

## Case study

### ***LACTOCOCCUS LACTIS endocarditis of the pulmonary valve on a complex congenital heart disease***

#### **Abstract:**

Lactococcus lactis (*L. lactis*) a gram-positive cocci used in the production of cheese and dairy products. Generally considered non-pathogenic in humans, but rare cases have been reported describing *L. lactis* infections. Of these, infective endocarditis has been reported in a small number of cases. We describe here the case of a young patient with endocarditis caused by *L. lactis*. To our knowledge, this is the first case of endocarditis caused by *L. lactis* of a pulmonary valve and complex congenital heart disease.

#### **Keywords:**

Infective endocarditis; Lactococcus lactis; pulmonary valve; congenital heart disease.

#### **Introduction :**

Lactococcus lactis (*L. lactis*), formerly known as Streptococcus lactis, is a gram-positive, catalase-negative, nonmotile, spherical cocci that can be found in pairs or in short chains(1). Widely used in the production of cheese and dairy products such as yogurt and fresh cream.

Despite the fact that *L. lactis* is generally considered non-pathogenic in humans, rare cases have been reported describing *L. lactis* infections in humans (2). Infectious endocarditis (IE) in adults and children has been reported in a small number of cases(3).

Here we describe the case of a young patient with endocarditis caused by *L. lactis*. To our knowledge, this is the first case of endocarditis caused by *L. lactis* of a pulmonary valve and complex congenital heart disease.

#### **Case presentation:**

A 27-year-old male patient, with a history of complex congenital heart disease and recurrent respiratory infections during infancy. The patient reports, on admission, NYHA stage III dyspnea, intermittent dry cough, inflammatory arthralgia of the large joints, with feverish sensations and profound asthenia. This symptomatology evolves three weeks before admission, without any notion of taking antibiotics or other therapies apart from paracetamol 1g in the presence of fever.

On admission, we found a slender patient with a funnel-shaped thoracic deformity (pectus excavatum), low weight with a BMI of 15, conscious (Glasgow score 15/15),

hemodynamically and respiratory stable with a blood pressure of 112/54 mmHg symmetrical to both upper limbs, a heart rate of 84 beats per minute, a respiratory rate of 20 breaths per minute, an oxygen saturation of 97% and a temperature of 38.6°C.

Examination found no signs of left or right heart failure. Auscultation revealed a regular rhythm with a diffuse systolic-diastolic murmur in wheel radius, with an intensity estimated at 4/6ths. Pulmonary auscultation was normal. No skin lesions or adenopathy or portal of entry were found. Joint examination without signs of septic arthritis.

The electrocardiogram shows a regular sinus rhythm, with signs of hypertrophy of the four chambers and secondary repolarization disorders.

Transthoracic echocardiography had objectified a complex congenital heart disease (Figures 1-4):

- Atrioventricular and ventriculoarterial discordance.
- A double outlet right ventricle.
- Aorta in an anterior and left position of the pulmonary artery.
- A 23 mm wide inlet interventricular communication, with a left to right shunt.
  - A moderately hypoplastic, non-hypertrophied left ventricle with preserved kinetics and systolic function.
  - Dilated, non-hypertrophied right ventricle with preserved longitudinal systolic function.
  - A dysplastic tricuspid pulmonary valve, with eversion of the posterior cusp, which sits, on its ventricular side, of a vegetation measuring 27.4 mm x 14.1 mm, mobile with a rocking movement in the trunk of the pulmonary artery during systole; it is also responsible for severe pulmonary regurgitation and a gradient of obstruction (maximum gradient at 85 mmHg, mean gradient at 53 mmHg).
  - Dilated pulmonary artery, measuring 59 mm, with an aneurysmal aspect (post-stenotic dilation).
  - Absence of persistent ductus arteriosus and coarctation of the aorta.

Blood tests on admission revealed an inflammatory syndrome with hyperleukocytosis at 13,470 / uL, predominantly neutrophils at 10,560 / uL, and C-reactive protein at 57 mg/l, renal function is normal with creatinine at 6.3 mg/L and a urea at 0.24 g/L. Liver function is normal with aspartate aminotransferase at 43 and alanine aminotransferase at 23.

An infectious assessment was carried out with negative viral serologies for hepatitis B and C, syphilis, and HIV. As for the blood cultures, they came back positive with identification of a Gram-Positive Cocci, type LACTOCOCCUS LACTIS,

unspecified subspecies, sensitive to Amoxicillin, Levofloxacin, Cefotaxime, Vancomycin, and Gentamicin; while it was resistant to Lincomycin and Erythromycin.

As part of the endocarditis extension assessment, a cerebral CT angiography and a thoraco-abdomino-pelvic CT scan did not reveal any abnormality (Figures 6-7).

The diagnosis of infective endocarditis of the pulmonary valve on complex congenital heart disease was retained according to the modified Duke criteria. The treatment was based on bi-antibiotic therapy based on Gentamycin 160 mg/d and Amoxicillin 12 g/d with good initial clinical and biological evolution. After a multidisciplinary discussion, a surgical decision was indicated given the characters of the vegetation and the major embolic risk.

The evolution was marked, on the 7th day of his hospitalization (the day before the day of his scheduled surgery), by acute respiratory distress and non-resuscitated cardiac arrest, probably secondary to a pulmonary septic embolism given the size, location and the mobile and tilting character in the trunk of the pulmonary artery.

#### Discussion:

*Lactococcus lactis* is a spherical microaerophilic mesophilic fermenting bacterium. The two most common bacteria among *Lactococcus* subspecies are *L. lactis* and *L. cremoris*, which appear to be skin commensals in cattle and are used to make cheese and fermented dairy products(4,5). *Lactococcus lactis* can sometimes be isolated as normal flora of the oropharynx, intestine or vagina. *L. lactis* is considered to have low virulence and low pathogenic potential although it has been associated with certain diseases in healthy, immunocompetent or immunocompromised patients(6–8).

It was noted that some patients had consumed unpasteurized milk, sour cream or yogurt. Other cases, however, had no history of consuming unpasteurized dairy products. Since *Lactococcus lactis* infections are rare, the origin of this infection has not been clearly established. Unpasteurized dairy products or direct intraluminal inoculation from contaminated hands are two theories about the origin of the infection(9–12).

A review of the current literature shows that there have been a total of 43, including this case, reported infections with *L. lactis*(13).

To our knowledge, our patient represents the 16th case of endocarditis caused by *Lactococcus lactis* reported in the literature. Among these cases, underlying heart disease predisposing to infective endocarditis is found in nine cases, including ours, while the rest of them had no history of valvular heart disease(3,14). Involvement of the mitral valve is the most frequently encountered, followed by the tricuspid and then aortic valve, the last case of which reported by Mitchell et al was complicated by cellulitis (14), and finally the pulmonary valve, of which our case is the unique in the literature (3) (Table 1).

For the first time in the literature, we report an infective endocarditis due to *Lactococcus Lactis* on a pulmonary valve and on a complex congenital heart disease with atrioventricular and ventriculo-arterial discordance with a right ventricle with double outlets, in a patient with history of raw milk consumption.

Infectious endocarditis of the pulmonary valve is a rare entity, representing 1.5 to 2% of cases of IE, with only 38 cases reported in the literature between 1960 and 2000 (15). In their review of Mayo Clinic experience between 2000 and 2014, Miranda et al, identified nine patients with pulmonary valve IE. The latter was isolated in 7 (78%) of the 9 cases. Three patients had congenital heart disease, two had central venous catheters, and three had cardiovascular implantable electronic devices. *Enterococcus faecalis* and *viridans* group streptococci were the most common pathogens, isolated in 22% of cases each (16). Risk factors reported in the literature include male gender, intravenous drug use, involved venous catheters, alcoholism, and congenital heart disease (15,16).

The diagnosis was retained in view of one major criterion and four minor among the Duke criteria, with positive blood cultures and an image of vegetation on the trans-thoracic and trans-oesophageal ultrasound. According to the literature, the rate of culture-negative endocarditis ranges from 2.1% to 35% (17).

Due to limited information on the susceptibility of this bacterium, there is no conventional antibiotic therapy strategy to treat infective endocarditis caused by *L. lactis*. In clinical practice, antibiotics are given empirically before culture results are available, or selected based on drug susceptibility results; third-generation penicillin and cephalosporin plus gentamicin are the most common choice for *L. lactis* infections (18).

The majority of cases reported by the authors experienced various severe complications including cerebral emboli, mycotic aneurysms, cardiac arrhythmias and septic pulmonary embolisms (2,11,19,20). The latter was encountered in a young child reported by Mansour et al (2). In our case, the characters of the vegetation let us suppose that the patient's death was linked to a septic pulmonary embolism. The ultimate evolution was favorable in the majority of cases, with the death of only three patients including our case(19,20).

### Conclusion:

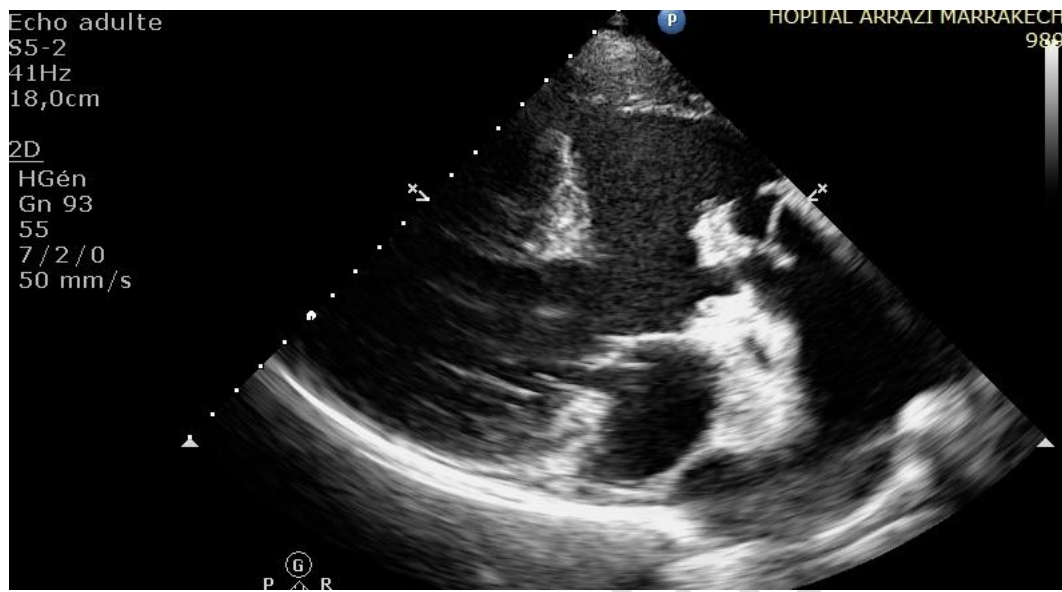
Despite its rarity, low virulence and pathogenic potential, *Lactococcus* should be treated as a serious infection due to its possible complications. The presence of signs of infective endocarditis and a history of consumption of unpasteurized dairy products or of coming into contact with farm animals should encourage clinicians to look for this germ, especially in cases of congenital heart disease.

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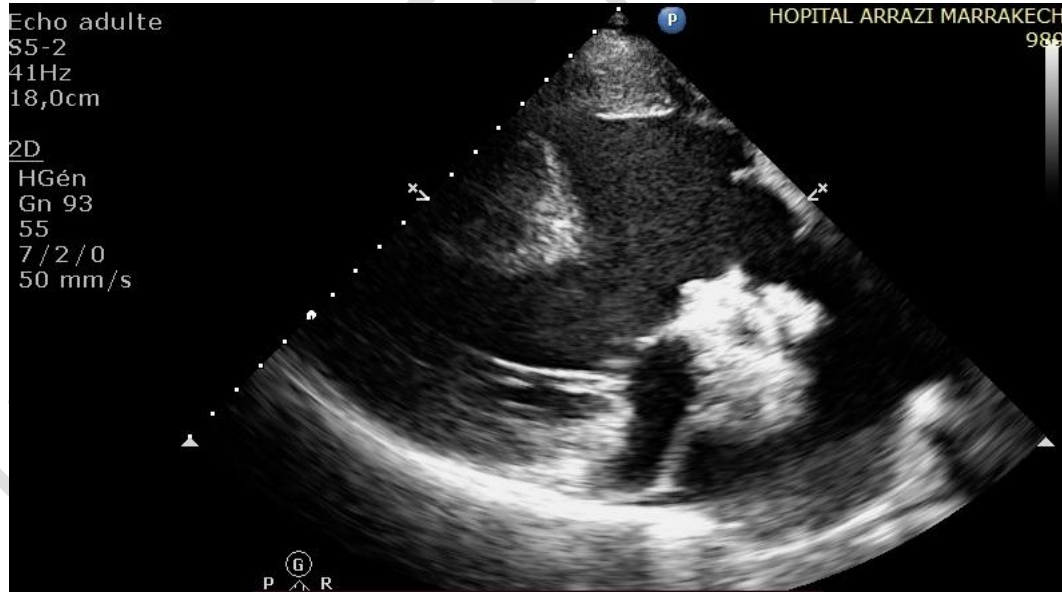
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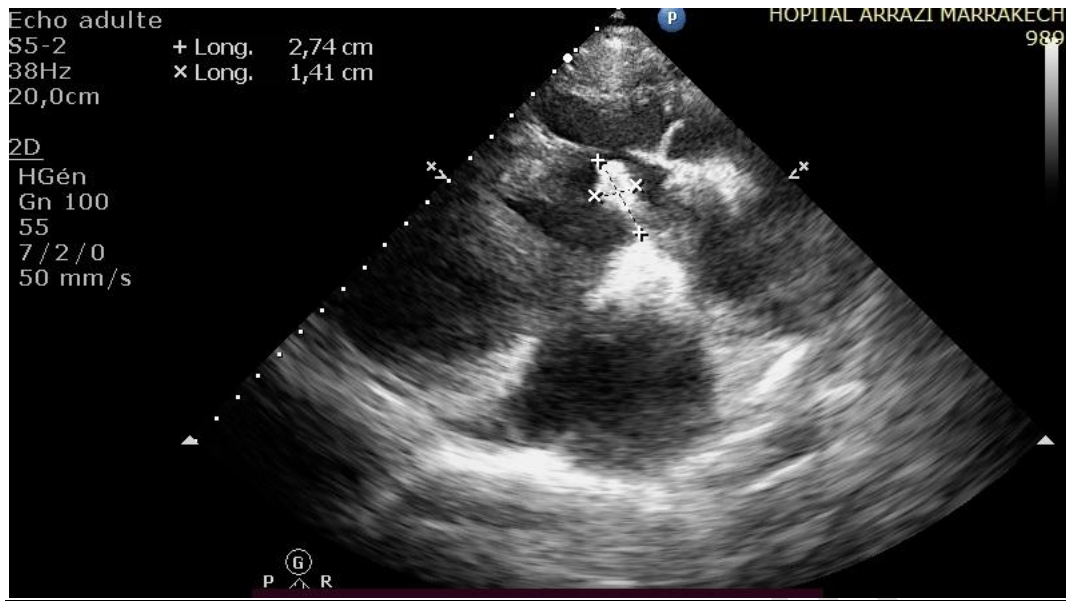
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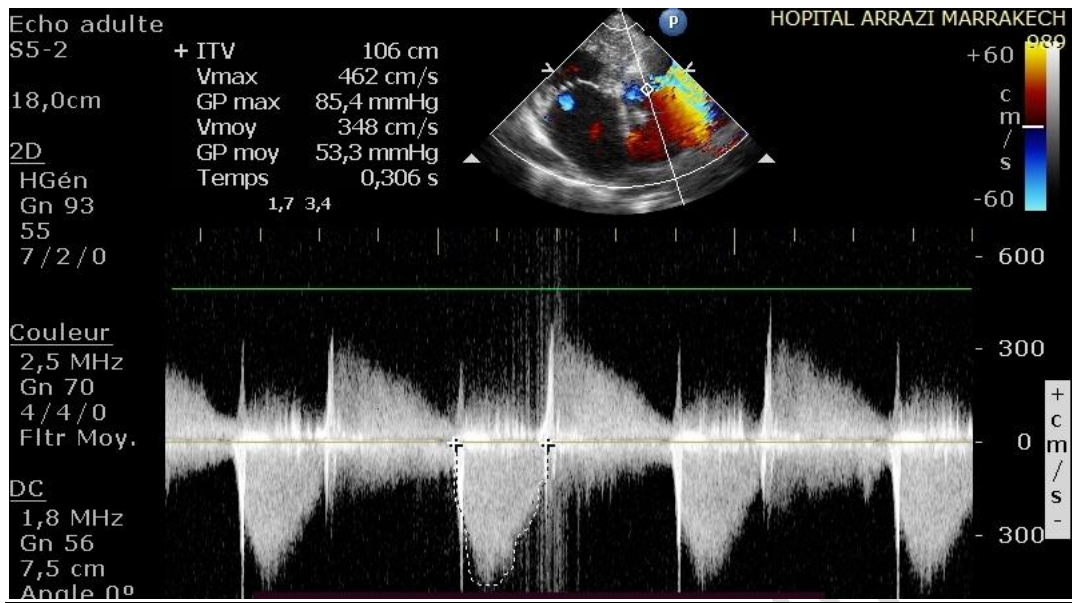
- **Figure 1: Pulmonary valve vegetation, on its ventricular side.**



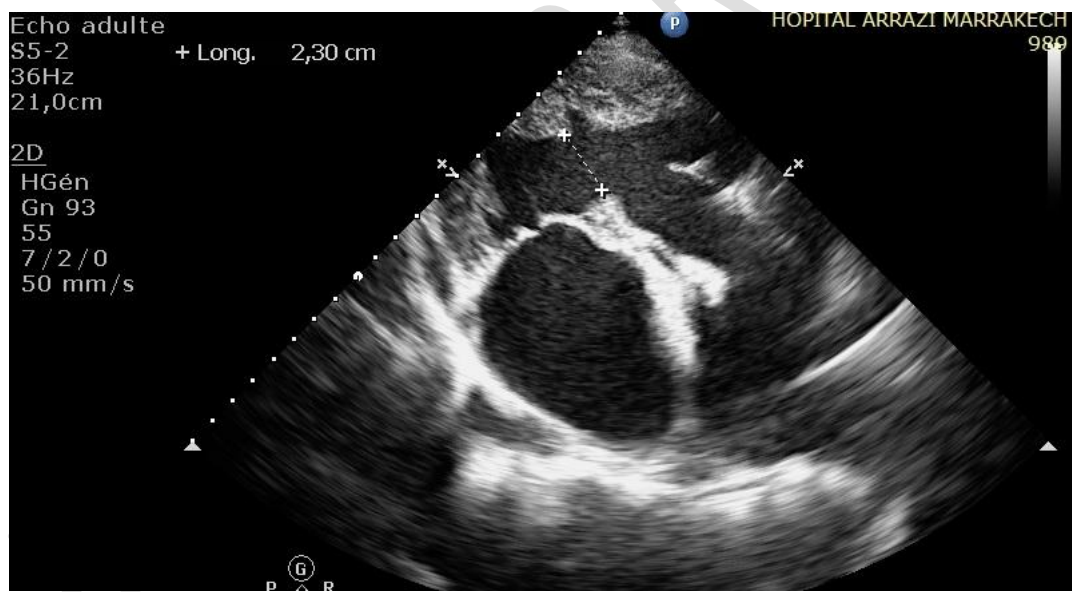
- **Figure 2: Pulmonary valve vegetation, on its ventricular side, with a rocking movement in the trunk of the pulmonary artery during systole.**



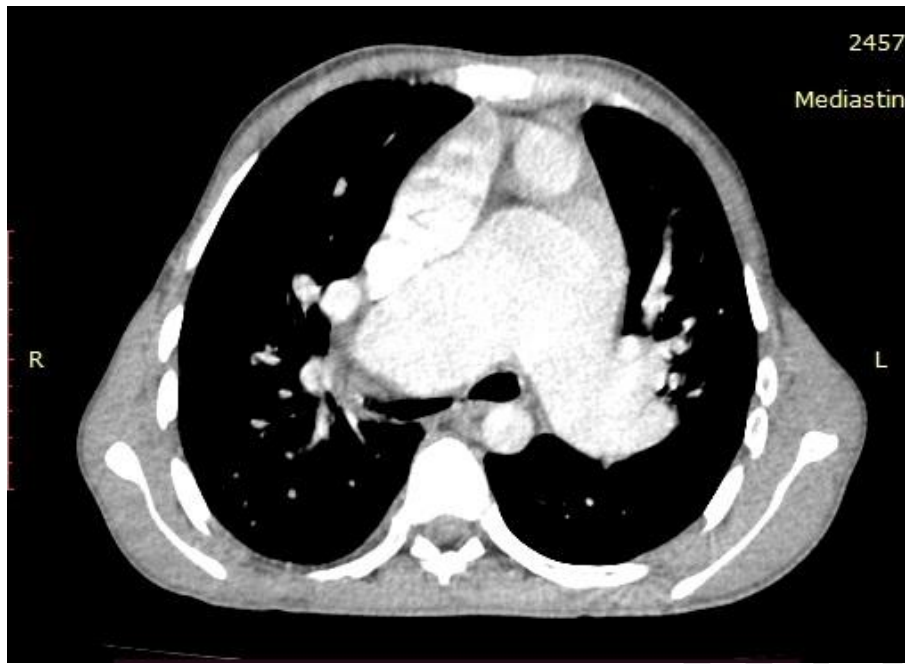
- **Figure 3: pulmonary valve vegetation measurement: 27.4 mm x 14.1 mm.**



- **Figure 4: Pulmonary regurgitation and the gradient of obstruction: maximum gradient at 85 mmHg, mean gradient at 53 mmHg.**



- **Figure 5: A 23 mm wide inlet interventricular communication.**



- Figure 6 - 7 (thoracic CT scan): Pulmonary artery arises from the left ventricle, with an increase in its caliber as well as that of its branches.

**Table 1: Reported cases of infectious endocarditis caused by *Lactococcus lactis*.**

Authors	Year	Subspecies	Unpasteurized dairy products consumption	Heart disease	Valve involved	Complications	Outcome
Wood et al.(9)	1955	<i>L. lactis</i> subsp. <i>lactis</i>	Yes (ice cream)	No history of heart disease	Unknown	None	Recovered
Mannion and Rothburn (21)	1990	<i>L. lactis</i> subsp. <i>lactis</i>	Unknown	Myocardial infarction, rheumatic mitral valve disease	Mitral	Infarction/dysphasia	Recovered
Pellizzer et al. (22)	1996	<i>L. lactis</i> subsp. <i>cremoris</i>	No	Mitral prolapse	Aortic	None	Recovered
Halldorsdotir et al.(10)	2002	<i>L. lactis</i> subsp. <i>cremoris</i>	Yes (milk)	No history of heart disease	Mitral	None	Recovered
Kiss et al.(23)	2005	Unknown	Unknown	Unknown	Unknown	Femoral osteomyelitis	Unknown
Zechini et al. L. (24)	2006	<i>lactis</i> subsp. <i>lactis</i>	Unknown	Atrial mixoma, mitral regurgitation	Mitral	None	Recovered after surgery
Resch et al.(11)	2006	<i>L. lactis</i> subsp. <i>cremoris</i>	Yes (cheese)	No history of heart disease	Aortic	Multiple mycotic aneurysms	Recovered after surgery
Lin et al.(19)	2009	<i>L. lactis</i> subsp. <i>cremoris</i>	No	No heart disease	Mitral	Intracerebral hemorrhage/infarction	Deceased
Rostagno et al. (25)	2012	Unknown	No	Mitral valve prolapse	Mitral	Embolic infarction	Recovered after surgery
Taniguchi et al.(20)	2015	Unknown	No	No heart disease	Mitral + tricuspid	Arrhythmia	Deceased

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Mansour et al.(2)	2016	Unknown	No	Ventricular septal defect	Tricuspid	septic emboli	Recovered
Georgountzos et al. (12)	2017	Unknown	No	No history of heart disease	Aortic	None	Recovered
Fei Chen et al.(18)	2018	L. lactis subsp. lactis	Unknown	Coronary heart disease	Mitral	None	Recovered
Lahlou et al. (3)	2021	L. lactis subsp. cremoris	Yes (milk)	No heart disease	Aortic	Liver abscess, splenic infarction, pleural bilateral effusion + right basal pneumonia	Recovered
Mitchell et al (14)	2022	Unknown	Yes (cheese)	Mild mitral valve regurgitation and stenosis and severe tricuspid regurgitation.	Aortic	Cellulitis	Recovered
Naaim et al	2023	Unknown	Yes (milk)	atrio-ventricular and ventriculo-arterial discordance and a double outlet right ventricle	Pulmonary	Probable pulmonary septic embolism	Deceased

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