE/CT	PV	No	Yes	*St. viridans*	OHS	U/E
7	F	15	2	Sub AoS	ETT	AoV	No	No	–	OHS	U/E
8	F	16	Several	–	ETT	PV	No	No	–	OHS	U/E
9	M	21	2	–	TTE/CT/MRI	PV	No	No	*St. mitis*	OHS	U/E
10	F	19	Several	–	TTE/CT	PV	No	Yes	*St. salivarius*	OHS	U/E
11	F	38	Several	Sub AoS	TTE/TEE/CT/ MRI	AoV, PV	No	No	*St. viridans*	OHS	Decease
12	M	26	1	–	TTE/TEE/MRI	–	No	No	*St. mitis*	OHS	U/E
13	F	23	2	–	TTE/CT	PV	No	Yes	*St. viridans*	OHS	U/E
14	M	14	1	–	TTE/TEE/CT/ MRI	–	No	No	*St. viridans*	OHS	U/E
15	M	33	Several	–	TTE/CT	AoV	No	Yes	–	OHS	U/E
16	M	16	1	–	TTE/CT	–	No	Yes	*St. mutans*	Amplatzer	U/E
17	M	14	Several	–	TTE/TEE/CT	PV	No	Yes	*St. viridans*	OHS	U/E

AoV - aortic valve; CT - computed tomography; F – female; M – male; MRI - magnetic resonance imaging; OHS – open-heart surgery; PA - pulmonary artery; PAn - pulmonary aneurysm; PEm - pulmonary embolism; PV - pulmonary valve; S - Staphylococcus; Sp - species; St - Streptococcus; Sub AoS - subaortic stenosis; TEE - transesophageal echocardiogram; TTE - transthoracic echocardiogram; U/E – uneventful; Veg - vegetations

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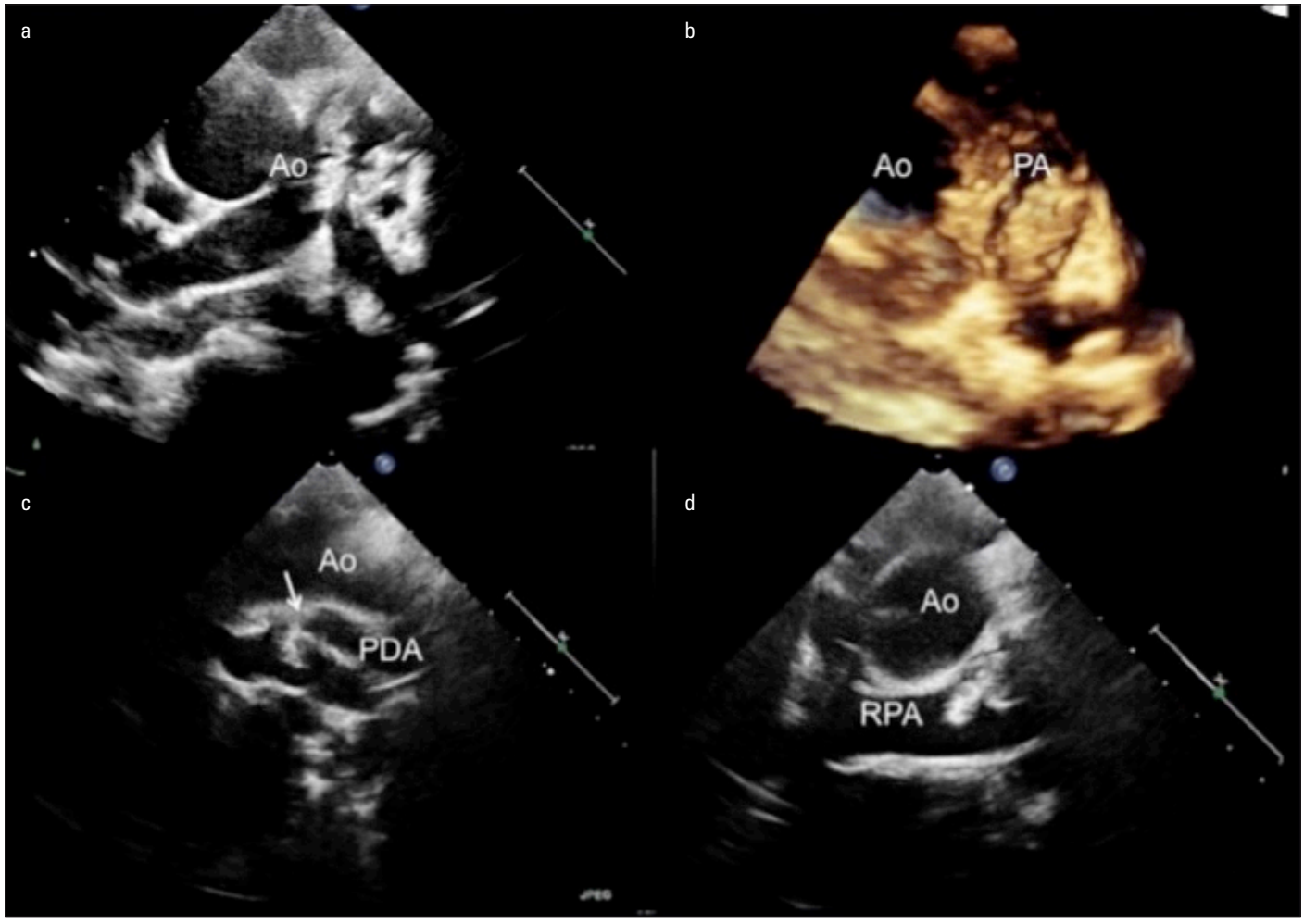

Figure 1. Transthoracic echocardiography images of a patient with infectious endarteritis associated with patent ductus arteriosus (PDA-IE), demonstrating multiple vegetations. A parasternal short-axis view shows two large vegetations in the valve and pulmonary trunk (a, b). The suprasternal axis view shows a large PDA (arrow) with vegetation (c, d)

vegetation size was 3–28 mm, and the prime morphology was filiform. In the remaining patients, the principal and minor diameters were similar. In all patients, at least one vegetation developed on the lateral wall of the DA (Fig. 1). In seven (41%) of the 17 patients, fragmentation of the vegetation led to septic PEm; in three patients, the embolism was caused by the whole vegetation. The size of the ductus did not determine the increase in pulmonary pressure nor was it related to the development of PEm. In one patient, the echocardiogram showed the development of PAn in the anterior wall, which initially developed on the site of the infectious vegetation implant. In nine patients, cardiac CT was performed; and in four cardiac patients, MRI was performed. The image studies helped establish the DA's size, infectious vegetations in the PA, and the cardiac valves (Table 1). Furthermore, they helped identify secondary pulmonary infarcts because of septic embolism and recognize PAn in segmentary pulmonary branches (Fig. 2 and Fig. 3).

Thirteen patients were surgically treated with extracorporeal circulation. Ductus ligatures were performed in three patients, and transpulmonary corrections were done in 10 patients. In the three remaining patients, a ligature of the DA without extracorporeal circulation was performed. Regarding valvular participation in the infectious process, owing to its proximity, the pulmonary valve (PV) was the most affected. In seven (41%) of the 17 patients, vegetations that caused mild to moderate valvular regurgitation were registered. The serial echocardiographic studies showed that antibiotic treatment reduced the size of the vegetations that were localized in PV and PA. The excellent clinical evolution allowed for the revision of only the ventral wall during the surgical correction of the DA in five patients. In the two remaining patients, the valvular damage motivated its replacement with a biological prosthesis. The aortic valve participated in the infectious process in four patients (23%). In three of them, the presence of a subvalvular aortic fibrous membrane promoted valvular damage and the development of vegetation. In the fourth patient, the aortic valve was bicuspid. In three patients, surgery included the replacement of the aortic valve and the resection of the subvalvular aortic membrane. In one of the five patients who required valvular replacement, it was necessary to change both the aortic and the PVs. In one patient, the treatment was percutaneous interventionism (Amplatzer device)

Figure 2. Chest computed tomography (CT) in coronal view (a) showing an aneurysm of the right lower pulmonary artery (PA) (arrowhead), followed by a periphery infarct (arrow). CT after two years (b) showing regression of the PA aneurysm. Patent ductus arteriosus in a candy cane aorta view before (c) and after (d)

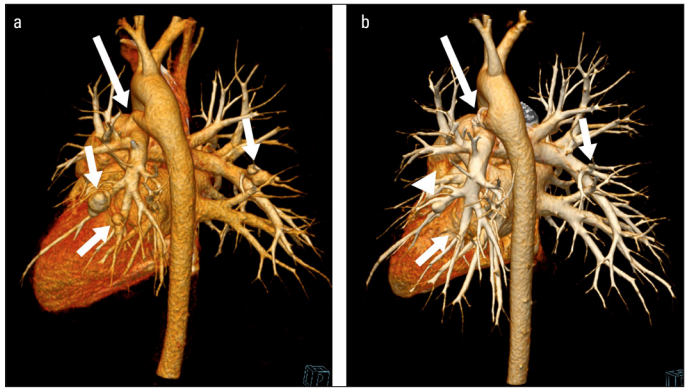

Figure 3. Computed tomography (CT) volume rendering in posterior view (a) showing bilateral pulmonary aneurysms (small arrows), and CT after two years (b) demonstrating a complete (small arrows) or partial (arrowhead) regression. Patent ductus arteriosus before (a) and after (b) percutaneous closure

three months after the IE resolution (Fig. 2). Resolution was satisfactory in 16 of the 17 patients, and only one patient who had a PDA-IE and subaortic stenosis with infective vegetations in the pulmonary and aortic valves died after surgery.

Discussion

This study reports the most extensive series of patients with PDA-IE studied by echocardiography (and some with cardiac MRI or cardiac CT) in the literature and presents similarities with some previous publications (Table 2) (2-28). In recent years, the incidence of PDA-IE has decreased owing to the use of antimicrobial prophylaxis in high-risk patients (prosthetic valve, previous IE, and congenital heart disease) (29-31).

We believe that the echocardiographic search of IE in PA should not only include cases with PDA and fever but should also be used in patients with bacteremia of uncertain origin and with any murmur and fever. The search should be performed mainly in children and young adults, although there are reports of PDA in patients between 75 and 95 years old who can have pulmonary IE and valvular endocarditis (32). The use of TTE has constituted an essential factor in the detection of PDA; when the TTE is negative and there is a high rate of probability of IE, or when the registers are of suboptimal quality, the echocardiographic study should be a TEE.

Associated cardiovascular defects were rarely reported in patients with endarteritis because of PDA. Only three patients were found in 24 publications (pulmonary stenosis, coarctation of the aorta, and rheumatic valve disease) (6-22). It is worth noting that subvalvular aortic stenosis was present in three of the 17 patients in our study group. The subaortic stenosis further facilitated the infectious implant in the aortic valve with the development of vegetations and the need to perform a valvular replacement. There was one death of an adult woman with a fibrous subaortic membrane and infectious endocarditis in the aortic and pulmonary valves. It should be recommended that in patients with PDA, an echocardiographic study, including the aortic subvalvular region, be done.

In patients with PDA-IE, serial echocardiograms should explore the PV because its participation in the infectious process is frequent [in 7 (41%) of 17 patients] (8-12). In these patients, adequate antibiotic treatments allow an excellent evolution, including reduction or even relapse of vegetations. This resulted in the corrective surgery limitation only to the DA's closure in five of seven patients; in the two remaining patients, a valvular replacement was necessary. The development of septic embolism from the vegetations in the PA is frequent. In the 27 publications with image studies, it was found in 36.5% of the 41 patients (Table 2). In our study series, it was detected in 41% patients. In most patients, the evolution of PEm is satisfactory with antibiotic treatment.

DA with remedied IE can be surgically or percutaneously treated. In our study group, 16 of the 17 patients were surgically treated; transpulmonary correction with extracorporeal circulation was performed in 13 patients; and a ligature of the DA was performed in the remaining three patients. The corrective surgery of DA with IE represented a spectacular change in the prognosis of these patients. In patients with an extensive infectious process that involves the PA wall or in those who do not respond to antibiotics, surgery with extracorporeal circulation is

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Table 2. Historical echocardiographic reports and clinical descriptions of patients with PDA-IE from 1985 to 2020

Author	Year	Sex	Age	Imaging method	PEm	PAn	Blood culture	Valvular SBE	Associated defects	Treatment	Follow-up
Vargas-Barron et al. (2)	1985	M	9	TTE	Yes	No	*Diphtheroids* sp.	No	No	Ligature	U/E
Chia et al. (3)	1987	F	16	TTE	No	No	*Candida parapsilosis*	No	No	OHS	U/E
Andrade-Freire et al. (4)	1987	F F	10 16	TTE TEE	No Yes	No No	– –	– –	– –	Ligature	U/E
Stejskal and Stark (5)	1992	F	7	TTE	Yes	No	*St. viridans*	No	No	OHS	U/E
Vargas-Barron et al. (6)	1992	F	11	TTE	No	Yes	*S. aureus*	No	AoCo	OHS / PAn resection	U/E
Balzer et al. (7)	1993	M	19	TTE	No	No	*S. aureus*	No	No	Ligature	U/E
Rivera et al. (8)	1997	F	7	TTE	Yes	No	*St. milleri*	PV	No	Ligature	U/E
Yanýk et al. (9)	2000	M	14	TTE	No	No	*St. viridans*	No	No	Ligature	U/E
Parthenakis et al. (10)	2000	F	18	TTE	No	No	*St. sanguis*	No	No	Ligature	U/E
Kouris et al. (11)	2003	F	43	TTE/TEE	Yes	No	*St. sanguis*	No	No	Ligature	U/E
Sadiq et al. (12)	2004	14 cases	less than 16	TTE	1/14	–	6/14 *St. viridans* (2) *S. aureus* (4)	PV (2)	No	Cath lab 8 Ligature 5 Antibiotics 1	U/E
Bilge et al. (13)	2004	F	11	TTE	Yes	No	*St. viridans*	No	No	Ligature	U/E
Kadakia et al. (14)	2004	M	25	TTE	No	No	*St. mutans*	No	No	Antibiotics	–
Cerruto and Mancuso (15)	2005	F	50	TTE/TEE	Yes	No	*Corynebacterium Pseudodiphtheria*	AoV	–	Antibiotics	AMI Death
Lankipalli et al. (16)	2005	M	64	TTE/TEE/MRI	No	No	*Gamella* Sp.	No	No	OHS	U/E
Cruz-González et al. (17)	2006	F	56	TTE	Yes	No	*St. viridans*	No	No	Antibiotics	–
Onji and Matsuura (18)	2007	M	49	TTE/CT	Yes	No	*St. mitis*	No	No	Ligature	U/E
Celebi et al. (19)	2007	M	2 months	TTE	No	No	*St. B Hemolytic*	No	No	Ligation	U/E
Kiani et al. (20)	2008	M	5	TTE	No	Yes	–	No	No	Ligation / Aneurysm resection	U/E
Bathoorn et al. (21)	2009	F	62	CT	Yes	No	–	No	No	Amplatzer	U/E
Cagli et al. (22)	2010	F	27	TTE	Yes	No	–	AoV/MV	RHD	OHS + MV and AoV prosthesis	U/E
Matsukuma et al. (23)	2011	M	35	TTE	Yes	No	*S. aureus*	No	No	OHS	U/E
Navaratnarajah et al. (24)	2011	M	34	TTE/TEE	Yes	No	*St. viridans*	No	No	OHS	U/E
Sugimura et al. (25)	2013	F	63	TEE/CT	No	No	Pseudomonas aerus	No	No	OHS	U/E
Miraclin et al. (26)	2017	F	54	CT/MRI	No	No	*Abiotrophia defective*	No	No	Antibiotics	U/E
Callegari et al. (27)	2019	M	7 weeks	TTE	No	No	*S. aureus*	No	No	Antibiotics	U/E
Lee et al. (28)	2020	F	42	CT	Yes	No	-	No	No	Antibiotics	Death

AMI - acute myocardial infarction; AoCo - aortic coarctation; AoV - aortic valve; CT - computed tomography; F – female; M – male; MRI - magnetic resonance imaging; MV - mitral valve; OHS - open-heart surgery; PV - pulmonary valve; S – staphylococcus; SBE - subacute bacterial endocarditis; Sp - species; St – streptococcus; TEE - transesophageal echocardiogram; TTE - transthoracic echocardiogram

a better option than a simple ligature. When the vegetations are small and reduced or disappear with antibiotics, a simple ligature is the best option (5, 32).

Nowadays, there is no disagreement with percutaneous closure as the elective treatment in infants with PDA (33). Percutaneous closure is suggested in adults also to prevent IE and heart failure and should be performed before decreased left ventricular ejection fraction. The presence of vegetations in the PA is not a contraindication for percutaneous closure of the PDA. In these patients, antibiotics are suggested under echocardiographic follow-up, and the device could be set once the infection has been controlled.

Study limitations

As it was a retrospective study, the prevalence of PDA-IE is unknown in a reference center, and the sample size was small.

Conclusion

The use of two-dimensional transthoracic echocardiography is trustworthy and reliable to confirm the diagnosis of infective endocarditis; the number and size of vegetations are variable. The main shape of the vegetations is filiform; in most patients, it is located on the lateral wall of the DA. The PV is frequently affected by continuity; fortunately, in most patients, it can be corrected with conservative medical treatment. Finally, serial echocardiographic studies help decide the type of corrective treatment, either percutaneous or surgical according to the vegetations' evolution.

Ethics approval: Ethics committee updated and approved by the Ethics and Research Committee of the National Institute of Cardiology "Ignacio Chávez". Date: September 20, 2021, Number: INCAR-DG-DC-CI-199-2021. This study is retrospective, and we only review clinical and echocardiography data.

Conflict of interest: None declared.

Peer-review: Externally peer-reviewed.

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Video 1. Two-dimensional transthoracic echocardiography in the parasternal short-axis view

Video 2. Three-dimensional transthoracic echocardiography showing two large vegetations on the valve and pulmonary trunk

Video 3. Two-dimensional transthoracic echocardiography in suprasternal view

Video 4. Two-dimensional transthoracic echocardiography in short suprasternal view

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