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Viral and Bacterial Causes of Labyrinthitis

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Labyrinthitis is a known inflammation of the membranous structure of the inner ear. Affected patients usually present with nausea and vomiting, vertigo, hearing loss/impairment, and tinnitus. Many etiologies have been proposed to lead to the development of labyrinthitis, including bacterial, viral, systemic, and iatrogenic causes and the most commonly reported causes include viral and bacterial infections. Not many investigations have elaborated on the viral and bacterial etiologies, and the evidence seems to be scattered across the different studies. In the present study, we have

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reviewed the literature to discuss the current evidence regarding the viral and bacterial causes of labyrinthitis. Many viruses and bacteria were reported in the literature to cause the condition. However, the most common pathogen includes cytomegalovirus and maternal rubella infections, leading to congenital hearing loss. Other viruses as measles and mumps might also lead to developing post-natal labyrinthitis. Studies also indicates that COVID-19 can be a recent cause of the disease. However, evidence regarding this information, similar to the case with other viral and bacterial etiologies, still needs further validation and reporting before making solid conclusions. Accordingly, we encourage researchers to furtherly report about similar cases and conduct epidemiological investigations to better understand the etiology of the disease.

Keywords: Labyrinthitis; viral; bacterial; etiology.

1. INTRODUCTION

Labyrinthitis is a known inflammation of the membranous structure of the inner ear. Affected patients usually have nausea and vomiting, vertigo, hearing loss/impairment, and tinnitus [1]. However, a previous study indicated that the incidence of the condition is directly correlated with age [2]. Many disorders can have clinical presentations similar to labyrinthitis, including cerebrovascular accidents, and therefore, conducting a proper differential diagnosis by carefully examining the patient and obtaining entire history is essential to establish a correct diagnosis [3]. The treatment of the condition is mainly based on symptomatic management of the patient, and dealing with the underlying etiology. Adequate treatment is also vital to enhance the prognosis because in some cases, hearing problems and residual balance might develop even after achieving complete recovery.

Many etiologies have been proposed to lead to the development of labyrinthitis, including bacterial, viral, systemic, and iatrogenic causes and the most commonly reported causes include viral and bacterial infections [4,5]. Not many investigations have elaborated on the viral and bacterial etiologies, and the evidence seems to be scattered across the different studies. Therefore, we aimed to conduct this study to better understand the viral and bacterial etiologies of labyrinthitis.

2. REVIEW

To better understand the etiology and pathophysiology of labyrinthitis, it is critical to understand the anatomical association of the labyrinth and the related structures of the mastoid, middle ear, and subarachnoid space. Furthermore, the labyrinth is composed of a membranous delicate network that involves the main bulk of the peripheral sensory structures for balance and hearing and is also found surrounded by an outer osseous framework [6,7]. The sensory organs that are present in this structure include the saccule, utricle, cochlea, and semicircular canals (Fig. 1). Labyrinthitis can be caused by induced inflammation or infection to the membranous labyrinth and can be caused by systemic, bacterial, and viral diseases [4]. Patients might present due to symptoms of labyrinthitis as a result of the presence of underlying etiology, including the aforementioned ones, and by inflammatory mediators, which attack the membranous labyrinth leading to significant damage in the related structures that might even end up with the hearing loss.Besides, it has been demonstrated that ina few cases with labyrinthitis, some complications including labyrinthitis ossificans, which is known as a pathological formation of new bone within the membranous structures of the labyrinth [8]. Accordingly, cochlear implantation decisions should be considered as early as possible in these situations to enhance the prognosis. Fibrosis and necrosis might also affect the labyrinth and membranous cochlea as a result of meningitis, which can significantly lead to the development of progressive hearing loss [9]. Studies also shows that labyrinthitis can also be termed as vestibular neuritis, and the two terms are widely used interchangeably in the literature [10]. However, it should be noted that the latter term should only be used in cases when the vestibular nerve is the only involved structure for a better nomination.

The labyrinth is located within the petrous part of the temporal bone near the mastoid cavity. Besides, it has also been found in direct relation with the round, and oval windows of the middle ear. The cochlear aqueduct and the internal auditory canal also maintain a connection between the labyrinth and the central nervous system. Consequently, microorganisms might get access to the labyrinth from these structures and

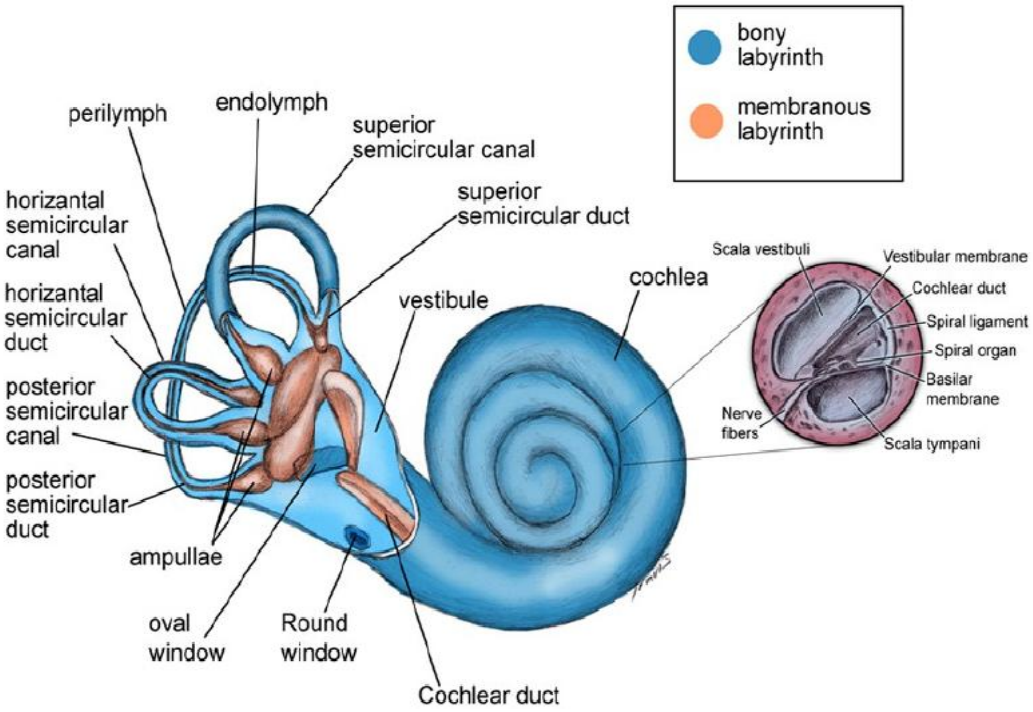

Fig. 1. Anatomical structure of the inner ear

cause the infection. Acquired or congenital defects of the bony labyrinth might also pave the way for bacterial and viral infections to induce labyrinthitis [6]. Hematogenous spread of the microorganisms was also previously indicated, and therefore, all of these pathways might help understand the pathology of labyrinthitis. Bacterial and viral labyrinthitis are common topics in this field that were adequately discussed in the literature and will be reviewed in the coming section of this article.

Viral etiologies of upper respiratory tract infections attribute to the most common causes of labyrinthitis. Besides, it has been demonstrated that cytomegalovirus or maternal rubella infection attribute to the most common causes of labyrinthitis-induced congenital deafness. In this context, estimates also show that the main causes of hearing loss within the post-natal period include measles and mumps infections [11-14]. Herpes zoster oticus or Ramsay-Hunt syndrome is also an infection to the labyrinth that is caused by reactivation of a latent infection by the varicella-zoster virus usually years, since the primary infection was first detected [15]. Evidence indicates that the main presentation of such infection can be mainly observed as a vesicular rash alongside the ear and oral mucosa, in addition to a classical paralysis of the peripheral facial nerve. It has been furtherly estimated that within up to 25% of the infected cases, the cochlear and vestibular nerves might be involved in the clinical presentation [16]. It should be noted that the etiology of the sensineuronal hearing loss secondary to cytomegalic viral infection is still of unknown mechanism. However, some authors suggested that inflammatory mediators might attribute to the development and pathology of the condition [17,18]. Little is known about the incidence of viral causes of labyrinthitis. Nevertheless, some epidemiological studies reported a variety of viruses that have been commonly associated with the development of labyrinthitis. Axonal degeneration of the vestibular nerve can predict the presence of viral labyrinthitis which might also perceed the development of vestibular neuritis [19]. Some of the reported virsus include influenza, parainfluenza, adenovirus, hipres simplex virus 1, coxsachievirus, rubella, respiratory syncetial, rubeola viruses, in addition to the previously mentioned varicella-zoster and mumps viruses, and cytomegalovirus. Recent data also indicated that COVID-19, a recent pandemic that is caused by severe acute respiratory syndrome (SARS)-2 virus, was also reported to be a common virological cause of labyrinthitis [20]. The damaging impact of COVID-19 on the hearing organs has been previously demonstrated. Nonetheless, the main mechanisms are not well

understood. On the other hand, it has been proposed that direct viral invasion and immune-medicated mechanisms secondary to systemic viral infections might be accepted theories for such infections of the labyrinth [21]. Investigations also demonstrated that otitis could result secondary to COVID-19 [22-26]. However, it should be noted that such events are not very common in this setting and are based on single case reports [22,27,28]. Furtherly, COVID-19 induced labyrinthitis usually develops within the acute phase of the infection based on the duration of patients' presentations with labyrinthitis-related symptoms and the time when COVID-19 diagnosis was established [20,29]. Another recent comparative investigation also indicates that cochlear involvement in COVID-19 is a frequent event, regardless of the presence of other COVID-19-related major manifestations [30].

On the other hand, estimates show that bacterial labyrinthitis usually develops due to otitis media and/or bacterial meningitis. Studies show that around 20% of children that have been diagnosed with bacterial meningitis, vestibular and auditory symptoms are usually observed among them [31,32]. It should be noted that the incidence of bacterial labyrinthitis has significantly decreased due to the administration of effective antibiotics to eliminate the infection before it can reach the labyrinth and induce the pathology of labyrinthitis. However, estimates indicated that meningitis-induced labyrinthitis is still a critical cause of hearing loss in clinical settings [32]. Otogenic infections usually attribute to a unilateral infection of one year, while meningitis-induced infections usually lead to a bilateral infection.Two different mechanisms might attribute to the development of this phenomenon. The inflammatory mediator or host cytokine and/or bacterial toxins with no detected bacteria might lead to the development of inflammation-induced serous labyrinthitis [33]. Studies show that this complication is a common sequela of otitis media and reports indicate that it is commonly associated with chronic and acute middle ear disorders. The central theme in the mechanism of serous labyrinthitis is the significant infiltration of the scala tympani by enzymes, toxins, and other inflammatory mediators leading to the development of a fine precipitate that lies medially to the membrane of the round window. A high frequency, mild-to-moderate sensorineural hearing loss might also develop due to endolymph penetration by the inflammatory mediators at the basilar part of the cochlea [16,18,34,35]. When effusion of the middle ear can still be detected, mixed hearing loss can significantly be revealed by audiometric testing. Furthermore, vestibular manifestations might also be associated. Nevertheless, these are not very common in this event. Adequate treatment can significantly enhance hearing functions. However, hearing loss can persist if adequate treatment modalities are not applied. Management of the condition is done by adequately cleaning the middle ear and eliminating the infection.

Bacteria can also be a direct cause of inflammation, and can directly lead to the development of suppurative labyrinthitis [33]. As previously mentioned, infecting bacteria can affect the labyrinth through the round and oval windows which connect it with the surrounding structures of the middle ear, or through the auditory canal and the cochlear aqueduct which connect it with the surrounding structures of the central nervous system, or through acquired and congenital defects as previously demonstrated [6,36].Moreover, a dehiscent horizontal semicircular can be the pathway for bacterial spread from the middle ear and mastoid to the labyrinth leading to the development of labyrinthitis.This has been observed in cases of cholesteatoma, which has been reported to be commonly associated with suppurative labyrinthitis and is a direct cause of the formation of this dehiscence. However, it should be noted that the incidence of suppurative labyrinthitis has also significantly decreased as a result of the administration of efficacious antibiotics. Severe vertigo, profound hearing loss, nausea and vomiting, and ataxia are common symptoms that are usually observed in patients with bacterial labyrinthitis. Some of the reported bacteria in the literature include *Moraxella catarrhalis, Streptococcus pneumoniae, Neisseria meningitidis, Haemophilus influenzae, Proteus species, Mycobacterium tuberculosis, Bacteroides species, Staphylococcus species, Streptococcus species, and Escherichia coli.* These bacteria are suggested based on the previous suggestion that the bacteria that can cause otitis and meningitis can significantly cause labyrinthitis. Finally, it has been estimated that gram-negative bacterial pathogens are more commonly observed when cholesteatoma is diagnosed alongside bacterial labyrinthitis.

Other causes of labyrinthitis that have been reported in the literature might also include autoimmune diseases. For instance, it has been

evidenced that granulomatosis with polyangiitis and polyarteritis nodosa might be complicated by the development of labyrinthitis is a rare event [37,38]. Human immunodeficiency virus and syphilis infections might also attribute to the development of labyrinthitis. However, evidence regarding the development of this phenomenon is scarce in the literature and the primary mechanism is not completely understood. However, some theories attribute it to the state of immunosuppression secondary to these infections, while others attribute it to the infecting viruses [3,39]. Iatrogenic causes of labyrinthitis were also reported in the literature secondary to the administration of some drugs as aminoglycosides, and furosemide for a prolonged period, and high doses of phenytoin, leading to significant toxicity. Alcohol abuse, direct trauma to the ear, ear tumors, and allergies might also precipitate the development of labyrinthitis. Besides, a differential diagnosis should also be established with similar conditions that might induce similar clinical manifestations to establish a proper diagnosis and plan adequate treatment plan to enhance the prognostic outcomes of the affected patients.

3. CONCLUSION

In the present study, we have reviewed the literature to discuss the current evidence regarding the viral and bacterial causes of labyrinthitis. Many viruses and bacteria were reported in the literature to cause the condition. However, the most common pathogen includes cytomegalovirus and maternal rubella infections, leading to congenital hearing loss. Other viruses such as measles and mumps might also lead to developing post-natal labyrinthitis. Recent evidence revealed that COVID-19 can be a recent cause of the disease. Nonetheless, evidence regarding this information, similar to the case with other viral and bacterial etiologies, still needs further validation and reporting before making solid conclusions. Accordingly, we encourage researchers to furtherly report about similar cases and conduct epidemiological investigations to better understand the etiology of the disease.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Wipperman J. Dizziness and vertigo. Prim Care. 2014;41(1):115-31.
2. Koo JW, et al. Prevalence of vestibular dysfunction and associated factors in South Korea. BMJ Open. 2015;5(10):e008224.
3. Barkwill D, Arora R. Labyrinthitis, in StatPearls. StatPearls Publishing Copyright © 2021, StatPearls Publishing LLC.: Treasure Island (FL); 2021.
4. Thompson TL, Amedee R. Vertigo: A review of common peripheral and central vestibular disorders. Ochsner J. 2009; 9(1):20-6.
5. Ortiz de Mendivil A, et al. Brainstem stroke: Anatomy, clinical and radiological findings. Semin Ultrasound CT MR. 2013; 34(2):131-41.
6. Sennaroğlu L, Bajin MD. Classification and Current Management of Inner Ear Malformations. Balkan Med J. 2017; 34(5):397-411.
7. Ekdale EG. Form and function of the mammalian inner ear. J Anat. 2016; 228(2):324-37.
8. Lin HY, et al. The incidence of tympanogenic labyrinthitis ossificans. J Laryngol Otol. 2014;128(7):618-20.
9. Berlow SJ, et al. Bacterial meningitis and sensorineural hearing loss: A prospective investigation. Laryngoscope. 1980;90(9): 1445-52.
10. Jeong SH, Kim HJ, Kim JS. Vestibular neuritis. Semin Neurol. 2013;33(3):185-94.
11. Hviid A, Rubin S, Mühlemann K. Mumps. Lancet. 2008;371(9616):932-44.
12. Moss WJ. Measles. Lancet. 2017; 390(10111):2490-2502.
13. Yazigi A, et al. Fetal and neonatal abnormalities due to congenital rubella syndrome: A review of literature. J Matern Fetal Neonatal Med. 2017;30(3):274-278.
14. Fowler KB, Boppana SB. Congenital cytomegalovirus infection. Semin Perinatol. 2018;42(3):149-154.
15. Jeon Y, Lee H. Ramsay Hunt syndrome. J Dent Anesth Pain Med. 2018;18(6):333-337.
16. Hato N, et al. Ramsay Hunt syndrome in children. Ann Neurol. 2000;48(2):254-6.

17. Kuhn M, et al. Sudden sensorineural hearing loss: A review of diagnosis, treatment, and prognosis. Trends Amplif. 2011;15(3):91-105.
18. Schraff SA, et al. Macrophage inflammatory proteins in cytomegalovirus-related inner ear injury. Otolaryngol Head Neck Surg. 2007;137(4):612-8.
19. Schuknecht HF, Kitamura K. Second Louis H. Clerf Lecture. Vestibular neuritis. Ann Otol Rhinol Laryngol Suppl. 1981;90(1 Pt 2):1-19.
20. Perret M, et al. Acute Labyrinthitis Revealing COVID-19. Diagnostics (Basel). 2021;11(3).
21. Merchant SN, Durand ML, Adams JC. Sudden deafness: Is it viral? ORL J Otorhinolaryngol Relat Spec. 2008;70(1): 52-60; Discussion 60-2.
22. Chirakkal P, et al. COVID-19 and Tinnitus. Ear Nose Throat J. 2021;100(2_suppl): 160s-162s.
23. Fidan V. New type of corona virus induced acute otitis media in adult. Am J Otolaryngol. 2020;41(3):102487.
24. Lamounier P, et al. A 67-Year-Old Woman with Sudden Hearing Loss Associated with SARS-CoV-2 Infection. Am J Case Rep. 2020;21:e927519.
25. Mohan S, et al. Considerations in Management of Acute Otitis Media in the COVID-19 Era. Ann Otol Rhinol Laryngol. 2021;130(5):520-527.
26. Chern A, et al. Bilateral Sudden Sensorineural Hearing Loss and Intralabyrinthine Hemorrhage in a Patient With COVID-19. Otol Neurotol. 2021;42(1):e10-e14.
27. Elibol E. Otolaryngological symptoms in COVID-19. Eur Arch Otorhinolaryngol. 2021;278(4):1233-1236.
28. Viola P, et al. Tinnitus and equilibrium disorders in COVID-19 patients: preliminary results. Eur Arch Otorhinolaryngol. 2021;278(10):3725-3730.
29. Rahman A, et al. Hematological Abnormalities in COVID-19: A Narrative Review. Am J Trop Med Hyg. 2021; 104(4):1188-201.
30. Mustafa MWM. Audiological profile of asymptomatic Covid-19 PCR-positive cases. Am J Otolaryngol. 2020;41(3):102483.
31. Nadol JB Jr. Hearing loss as a sequela of meningitis. Laryngoscope. 1978;88(5):739-55.
32. Wu JF, et al. Extracranial and intracranial complications of otitis media: 22-year clinical experience and analysis. Acta Otolaryngol. 2012;132(3):261-5.
33. Jang CH, Park SY, Wang PC. A case of tympanogenic labyrinthitis complicated by acute otitis media. Yonsei Med J. 2005; 46(1):161-5.
34. Kuhweide R, et al. Ramsay Hunt syndrome: pathophysiology of cochleovestibular symptoms. J Laryngol Otol. 2002;116(10):844-8.
35. Thieu H, et al. Antibiotic resistance of Helicobacter pylori infection in a children's hospital in Vietnam: prevalence and associated factors. Minerva Med. 2020;111(5):498-501.
36. Nguyen TM, et al. Clinical features and outcomes of neonatal dengue at the Children's Hospital 1, Ho Chi Minh, Vietnam. J Clin Virol. 2021;138:104758.
37. Broughton SS, Meyerhoff WE, Cohen SB. Immune-mediated inner ear disease: 10-year experience. Semin Arthritis Rheum. 2004;34(2):544-8.
38. Harris JP, Ryan AF. Fundamental immune mechanisms of the brain and inner ear. Otolaryngol Head Neck Surg. 1995; 112(6):639-53.
39. de Jong MA, Luder A, Gross M. Main Aspects of peripheral and central hearing system involvement in Unexplained HIV-Related Hearing Complaints. Front Neurol. 2019;10:845.

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