

## Huge *Candida albicans* normal native tricuspid valve endocarditis

Massimiliano Guerriero<sup>a</sup>, Francesco Colasurdo<sup>b</sup>, Anna Maria Pollio<sup>a</sup>

**How to cite:** Guerriero M, Colasurdo F, Pollio AM. Huge *Candida albicans* normal native tricuspid valve endocarditis. *Autops Case Rep* [Internet]. 2018;8(2):e2018021. <http://dx.doi.org/10.4322/acr.2018.021>

### ABSTRACT

Fungal endocarditis has become an important infection associated with medical progress and the modern lifestyle. In particular, *Candida* spp. is a rare but important cause of infective endocarditis. We report the case of a 28-year-old woman—quadriplegic and bedridden from birth—who died after repeated episodes of pneumonia treated with different regimens of intravenous antibiotics. A medico legal autopsy was performed, which diagnosed severe *Candida* native valve infective endocarditis (CIE). This case report illustrates the prolonged use of antibiotic treatment as a possible risk factor for the development of CIE. We also considered how the bedridden condition and the presence of a central venous catheter may be additional risk factors for the development of this entity. Finally, we examined the absence of peripheral embolization in the setting of endocarditis of the right side of the heart.

### Keywords

*Candida albicans*; Endocarditis; Quadriplegia; Tricuspid Valve.

### INTRODUCTION

Bedridden and/or non-autonomous patients, structural heart disease, intravascular catheters, and invasive procedures are predisposing factors for the development of infective endocarditis. Among the varied etiological agents, fungal endocarditis is uncommon and is associated with high mortality (56%-70%).<sup>1</sup>

In English medical literature from 1965 to 2000 there were two important review articles encompassing 422 cases of fungal endocarditis (152 cases in one review and 270 cases in the other) comprising all age groups.<sup>2,3</sup>

In adults, only rare individual cases of *Candida* infective endocarditis (CIE) on normal valves have been described; in contrast, eight cases of CIE have been described in children with structurally normal hearts.<sup>4</sup>

### CASE REPORT

A 28-year-old woman who suffered a severe neonatal hypoxic-ischemic brain injury, grew up presenting spastic quadriplegia with epilepsy. Due to major swallowing disorders, from the age of 20 the patient developed numerous episodes of aspiration pneumonia, which subsequently worsened with marked respiratory failure, high fever, and leukocytosis. Over the following 8 years, bronchial lavage aspirate cultures isolated *Escherichia coli*, *Streptococcus agalactiae*, and *Pseudomonas aeruginosa*.

A central venous catheter/PORT type was inserted in the patient's left subclavian vein to ensure a proper antibiotic infusion, and a percutaneous endoscopic gastrostomy (PEG) was performed to avoid further episodes of oropharyngeal content aspiration.

<sup>a</sup> Antonio Cardarelli Regional Hospital, Regional Health Authority of Molise (ASReM), Department of Pathology. Campobasso, CB, Italy.

<sup>b</sup> Independent scholar, Campobasso, CB, Italy.



Two months after the PORT-A-CATH® insertion, three different blood culture samples were positive for *Candida albicans*. Although the candidemia could be associated with the catheter colonization, the catheter was not removed because of the difficulty in obtaining other intravenous (IV) access. A transthoracic echocardiogram was performed twice and did not reveal any valvar dysfunction or structural alteration, despite the lower sensitivity for the diagnosis of infective endocarditis, compared to the transesophageal examination. Fortunately, after IV fluconazole 800 mg, every 24 hours, successive blood cultures became negative. Having reached clinical stability, the patient was discharged from the hospital to home care assistance; however, the antimicrobial regimen (IV fluconazole 800 mg every 24 hours added to IV piperacillin and tazobactam 4 g every 12 hours for 10 days) was maintained. Unfortunately, 6 weeks later, the patient was re-admitted to the hospital for a new episode of severe respiratory and cardiac failure. Over a few hours, she developed severe hypotension, which was unresponsive to a vasoactive drugs infusion (dopamine and norepinephrine) and evolved to bradycardia, asystole, and death.

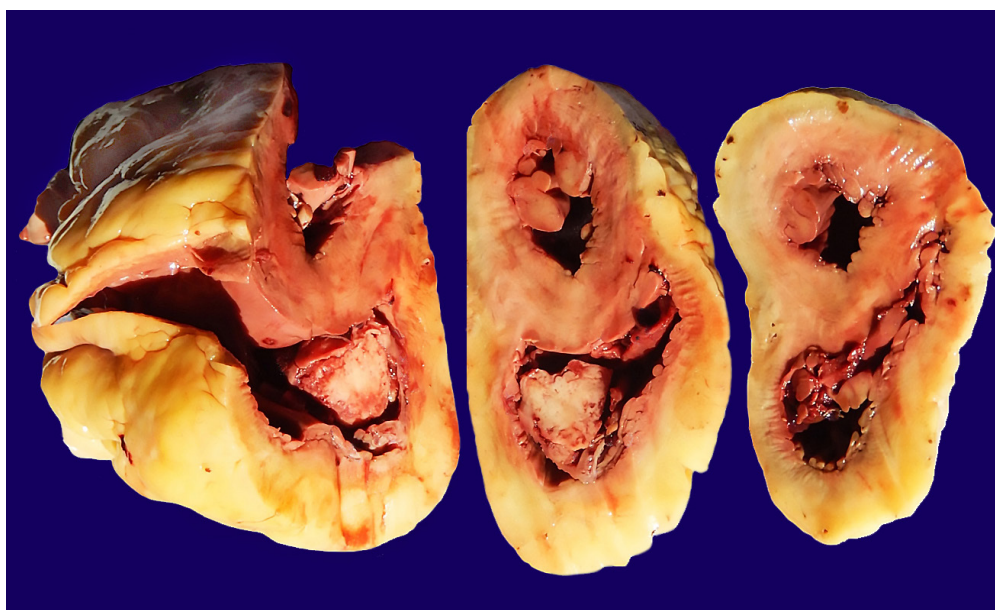
### Autopsy Findings

The corpse's external examination revealed an undeveloped body for her chronological age; in fact, she looked no more than 11 or 12 years old (height 146 cm;

weight 38 kg). She was a very thin person with a prepuberal appearance, a clearly visible rib cage, minimal fat tissue, and marked sarcopenia. The physical posture was typical of a quadriplegic person: arms in adduction and intra-rotated with the elbow's flexion; flexion of the wrists, fingers and knees; and equine feet. A clearly identifiable deformity of the spine was depicted with a C-shaped significant scoliosis curved to the left in the coronal plane, which was evident after evisceration. The patient had lost most of her teeth.

Grade 4 bedsores were present in the sacral region along with vulvar and perianal erythema. The central venous catheter was in the upper left hemithorax, and the output of the PEG valve was in the epigastrium.

The mediastinal organs were small. The heart weighted 184 g (reference range [RR] 251 g), and 80 mL of pericardial serous effusion was drained after its overture. The thickness of the left ventricle wall was 13 mm (RR: 15 mm), while the wall of the right ventricle measured 3 mm (RR: 2-4 mm).<sup>5</sup> The coronary arteries examination showed regular size in their origin, and no thrombi were not found within their lumen. At the opening of the heart chambers (Figure 1), a nodular vegetation of 2.5 cm originating from the tricuspid valve was evident. The posterior cusp of the tricuspid atrioventricular valve was completely destroyed by the infection.



**Figure 1.** Gross view of multiple heart cross sections from the apex to the base showing the endocarditic vegetation attached to the tricuspid valve, and partly filling the right ventricle and right atrium.

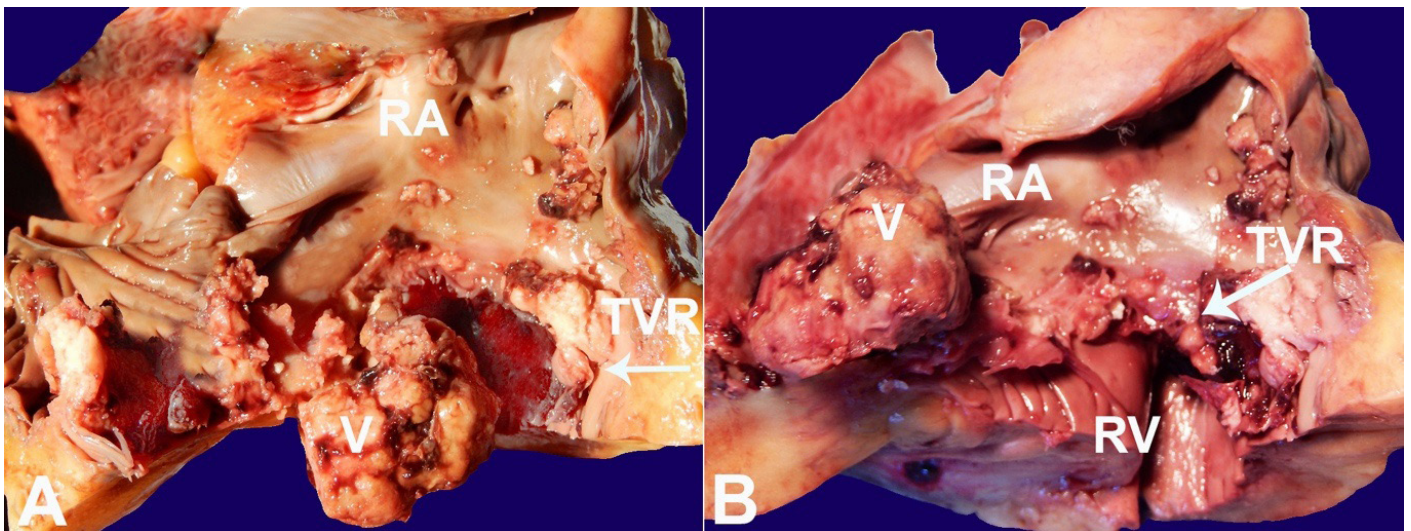


This lesion completely destroyed the tricuspid valve and occupied almost the entire right atrium chamber and part of the right ventricle (Figure 2A and 2B).

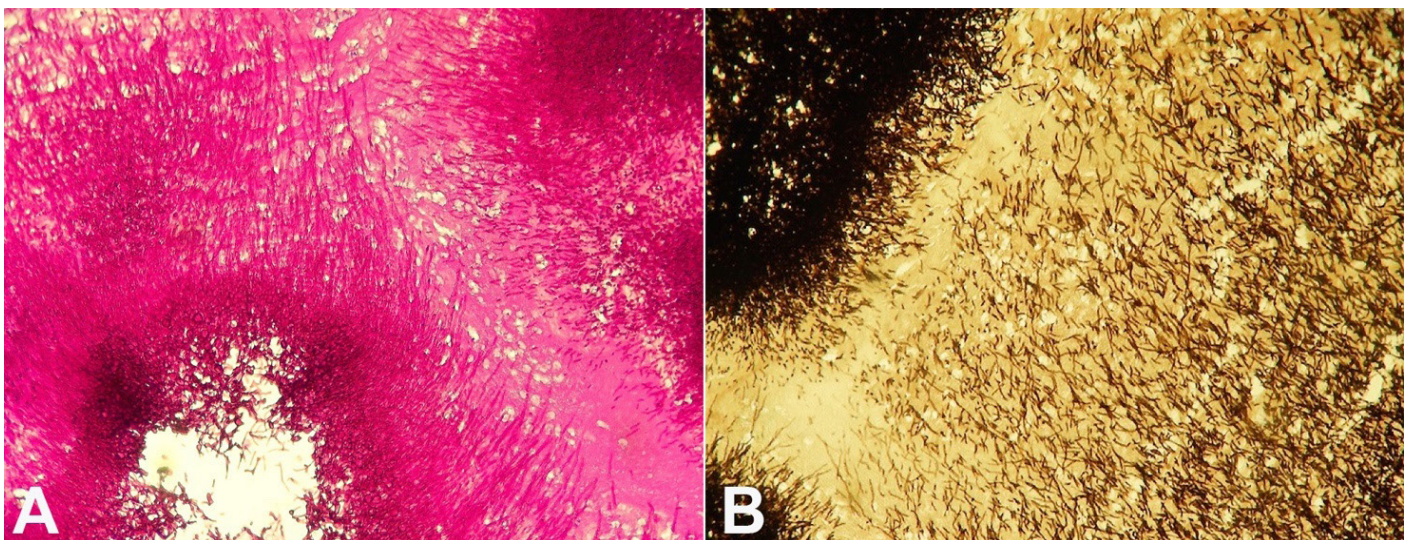
The histological evaluation of this lesion (Figure 3 A–B) showed fungal endocarditis. Both hematoxylin and eosin, and Grocott's staining, revealed fibrinonecrotic material with neutrophils, fungal budding yeast, hyphae, and abundant pseudohyphae. The pseudohyphae—which represent elongated buds that have failed to dissociate from the mother cell and from one another—have been referred to as “links of

sausage.” *C. albicans* also have the ability to produce true hyphae. The above-mentioned morphological characteristics, and the three positive blood cultures, were consistent with *C. albicans* endocarditis.

The left lung weighed 344 g (RR for a normal woman aged 28: 403 g; however, the RR for a normal woman aged 12 [the approximate anthropometric measures of the patient]: 275 g). The right lung weighed 370 g (RR: 435 g; RR for a normal woman aged 12 [approximate anthropometric measures of the patient]: 290 g) (Figure 4). Confluent foci of

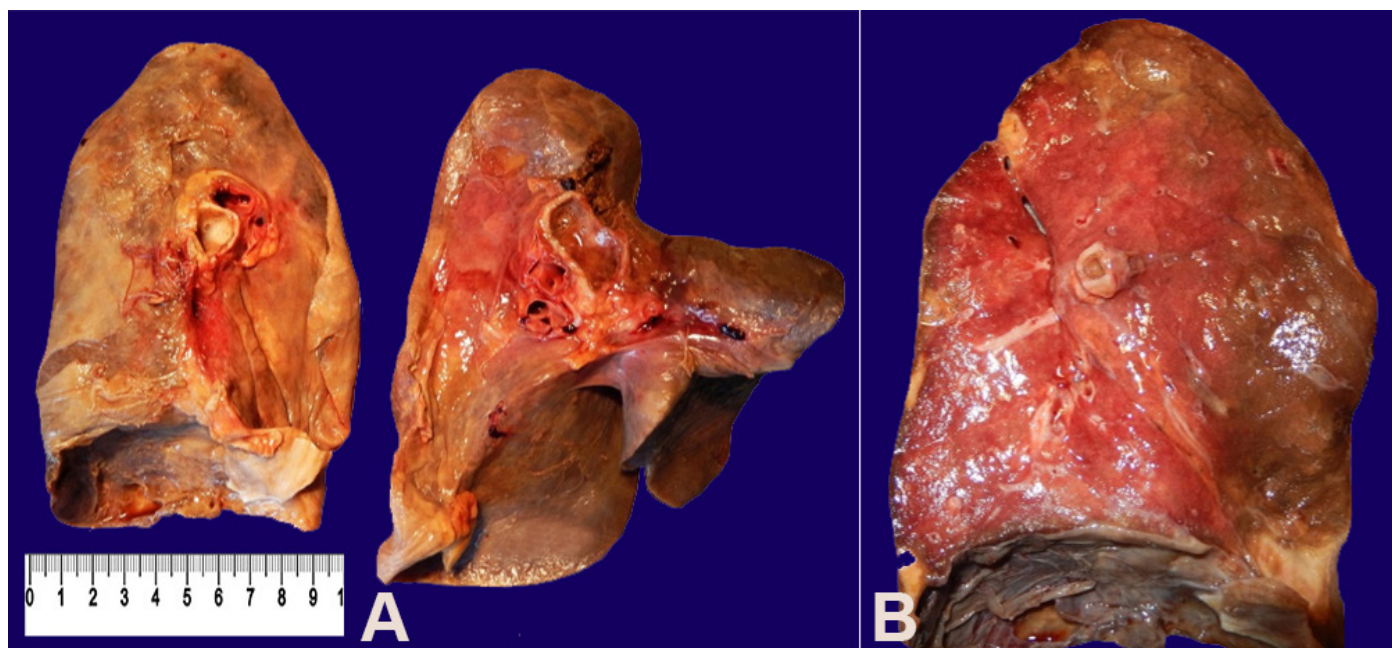


**Figure 2.** Gross examination of the heart, from the right atrium view, showing the nodular vegetation arising from the tricuspid valve. **A** – The vegetation occupied the whole valve cusp; **B** – After removal of the vegetation, the valve cusp appeared completely destroyed. RA = right atrium; RV = right ventricle; TVR = tricuspid valve ring; V = vegetation.



**Figure 3.** Photomicrographs of the endocardial vegetation with necrotic debris, fibrin, neutrophils, rare macrophages, and fungal budding yeast, hyphae and abundant pseudohyphae. The *Candida pseudohyphae* were usually evident in the H&E-stained slides, (**A** – H&E, 100X) and were positive by Grocott's stain (**B** – Grocott's stain, 100X).





**Figure 4.** Gross findings of the lungs (**A** – Left and right lungs, medial vision; **B** – Left lung, aspect to the cut section). The lungs appeared diffusely boggy and hardened, with edema and different nodular areas of consolidation that were white/yellow in color.

bronchopneumonia were evident in both lungs. Other findings included fibrosis, diffuse micro calcifications, and bronchiectasis, which may be related to the repeated episodes of aspiration pneumonia.

The brain weighed 640 g (RR: 1210 g) and showed several cystic lesions in the white matter, which were related to cerebral infarcts and ischemic lesions that may have occurred at birth (Figure 5). The cortex above was characterized by ulegyria (pathognomonic of perinatal injury), which explained the origin of spastic quadriplegia of perinatal hypoxic damage. This finding appeared to be of cicatricial origin, especially in the cortex sulci with the overlying convolution looking vaguely polypoid.

The remaining organs were macroscopically unremarkable.

Histological examination confirmed the presence of bronchopneumonia and pulmonary edema, plus micro calcifications and diffuse fibrosis, which were consistent with signs of chronic lung damage associated with repeated aspiration. Although the lungs were thoroughly searched, no fungus lesions were found.

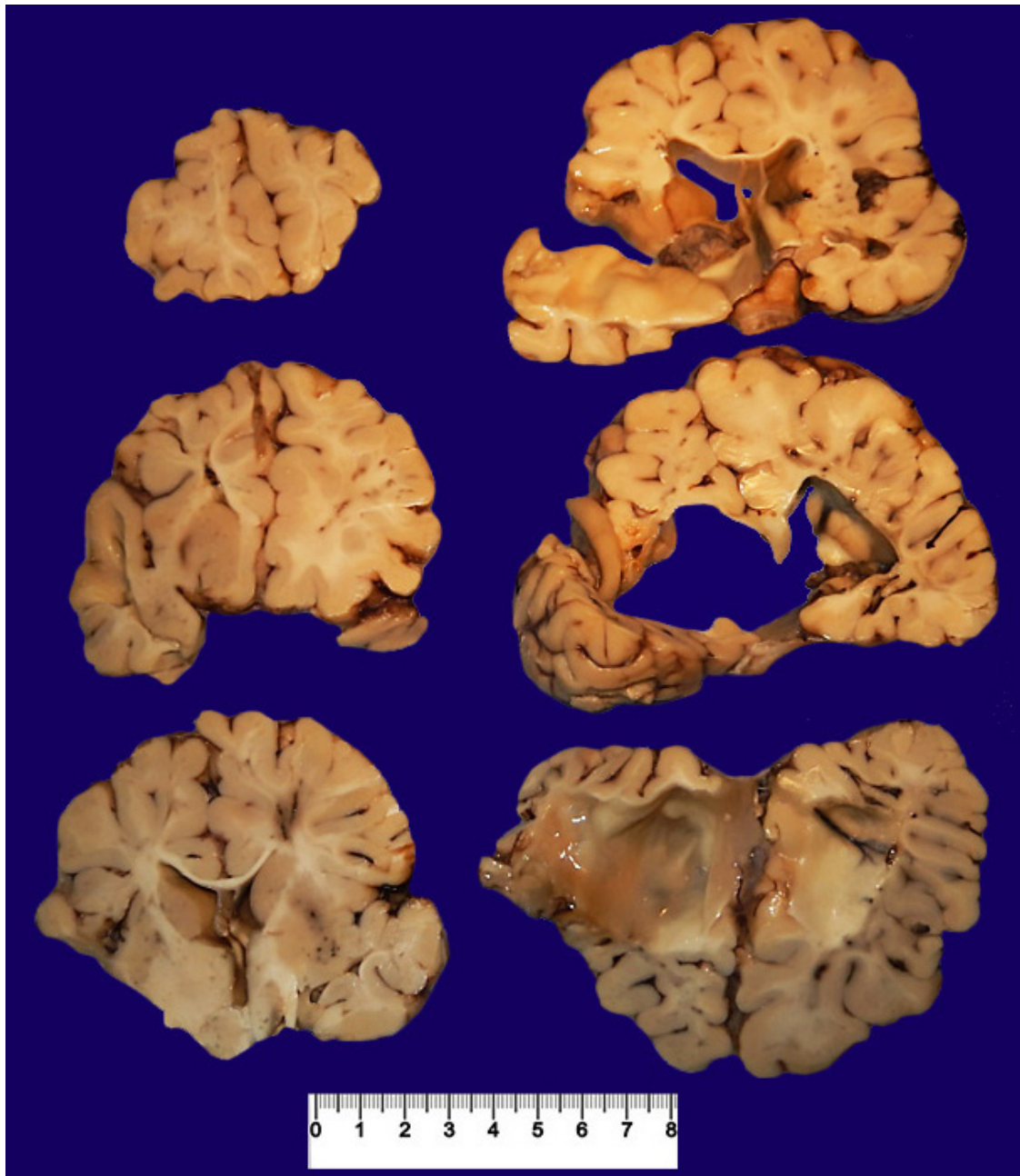
In summary, the autopsy findings were consistent with the diagnosis of acute respiratory failure caused by massive bilateral bronchopneumonia in a patient

with native tricuspid valve fungal endocarditis, cerebral ulegyria, quadriplegia, and repeated episodes of aspiration pneumonia. Other findings included stage 4 bedsores, a PEG valve and a central venous catheter.

## DISCUSSION

Fungal endocarditis is rare but often fatal. In this setting, the most commonly isolated pathogens are *Candida* spp. (as in our case) and *Aspergillus* spp. Other, less frequently occurring fungal pathogens, include the genera *Coccidioides*, *Cryptococcus*, *Histoplasma* and *Blastomyces*. Embolization is quite common in these cases; however, in our case, after careful research, no pulmonary embolization was detected, which was probably due to the timely treatment with antifungal drugs. In fact, antimicrobial therapy could have countered the spread of *Candida* spp. into the patient's other organs.

Infective endocarditis caused by *Candida* spp. represents only 1%-2% of the overall number of cases of infective endocarditis.<sup>6</sup> This kind of infection is associated with a high mortality rate that ranges between 30% and 80%.<sup>7</sup> Recently, episodes of fungemia have substantially increased because of the increasing number of risk and predisposing factors.



**Figure 5.** Gross examination of the central nervous system showing “mushroom shaped” gyri and cystic dilatation of the lateral ventricles due to white matter atrophy.

In our case, we dare to consider that an additional risk factor could have been the bedridden condition of the patient accompanied by an extensive degree of neuropsychic motor impairment. However, there are no data in the medical literature that relate this condition with endocarditis (bacterial or fungal).

A recent study, by an Italian group,<sup>8</sup> gathered 140 cases of CIE on native valve endocarditis (NVE) and prosthetic valve endocarditis (PVE). Patients with a history of abdominal surgery and antibiotic exposure had a higher probability of developing NVE rather than

PVE; in our case, the prolonged antibiotic therapy due to the episodes of bronchial pneumonia was also an important risk factor for *Candida* spp. infection.<sup>9</sup>

Right-side endocarditis (RSE) is quite common in intravenous drug users (IDU), and usually involves the tricuspid valve and—more rarely—the pulmonary valve. However, the mechanism that leads to endothelial damage is particular, because it is linked to the drug itself; in these cases it is almost always a bacterial endocarditis.<sup>10</sup> The clinical presentation and outcome of RSE are distinct from left-sided endocarditis.

RSE accounts for 5%-10% of all infectious endocarditis (IE) and is mostly diagnosed in IDU; in contrast, isolated RSE in the non-IDU population occurs in those with congenital heart diseases, permanent pacemakers, implantable cardioverter defibrillators, or central venous catheters. (Among these, the latter is the only risk factor present in our case.)<sup>11</sup> Septic pulmonary embolism with multiple pulmonary emboli is a very common condition in RSE. In 40% of IE episodes, peripheral embolization has been observed.<sup>11</sup> In our case, the accurate analysis of numerous pulmonary samples, which was carried out by two different pathologists, did not reveal the presence of peripheral emboli.

## CONCLUSION

The positive blood culture for *Candida* spp. in the setting of protracted antibiotic regimens should never be underestimated. The rates of candidemia have increased by as much as 128% in recent years because of a growing number of patients at risk. However, the diagnosis of endocarditis is overlooked. It is important to emphasize, in this case, all the challenges faced during the care of the patient due to difficulties in communication.

For these reasons, in patients with several risk factors, the possibility of fungal endocarditis always should be considered. In this case, the autopsy was important because it highlighted an unrecognized diagnosis.

This case report is in accordance with the Italian medical publication's ethics committee. The autopsy was performed under legal request and the publication was authorized after the the judicious investigation.

## REFERENCES

1. Kumar P, Muranjan MN, Tullu MS, Vaideeswar P, Kher A, Lahiri KR. *Candida tropicalis* endocarditis: treatment in a resource-poor setting. *Ann Pediatr Cardiol*.

2010;3(2):174-7. <http://dx.doi.org/10.4103/0974-2069.74051>. PMID:21234200.

2. Pierrotti LC, Baddour LM. Fungal endocarditis, 1995-2000. *Chest*. 2002;122(1):302-10. <http://dx.doi.org/10.1378/chest.122.1.302>. PMID:12114375.

3. Ellis ME, Al-Abdely H, Sandridge A, Greer W, Ventura W. Fungal endocarditis: evidence in the world literature, 1965-1995. *Clin Infect Dis*. 2001;32(1):50-62. <http://dx.doi.org/10.1086/317550>. PMID:11118386.

4. Marom D, Ashkenazi S, Samra Z, Birk E. Infective endocarditis in previously healthy children with structurally normal hearts. *Pediatr Cardiol*. 2013;34(6):1415-21. <http://dx.doi.org/10.1007/s00246-013-0665-9>. PMID:23483241.

5. Finkbeiner WE, Ursell PC, Davis RL. *Autopsy pathology: a manual and atlas, expert consult – online and print*. London: Elsevier Health Sciences; 2009.

6. Baddley JW, Benjamin DK Jr, Patel M, et al. *Candida* infective endocarditis. *Eur J Clin Microbiol Infect Dis*. 2008;27(7):519-29. <http://dx.doi.org/10.1007/s10096-008-0466-x>. PMID:18283504.

7. Arnold CJ, Johnson M, Bayer AS, et al. *Candida* infective endocarditis: an observational cohort study with a focus on therapy. *Antimicrob Agents Chemother*. 2015;59(4):2365-73. <http://dx.doi.org/10.1128/AAC.04867-14>. PMID:25645855.

8. Giuliano S, Guastalegname M, Russo A, et al. *Candida* endocarditis: systematic literature review from 1997 to 2014 and analysis of 29 cases from the Italian Study of Endocarditis. *Expert Rev Anti Infect Ther*. 2017;15(9):807-18. <http://dx.doi.org/10.1080/14787210.2017.1372749>. PMID:28903607.

9. León C, Ruiz-Santana S, Saavedra P, et al. A bedside scoring system ("Candida score") for early antifungal treatment in nonneutropenic critically ill patients with *Candida* colonization. *Crit Care Med*. 2006;34(3):730-7. <http://dx.doi.org/10.1097/01.CCM.0000202208.37364.7D>. PMID:16505659.

10. Frontera JA, Gradon JD. Right-side endocarditis in injection drug users: review of proposed mechanisms of pathogenesis. *Clin Infect Dis*. 2000;30(2):374-9. <http://dx.doi.org/10.1086/313664>. PMID:10671344.

11. Procop GW, Pritt BS. *Pathology of infectious diseases*. USA: Philadelphia Elsevier Saunders; 2015.

**Authors contributions:** Guerriero M. performed the autopsy, designed wrote the manuscript and was responsible for the literature data search, Colasurdo F. was the technician of the autopsy and Pollio AM supervised the autopsy performance and guided the organs representation.

**Conflict of interest:** None

**Financial support:** None

**Submitted on:** December 17<sup>th</sup>, 2017

**Accepted on:** March 24<sup>th</sup>, 2018

**Correspondence**

Massimiliano Guerriero

Department of Pathology - Regional Health Authority of Molise (ASReM) - Antonio Cardelli Regional Hospital

Contrada Tappino s.n.c. – Campobasso/CB – Italy

86100

Phone: +39 (0874) 409-205

ilguerrierochecorre@gmail.com