mild respiratory disease from 2009 to 2012; and Zhang et al.[10] only detected one case from 2011 to 2015, representing 18% of all the isolates. The 2015 comparative study of the circulation of EV-D68 in Europe and the United States by Poelman et al.[11] confirmed the low prevalence of this virus in Europe and the lower morbidity during the North American outbreak. In Spain in 2014, Gimferrer et al.[5] were the first to report two cases (40%) in adults, in a group of five hospitalised patients; neither of them required intensive care.

None of these studies detected severe neurological disorders or flaccid paralysis in adults as are found in children. It is possible that after multiple and continuous infections by different enteroviruses during childhood, the adult population has heterotypic neutralising antibodies which protect them from the severe forms of this infection.[7–9] In spite of that, the first reported case of infection by EV-D68 in an adult in the United States was a pregnant woman, suggesting that her pregnancy could have made her more susceptible to the infection.[7]

From a virology point of view, these 12 cases could be considered as an outbreak as, apart from having been concentrated in a period of about seven weeks, all EV-D68 belonged to clade A, subclade A1 which had circulated before 2014, while in a multicentre study conducted in Spain, all EV-D68 belonged to clade B and were genetically related to those detected in the United States and Canada in 2014.[2,6,7]

Acute respiratory infections caused by EV-D68 do not appear to have the same morbidity or virulence as the cases in the paediatric population. In spite of this, their incidence should continue to be monitored and, as far as possible, they should be genetically characterised.

## Conflicts of interest

The authors declare that they have no conflicts of interest.

## References

1. Schieble JH, Fox VL, Lennette EH. A probable new human picornavirus associated with respiratory diseases. Am J Epidemiol. 1967;85:297–310.
2. Messacar K, Abzug MJ, Dominguez SR. 2014 Outbreak of enterovirus D68 in North America. J Med Virol. 2016;88:739–45.
3. Böttcher S, Prifert C, Weinbrich B, Adams O, Aldabbagh S, Eis-Hübinger AM, et al. Detection of enterovirus D68 in patients hospitalised in three tertiary university hospitals in Germany, 2013 to 2014. Euro Surveill. 2016;21, pii=30227.
4. Schuffenecker I, Mirand A, Josset L, Henquell C, Hecquet D, Pilorge L, et al. Epidemiological and clinical characteristics of patients infected with enterovirus D68, France, July to December 2014. Euro Surveill. 2016;21, pii=30226.
5. Gimferrer L, Campins M, Codina MG, Esperalba J, Martin MC, Fuentes F, et al. First enterovirus D68 (EV-D68) cases detected in hospitalised patients in a tertiary care university hospital in Spain, October 2014. Enferm Infecc Microbiol Clin. 2015;33:585–9.
6. González R, Taravillo I, Reina J, Navascuences A, Moreno-Docón A, Aranzamendi M, et al. Spanish enteroviruses surveillance in respiratory infections and molecular epidemiology of EV-D68, 2014–2018. In: 21st European Society for Clinical Virology (ESCV). 2018. Oral Presentation O02, pp.12.
7. Ward NS, Hughes BL, Mermel LA. Enterovirus D68 infection in an adult. Am J Crit Care. 2016;25:178–80.
8. Meijer A, van der Sanden S, Snijders BE, Jaramillo-Gutierrez G, Bont L, van der Ent C, et al. Emergence and epidemic occurrence of enterovirus 68 respiratory infections in The Netherlands in 2010. Virology. 2012;423:49–57.
9. Lu QB, Wo Y, Wang HY, Wei MT, Zhang L, Yang H, et al. Detection of enterovirus 68 as one of the commonest types of enterovirus found in patients with acute respiratory tract infection in China. J Med Microbiol. 2014;63:408–14.
10. Zhang T, Li A, Chen M, Wu J, Huang F. Respiratory infections associated with enterovirus D68 from 2011 to 2015 in Beijing, China. J Med Virol. 2016;88:1529–34.
11. Poelman R, Schuffenecker I, van Leer-Buter C, Josset L, Niesters HG, Lina B, et al. European surveillance for enterovirus D68 during the emerging North-American outbreak in 2014. J Clin Virol. 2015;71:1–9.

Jordi Reina[a,*], María Cabrerizo[b], Ester del Barrio[a]

[a] *Unidad de Virología, Servicio de Microbiología, Hospital Universitario Son Espases, Palma de Mallorca, Spain*
[b] *Laboratorio de Enterovirus, Centro Nacional de Microbiología, Majadahonda, Madrid, Spain*

* Corresponding author.
*E-mail address:* jorge.reina@ssib.es (J. Reina).

2529-993X/


## Bilateral endophthalmitis as the initial presentation of pneumococcal endocarditis☆

### *Endoftalmitis bilateral como forma de presentación de una endocarditis neumocócica*

Endogenous or metastatic endophthalmitis due to haematogenous spread from an extraocular septic focus represents less than 10% of all forms of endophthalmitis.[1] Diabetes, immunosuppression and the use of parenteral drugs are well established risk factors. Bilateral involvement is rare and is more commonly seen in forms involving fungal aetiology.[1] Here we describe a case of bilateral endophthalmitis as the first manifestation of pneumococcal endocarditis and discuss our literature review on this clinical scenario.

The patient was an 80-year-old woman with a history of high blood pressure, morbid obesity, sleep apnoea-hypopnoea syndrome and obesity-hypoventilation syndrome, with chronic respiratory failure and permanent atrial fibrillation. A transthoracic echocardiogram performed one year prior showed a degenerative aortic valve with slightly decreased opening and mild regurgitation. Her usual treatment consisted of furosemide, acenocoumarol, candesartan and omeprazole. She had received the pneumococcal polysaccharide vaccine at the age of 66 years. The patient was assessed in the Accident and Emergency Department for general malaise, feeling hot and cold, drowsiness and sharp decrease in visual acuity in both eyes for 48 h. Physical examination revealed an axillary temperature of 39 °C with no data to suggest haemodynamic instability (blood pressure of 142/75 mmHg, heart rate of 98 bpm), a systolic murmur in aortic focus of intensity III/VI and bilateral ankle oedema. Eye examination revealed hyperaemic conjunctiva with transparent cornea and hypopyon in both eyes (more evident in the right), while the fundoscopy did not allow visualisation of the retinal structures due to opacity of the anterior media. Blood analysis showed thrombocytopenia ($76 \times 1000$ platelets/μl), deterioration in renal function (serum creatinine: 1.60 mg/dl) and elevated C-reactive protein (23.5 mg/dl [normal range: 0.10–0.50]). In view of suspected endogenous endophthalmitis, the patient was started on intravitreal treatment with ceftazidime and vancomycin (0.5 ml), in addition to systemic antibiotic therapy with piperacillin/tazobactam (4/0.5 g/6 h), levofloxacin (500 mg/12 h) and linezolid (600 mg/12 h). An emergency transthoracic echocardiogram revealed a mobile Image $1 \times 1.3$ cm

DOI of original article: https://doi.org/10.1016/j.eimc.2018.10.018.
☆ Please cite this article as: Fernández-Ruiz M, Vargas JC, Ruiz-Ruigómez M. Endoftalmitis bilateral como forma de presentación de una endocarditis neumocócica. Enferm Infecc Microbiol Clin. 2019;37:488–490.

**Table 1**
Cases reported in the literature of endogenous endophthalmitis in the context of pneumococcal endocarditis.

| Case, year | Gender, age | Predisposing factors | Valve affected | Characteristics of the endophthalmitis | Other manifestations | Systemic treatment | Intravitreous treatment and vitrectomy | Outcome |
|---|---|---|---|---|---|---|---|---|
| Case 1, 1996[2] | Male, 34 years | Chronic alcoholism | Mitral (native) | Bilateral | Meningitis | Ceftriaxone and thiamphenicol; valve resection with prosthesis implant | Thiamphenicol; vitrectomy | No perception of light in either eye |
| Case 2, 2003[3] | Male, 43 years | Diabetes | Aortic (native) | Unilateral (LE) | Pneumonia, perivalvular abscess, 2nd-degree AVB, purulent pericarditis | Ceftriaxone, vancomycin, gentamicin; valve resection with prosthesis implant | Ceftazidime and vancomycin | Death |
| Case 3, 2004[4] | Male, 55 years | No | Mitral (native) | Bilateral | No | Penicillin G and gentamicin; valve resection with prosthesis implant | Ceftazidime and vancomycin, radical vitrectomy | Partial recovery of VA (0.2 in RE and 0.25 in LE) |
| Case 4, 2005[5] | Male, 42 years | Alcoholism | Tricuspid (native) | Unilateral (RE) | No | Penicillin G and gentamicin ceftriaxone and vancomycin; valve resection with prosthesis implant | No | No perception of light in RE |
| Case 5, 2005[6] | Female, 50 years | No | Mitral (native) | Unilateral (RE) | Pneumonia, severe valve regurgitation | Not specified; valve resection with prosthesis implant | No | Death |
| Case 6, 2011[7] | Female, 63 years | Previous *S. agalactiae* endocarditis | Aortic (prosthetic) | Unilateral (RE), periorbital cellulitis | Perivalvular abscess, Mobitz type II 2nd-degree AVB | Vancomycin and gentamicin, linezolid moxifloxacin | Vancomycin and amikacin | No perception of light in RE |
| Case 7, 2014[8] | Female, 69 years | Diabetes, recurrent otitis media, heart valve disease | Aortic (native) | Bilateral (LE more affected) | No | Ceftriaxone and levofloxacin | No | No perception of light in LE, perception of light in RE |
| Case 8, 2015[9] | Male, 48 years | Rheumatic heart disease | Aortic and mitral (native) | Not specified | Liver and spleen abscess | Ceftriaxone and vancomycin penicillin G | Not specified | Cure (residual VA not specified) |
| Case 9, 2018[10] | Male, 56 years | Diabetes, otitis media | Aortic (native) | Bilateral | No | Ceftriaxone; valve resection with prosthesis implant | Ceftazidime and vancomycin | Perception of light in RE, partial recovery of VA (0.8) in LE |
| Our case | Female, 80 years | Degenerative heart valve disease | Mitral (native) | Bilateral (RE more affected) | No | Piperacillin/tazobactam, levofloxacin, linezolid ceftriaxone, ampicillin | Ceftazidime and vancomycin | Death |

AVB: atrioventricular block; LE: left eye; RE: right eye; VA: visual acuity.

in size in the anterior leaflet of the mitral valve protruding towards the left atrium, plus a second smaller lesion (0.5 × 0.5 cm) in the posterior leaflet, which was protruding towards the ventricle. These findings were compatible with endocarditis vegetations. In the two sets of blood cultures extracted when the patient arrived (time to positivity less than 12 h), the preliminary identification was of Gram-positive cocci in chains, so the systemic treatment was changed to ceftriaxone (2 g/24 h) and ampicillin (2 g/ h), continuing linezolid. In the end, isolation of *Streptococcus pneumoniae* was confirmed, with intermediate sensitivity to penicillin G (minimum inhibitory concentration: 1 mg/l), so the ampicillin was discontinued. A surgical approach to the endocarditis was ruled out because of the patient's poor baseline functional status and high burden of comorbidity. There was a slight improvement in the endophthalmitis in her right eye, with a decrease in hypopyon (1 mm). However, over the following 48 h the patient's clinical situation progressively deteriorated, resulting in her death due to multiple organ failure.

Endogenous endophthalmitis is an uncommon complication in the course of bacteraemia and tends to be devastating in terms of visual prognosis, with any delay in diagnosis being a further contributory factor. The microorganism penetrates the eyeball through the vessels of the posterior pole and, after crossing the blood/eye barrier, it spreads from the retina and choroid to the vitreous body and, finally, the anterior chamber. The sources of bacteraemia most commonly reported in the literature include intravascular catheters, endocarditis and, more rarely, liver abscesses, while *Klebsiella pneumoniae* (particularly strains of serotypes K1 and K2 carrying the *magA* gene associated with hypermucoviscosity in Asian series), *Staphylococcus aureus* and streptococci are the most common agents.[1]

Although *Streptococcus pneumoniae* has been described in some series as the fourth leading cause of endogenous endophthalmitis,[1] bilateral involvement as a form of presentation of pneumococcal endocarditis is unusual. We searched the PubMed database (MeSH terms: "*Streptococcus pneumoniae*" or "*pneumococcus*" plus "*endophthalmitis*" plus "*endocarditis*"), and did a manual review of the list of references of the identified articles, revealing nine additional cases[2–10] reported up to September 2018 (Table 1). There was a predominance of native valve endocarditis[2–6,8–10] and in four patients (40%) other concurrent manifestations of invasive pneumococcal disease were associated, such as meningitis,[2] pneumonia[3,6] and visceral abscesses.[9] The endophthalmitis was bilateral in half of the series. In six of the cases with available information (66.7%), intravitreal antibiotic treatment was administered,[2–4,7,10] although the utility of this strategy in endogenous endophthalmitis is less established than in exogenous forms, probably due to the low incidence of the complication. For that reason, systemic treatment should include antibiotics with good penetration into the eyeball, such as linezolid or fluoroquinolones.[7,8] Only two of the cases reviewed involved vitrectomy.[2,4] However, vitrectomy should not be delayed in the forms caused by aggressive microorganisms such as *S. aureus* or *K. pneumoniae*.[1] The outcomes were adverse in general terms, as two patients[3,6] (in addition to our case) died, while among the survivors, there was only partial recovery in visual acuity in three of the 10 affected eyes.[4,10]

In conclusion, in a patient with bilateral endophthalmitis, an endogenous mechanism secondary to haematogenous spread from an extraocular focus should be considered. On rare occasions, pneumococcal endocarditis could constitute the underlying disease. The poor prognosis in terms of visual sequelae and the life-threatening nature of this disorder, demonstrated by our experience and in the review of the literature, means that a high degree of clinical suspicion is vital, followed by an aggressive diagnostic approach for early instigation of the appropriate systemic and intraocular treatment.

## Acknowledgements

The authors would like to thank the staff of the Hospital Universitario 12 de Octubre library for their help in obtaining the articles included in this literature review.

## References

1. Durand ML. Bacterial and fungal endophthalmitis. Clin Microbiol Rev. 2017;30:597–613.
2. Magadur-Joly G, Raffi F, Bouchut P, Chevalet P, Merrien D, Struillou L, et al. [Hematogenic bacterial endophthalmitis. A rare infection with very poor functional prognosis]. Ann Med Interne (Paris). 1996;147:212–7 (in French).
3. Rubin RH, King ME, Mark EJ. Case record of the Massachusetts General Hospital. Weekly clinicopathological exercises. Case 7-2003. A 43-year-old man with fever, rapid loss of vision in the left eye, and cardiac findings. N Engl J Med. 2003;348:834–43.
4. Christensen SR, Hansen AB, la Cour M, Fledelius HC. Bilateral endogenous bacterial endophthalmitis: a report of four cases. Acta Ophthalmol Scand. 2004;82:306–10.
5. Akcam FZ, Yayli G, Kaya O, Gonen I. Unusual presentation of infective endocarditis caused by *Streptococcus pneumoniae* on native tricuspid valve. Saudi Med J. 2005;26:334–5.
6. Ortiz P, Monivas V, Fuentes R, Toquero J. Endophthalmitis, pneumonia, and a heart murmur. Heart. 2005;91:532.
7. O'Brien S, Dayer M, Benzimra J, Hardman S, Townsend M. Streptococcus pneumoniae endocarditis on replacement aortic valve with panopthalmitis and pseudoabscess. BMJ Case Rep. 2011, http://dx.doi.org/10.1136/bcr.06.2011.4304.
8. Thaisiam P, Rattanaumpawan P. Rare manifestations of *Streptococcus pneumoniae* infection; the first case report in Thailand and literature review of pneumococcal endophthalmitis and endocarditis. J Med Assoc Thai. 2014;97:1364–9.
9. De Egea V, Muñoz P, Valerio M, de Alarcón A, Lepe JA, Miró JM, et al. Characteristics and outcome of *Streptococcus pneumoniae* endocarditis in the XXI Century: a systematic review of 111 cases (2000–2013). Medicine (Baltimore). 2015;94:e1562, http://dx.doi.org/10.1097/MD.0000000000001562.
10. Brill DA, Farley ND, Albert DC, Sassalos TM, Sangave AA, Desai UR. Bilateral endogenous endophthalmitis from *Streptococcus pneumoniae*. Retin Cases Brief Rep. 2018, http://dx.doi.org/10.1097/ICB.0000000000000760.

Mario Fernández-Ruiz [a,*], Julio César Vargas [b,1], María Ruiz-Ruigómez [a]

[a] *Unidad de Enfermedades Infecciosas, Hospital Universitario 12 de Octubre, Instituto de Investigación Hospital 12 de Octubre (imas12), Madrid, Spain*
[b] *Servicio de Medicina Interna, Sanatorio Internacional, Ciudad del Este, Paraguay*

* Corresponding author.
*E-mail address:* mario_fdezruiz@yahoo.es (M. Fernández-Ruiz).
[1] The affiliation of Julio César Vargas at the time of this article was Internal Medicine Service of the Hospital Universitario 12 de Octubre, Madrid, Spain.

2529-993X/