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What differences lymphoma from vestibular schwannoma?

O que diferencia o linfoma do schwannoma vestibular?

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ABSTRACT

Introduction: Vestibular schwannoma (VS) is a benign tumor originating in the Schwann cells surrounding the vestibular nerve. Its initial symptoms include progressive hearing loss in one ear, representing an intracranial threat due to the mass effect. On the other hand, cerebral lymphomas, although rare, present with a variety of focal and non-focal neurological symptoms. The association of rapidly progressive unilateral hearing loss, tinnitus and vestibular dysfunction suggests VS.

Objective: To search for cases of lymphoma mimicry in relation to vestibular schwannoma, to describe the differential diagnosis and events associated with it.

Method: Integrative review conducted with methodological rigor, gathering evidence for clinical practice. It was performed in the PubMed and Medline databases, using the Boolean operator "AND" to associate relevant descriptors.

Result: Of the 96 articles found, 8 were selected based on the guiding question. Original studies in English or Spanish were included. Early diagnosis of VS is based on magnetic resonance imaging and hearing tests. Radiotherapy is a viable alternative. Furthermore, intracanalicular lesions of the internal auditory nerve are frequently VSs, but differential diagnoses should consider other possibilities, such as facial neuroma. The radiological features of VSs are not specific, and differential diagnoses need to be considered.

Conclusion: Differentiating lymphomas located in the cerebellopontine angle from VSs is crucial to avoid inappropriate treatments. Radiosurgery proposed for presumed small VSss may be inappropriate if the diagnosis is another one, such as lymphoma. Therefore, it is essential to obtain an accurate histopathological diagnosis to guide appropriate treatment.

KEYWORDS: Lymphoma. Auditory nerve. Acoustic neuroma. Vestibular schwannoma.

RESUMO

Introdução: O schwannoma vestibular (SV) é tumor benigno originado nas células de Schwann que circundam o nervo vestibular. Seus sintomas iniciais incluem perda auditiva progressiva em um dos ouvidos, representando ameaça intracraniana pelo efeito de massa. Por outro lado, os linfomas cerebrais, embora raros, apresentam-se com variedade de sintomas neurológicos focais e não focais. A associação de perda auditiva unilateral rapidamente progressiva, zumbido e disfunção vestibular sugere SV.

Objetivo: Buscar casos de mimetismo de linfomas em relação ao schwannoma vestibular, para descrever o diagnóstico diferencial e os eventos associados a ele.

Método: Revisão integrativa conduzida com rigor metodológico, reunindo evidências para a prática clínica. Foi realizada nas bases de dados PubMed e Medline, utilizando o operador booleano "AND" para associar descritores relevantes.

Resultado: Dos 96 artigos encontrados, 8 foram selecionados com base na questão norteadora. Foram incluídos estudos originais em inglês ou espanhol. O diagnóstico precoce do SV baseia-se em ressonância magnética e testes auditivos. A radioterapia é alternativa viável. Além disso, lesões intracanaliculares do nervo auditivo interno são frequentemente SVs, mas diagnósticos diferenciais devem considerar outras possibilidades, como neuroma facial. As características radiológicas do SV não são específicas, e diagnósticos diferenciais precisam ser considerados.

Conclusão: Diferenciar linfomas localizados no ângulo pontocerebelar de SV é crucial para evitar tratamentos inadequados. A radiocirurgia proposta para supostos SVs pequenos pode ser inapropriada se o diagnóstico for outro, como um linfoma. Assim, é fundamental obter diagnóstico histopatológico preciso para orientar o tratamento adequado.

PALAVRAS-CHAVE: Linfoma. Nervo auditivo. Neuroma acústico. Schwannoma vestibular.

Central Message

The article explores the differential diagnosis between vestibular schwannoma and intracranial lymphoma, highlighting the clinical and radiological similarities that can lead to misdiagnosis. Accurate identification of these conditions is essential to ensure correct treatment, avoiding inappropriate interventions, such as radiosurgery in cases of lymphoma.

Perspective

The review reinforces the importance of early differentiation between vestibular schwannoma and lymphoma, using advanced imaging techniques and collaboration with neuroradiologists. The article highlights that inaccurate diagnoses can result in inaccurate treatments, underlining the need for rigor in the diagnostic process.

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INTRODUCTION

Vestibular schwannoma (VS) is a benign tumor that originates in the cells surrounding the vestibular nerve (Schwann cells). Initial symptoms, as the tumor grows and presses on the auditory nerve, include progressive hearing loss in one ear. It poses a threat to intracranial structures due to the mass effect and presents a small risk of malignant transformation.[1]

Regarding lymphomas, the incidence varies from 0.[4] to 0.5 per 100,000 inhabitants per year, corresponding to less than 1% of all non-Hodgkin's lymphomas and 3% of all brain malignancies. Presents with focal neurologic deficits (70–73%), neuropsychiatric symptoms (28–43%), seizures (9–14%), ocular symptoms (4%), and increased intracranial pressure (3–33%). Most lymphomas are supratentorial and localized intra-axially. Most supratentorial lesions occur in the cerebral white matter or corpus callosum, some in the deep central gray nucleus, the posterior fossa, and rarely in the spinal cord.[2]

The association of rapidly progressive unilateral hearing loss, tinnitus, and vestibular dysfunction in combination with a contrast-enhanced mass within the internal auditory canal on magnetic resonance imaging (MRI) suggests VS.[3] In this sense, the scope of the present review was to search the literature for cases of lymphoma mimicry in relation to VS, in order to describe the differential diagnosis and the events associated with this distinction.

METHOD

This article is an integrative literature review, a methodical analysis method that gathers evidence for clinical practice, through search, evaluation and synthesis of available information on the specific topic to be analyzed. To carry out the present study, the following methodological steps were followed: identification of the theme and guiding question of the research; definition of inclusion and exclusion criteria; identification of the information to be extracted from the selected articles; analysis and interpretation of the results and presentation of the review.

At first, the theme "vestibular schwannoma and its neurosurgical approaches" was established. Next, the guiding question was defined: "How can lymphoma mimic a vestibular schwannoma?".

For scientific basis, searches were carried out in the PubMed and Medline databases, using the Boolean operator "AND" to associate the descriptors in the search.

Of the 96 articles found, 7 were chosen with a view to reading the article and selection based on relevant aspects of the guiding question, series and case reports on lymphomas mimicking VS were chosen to compose the present review.

Only original studies related to the theme that answered the guiding question in English or Spanish were included. At the same time, duplicate articles, review articles, and those that do not fit the theme of the present review were excluded, resulting in 36 articles in Pubmed and 46 in Medline.

DISCUSSION

Early diagnosis of VS is based on MRI and hearing tests. It is usually unilateral but may be bilateral in neurofibromatosis type 2. In addition, there are several surgical techniques to remove VS, the most common being translabyrinthine and rectosigmoid approaches. Due to surgical risks, such as hearing loss, facial nerve dysfunction, postoperative headache, and cerebrospinal fluid leakage, a "look and re-examine" approach is adopted for most patients. Radiotherapy is a useful alternative and has been shown to have a similar response to growth restriction.[4]

Intracanalicular injury of the internal auditory nerve represents VS in most cases. In the presence of facial paralysis, this could possibly represent facial neuroma, although they involve the labyrinthine/tympanic or mastoid segment of the facial nerve. The rare but possible differential diagnosis of the lesions needs to be considered when dealing with the reviewed region carefully before concluding the lesion as VS exclusively. With the improvement of imaging modalities, attention should be paid to detailed MRI. Discussing the case with the neuroradiology team should be a routine protocol that could help avoid misdiagnoses of the disease.[5]

The radiological characteristics of this tumor are not specific in conventional MRI, and advanced imaging techniques, such as diffusion-weighted MRI (DWI), diffusion tensor imaging, MRI perfusion, and MRI spectroscopy, have been shown to be useful for differentiating primary lymphomas of the central nervous system from other neoplasms. According to Arcuri et al.[6] MR spectroscopy played an important role in the diagnosis of primary cerebellopontine angle lymphoma and in the differentiation of this from acoustic schwannoma or meningioma.

Lymphoma can occasionally mimic VS, presenting diagnostic challenges due to clinical and radiographic similarities. The correct identification of these masses is crucial for proper management. Masses in the cerebellopontine and intracanalicular angle may be misdiagnosed as VSs, with a small percentage revealing themselves as other diagnoses, including lymphoma. The clinical presentation of unilateral progressive sensorineural hearing loss, tinnitus, and vestibular dysfunction, together with a contrast-enhancing mass in the internal auditory canal on MRI, is suggestive of VS, but may be lymphoma, especially in patients with HIV. Its most common symptoms include hearing loss and tinnitus, with only half of patients experiencing vertigo attacks, which can be similar to the clinical presentation of VS-mimicking lymphomas.[7]

Epidemiology and etiology

Schwannomas account for 8-10% of all intracranial tumors and 75% of tumors cerebellopontine angle. The overall incidence is 3-5 cases per 100,000 person-years, and in the age group over 70 years, the incidence rises to 20 cases per 100,000 person-years. This estimate has increased in recent decades due to the dissemination of more accurate imaging tests, such as contrast-enhanced MRI. However, it is believed that the prevalence is higher than what has already been verified, since many cases are asymptomatic and have slow growth.[1]

VS is unilateral 95% of the time and usually has sporadic onset. However, the relationship with the highest incidence of these tumors in patients with neurofibromatosis is known. The bilateral presentation is pathognomonic of neurofibromatosis type 2. This relationship should also be suspected in patients with unilateral tumors and younger than 40 years of age, since most sporadic cases are diagnosed between the sixth and seventh decade of life.[1,2] These tumors originate due to the loss of a tumor suppressor gene on the long arm of chromosome 22. In cases of neurofibromatosis type 2, this condition can be inherited or passed on to the next generations in an autosomal dominant manner.[2]

Clinical presentation

Clinical manifestations vary considerably depending on the location and size of the tumor, as well as the compression of other nearby cranial nerves. The classic symptomatic triad is ipsilateral hearing loss (>90%), asymmetric tinnitus (55%), and dizziness or imbalance (up to 61%).[1]

Initially, due to the involvement of the vestibular portion of the VIII nerve, imbalance occurs, and in less than 20% of cases, true vertigo may occur. However, as the tumor grows, vestibular function is centrally compensated, which reduces the intensity and perception of this symptom. A clinical sign that may be present is nystagmus or electronystagmography altered by caloric stimulation.

Sensorineural hearing loss and high-pitched tinnitus occur when there is compression of the auditory nerve in the internal auditory canal, which is usually the main complaint that leads to seeking medical attention. The more lateralized the tumor is in the internal auditory canal, the earlier the hearing loss. Hearing loss tends to be unilateral, progressive, and insidious. Up to 70% of patients have hearing loss with predominance in high frequencies (4,000 to 5,000 Hertz) and decreased word discrimination. Although less frequent, about 10% may report sudden hearing loss. Therefore, VS should always be considered as a differential diagnosis in patients with sudden deafness.[2]

Larger tumors can compress the facial nerve and trigeminal nerve, causing hypoesthesia with trigeminal distribution, secondary trigeminal neuralgia, paresthesia, facial weakness and spasms, and even changes in taste. In addition, compression of the brainstem and lower cranial nerves may occur, resulting in symptoms depending on the function of the affected structure. Compression of the cerebellum can lead to dysbasia, dysmetria, or cerebellar ataxia. Schwannomas larger than 4 cm can lead to secondary hydrocephalus due to obstruction that hinders cerebrospinal fluid resorption.

Symptoms arising from facial nerve, trigeminal motor, or lower cranial nerve dysfunction are possible, but are uncommon even in large tumors. Therefore, when present, they should be considered differential diagnoses.[1]

Diagnosis

Currently, the gold standard in tumor investigation is gadolinium contrast MRI, due to its high sensitivity (98%) and excellent specificity, allowing the detection of even very small tumors. However, in cases of unavailability of this exam or contraindication, it is possible to resort to contrast-enhanced computed tomography.

Tumors that have a rounded or oval shape in the center of the internal auditory canal are suggestive of VS, as well as narrowing of the base of the internal auditory canal. These tumors may present isointensity or hyperintensity on T1-weighted sequences and hyperintensity on T2-weighted sequences, in addition to exhibiting heterogeneity in contrast uptake.[1-3] It is important to note that schwannomas larger than 3 cm in diameter can also resemble cystic areas, despite being predominantly solid.

It is essential to perform the differential diagnosis with other tumors that affect the cerebellopontine angle, such as meningiomas, epidermoid tumors, arachnoid cysts, and metastases.

Evaluation

In addition to imaging tests, audiometric evaluation is recommended, including pure-tone audiogram and vocal discrimination tests. For patients with small tumors (1.5 cm or less), nystagmography and vestibular evoked myogenic potential, which evaluate the upper and lower division of the vestibular nerve, respectively, is advisable. These tests help in understanding the location of the tumor in relation to its depth and proximity to the cochlear nerve. In addition, auditory brainstem response testing can provide information about the prognosis of hearing preservation.

Evolution

VS usually exhibits indolent behavior and may remain stable for long periods or have extremely gradual growth. It is considered slow growing when it reaches up to 2 mm per year, while it is classified as fast when it exceeds 1 cm per year. In addition, it is important to note that some tumors can regress, involuting up to about 1 mm per year.

Various series demonstrate different growth rates, with averages ranging from 1 mm/year, and in some cases, up to 40% of tumors remained unchanged

for up to 80 months.[3] Other studies indicate even more frequent and lasting stability, with 52% of cases without growth in a 9-year period, and 76% of patients under observation not requiring treatment during this period.[3]

In the last 15 years, it has been reported that only 22-48% of tumors showed growth over 2.[6-7.3] years of follow-up.[1]

It is crucial to emphasize that the worsening of audiovestibular symptoms is not a reliable indicator of tumor growth.[1]

Treatment

To determine the treatment approach, it is essential to consider several factors, including the size of the tumor, the patient's neurological condition, their age, other coexisting medical conditions, and the patient's own preference. This may lead to a choice between expectant management or the implementation of active treatment.

Conservative management involves observation of symptoms, hearing, and tumor growth with periodic imaging tests. If there is evidence of progression of the VS (growth greater than 2 mm), intervention is indicated. During the first 2 years after diagnosis, MRI is recommended every 6 months. If the tumor remains stable, annual examinations are sufficient in subsequent years, with repeated programs for 5, 7, 9, and 14 years after diagnosis.[2] The audiological evaluation must be carried out annually. For continuous surveillance, contrast-enhanced MRI or high-contrast T2-weighted, thin-slice MRI cisternography can be used.

Therapeutic options include radiosurgery, microsurgery or chemotherapy, and can be applied alone or in combination.

For patients with small tumors (<15 mm) and functional hearing, expectant management is indicated. Medium-sized tumors (15-20 mm) are preferentially treated, especially in the young, but may be seen if multiple comorbidities are present or if the patient is elderly. On the other hand, for large tumors (>25 mm), the recommendation is always to treat, regardless of age.[2]

Observational management can prevent morbidities and even treatment-related mortality. However, the increase in tumor size over time can make the operation more challenging. In addition, it is important to highlight that hearing loss is a natural evolution of the disease that can occur regardless of the treatment chosen and does not present a greater risk in cases where expectant management is adopted.[1]

In patients with neurofibromatosis type 2, the approach should be evaluated on an individual basis, as they often have a more challenging prognosis in the management of tumors, with higher rates of recurrences and nerve deficits. Early treatment is generally considered the best option, and in some cases, chemotherapy, such as the use of bevacizumab, may offer a satisfactory response.[2]

Radiosurgery aims to slow tumor growth, but it does not lead to a cure or removal of dysfunctional tissue. It is important to note that in the first 3 years after radiosurgery, there may be a transient increase in the volume of the schwannoma, but in more than 50% of cases, the tumor involutes after treatment. Follow-up after radiosurgery should include audiological evaluations and MRI every 2 years for the first 10 years and then every 5 years indefinitely. Studies have demonstrated efficacy in tumor control in more than 90% of VS cases over a 10-year period. However, failure may occur that requires further intervention, such as in cases of symptoms caused by the mass effect, persistent growth after 3 years, or accelerated growth. The main indication for radiosurgery is the treatment of tumors less than 2.5 cm in diameter, but it can be considered in tumors smaller than 3 cm. It is important to note that there are associated risks, such as permanent facial nerve weakness, trigeminal neuropathy, secondary neoplasia, among others.

Microsurgery can be performed on tumors of all sizes, but it is the conduct of choice for bulky tumors with a mass effect. There are several possible access routes, including the retrosigmoid, translabyrinthine and middle fossa. Advances in surgical techniques, the use of surgical microscopes, and intraoperative neurophysiological monitoring have led to better rates of facial nerve preservation and postoperative hearing.

The retrosigmoid approach is capable of preserving hearing, while the translabyrinthine generally does not, becoming more indicated when the patient does not have functional hearing. Midfossa access is recommended for small, lateralized tumors with hearing-preserving potential, but may present a higher risk of facial nerve damage, especially if the surgeon is less experienced.[2]

After the operation, patients may experience continuous fatigue and imbalance, which tend to disappear within 3 months. Follow-up with MRI should be performed for the first 12 months, followed by periodic surveillance according to the specific indications of each case. Risks associated with the operation include decreased facial nerve function and hearing, which are related to the size of the tumor and the complexity of the surgical procedure. Other possible complications include postoperative cerebrospinal fluid fistula (9-13%), aseptic meningitis (2-4%), bacterial meningitis (1%) among others.[1]

The objective of microsurgery, regardless of the route chosen, is the maximum excision of the tumor with preservation of neurological functions. In cases of strong adherence of the tumor to the 7th, cranial nerve or to the brainstem, it may be necessary to perform almost total or subtotal resection of the tumor and to monitor the tumor remnant with serial imaging tests.

Some patients may require rehabilitation intervention such as those who have had facial nerve palsy, bilateral hearing loss, dizziness, or chronic imbalance. In cases of hearing loss, it is also possible

to consider operations for bone conduction implants or the use of non-surgical hearing devices, such as hearing aids, to improve this function.

Tumor-related facial nerve topography

Predicting the course of the facial nerve by means of preoperative imaging tests is of great importance for the establishment of a more appropriate surgical plan and the reduction of complications, in addition to presuming the estimation of postoperative results in relation to the functional preservation of the facial nerve.

Several factors are associated with the risk of facial paralysis after surgical resection, including previous radiation therapy, tumor location, direction of growth, and size. These factors can lead to displacement of the facial nerve and adhesion or stretching of its nerve fibers over the mass.[4]

The rate of anatomical injury of the facial nerve due to the operation is generally less than 5% in different series. However, the long-term preservation rate of facial nerve functional integrity (assessed as grade I of the House-Brackmann scale) is about 60% in some studies involving large SVs.[5]

The position of the facial nerve in relation to the tumor can vary and there are more frequent standard conditions: anterior or ventral, anterosuperior, anteroinferior and dorsal or posterior. The 7th cranial nerve, in its anatomical position, usually occupies the anterosuperior quadrant of the internal auditory canal, and its course varies according to the size of the tumor, site of origin, and degree of adhesion.[6,7]

Studies carried out to assess the position and path of the facial nerve confirm these variations and highlight what is most frequently seen in practice. For example, a series of 100 patients undergoing VS microsurgery found the anterosuperior position to be predominant, especially in small tumors (<15 mm), while larger tumors showed an increase in the incidence of anterior and anteroinferior patterns, with no case reported in the posterior position. This study also suggested that anterosuperior and anteroinferior patterns are associated with better postoperative outcomes in preserving facial nerve function. In addition, tumors larger than 3 cm in diameter showed greater adhesion of the facial nerve to the tumor capsule, leading to more neural deficits after the procedure.[6]

In contrast to these results, another series of patients, consisting of 356 cases, reported a predominance of the anterior position in small schwannomas.[8] Similar to what was found in a larger series, involving 1,006 cases, Sampath et al.[9] described the predominance of facial nerve presentation anteriorly in all tumor sizes, as the second highest frequency in the anterosuperior position.

Although advances in the field of imaging have been made, accurate identification of the preoperative facial nerve is still challenging. Currently, the most reliable method is the use of the surgical microscope associated with repeated intraoperative nerve stimulation. Other options that can aid in surgical planning include cisternography and tractography.[10]

Diffusion tractography is a modern MRI technique that can provide three-dimensional images of white matter fibers, but it still has some limitations, such as the difficulty in distinguishing the facial nerve from the vestibular nerve and the possibility of focal deletion due to the effect of tumor mass. Therefore, validation by intraoperative monitoring is essential.[5]

A retrospective study with 19 cases evaluated the accuracy of tractography in comparison with the result obtained by describing the intraoperative course of the 7th nerve. In 84% of the cases, the tractography was successful, and in 94% of them, it corresponded to the intraoperative description of the nerve position. However, it is important to exercise caution when using this technology, since it presented significant discrepancies in relation to the actual position (3D tumor model) compared to that of tractography, reaching up to 3.7 mm (+/- 4.[2] mm) difference.[11]

Furthermore, in another study, Borkar et al.[12,] found an accuracy of 90.9% in a sample with 22 patients. Similarly, other authors[9] reported an accuracy of 71% when analyzing 21 patients, while Borkar et al.[12] described an accuracy of 89% in 16 treated patients.

CONCLUSION

Although VS is characterized by symptoms such as hearing loss and tinnitus, other conditions, including lymphoma, may present with similar clinical symptoms and radiological findings. Accurate identification of these masses is essential, as treatment and prognosis can vary significantly. Awareness of the possibility of lymphoma in patients with typical VS symptoms, especially in immunosuppressive settings such as HIV, is important for differential diagnosis. The importance of the review as a way to address the risk factors and diagnosis of VS, was observed due to the chance of medical treating in specific cases that require surgical treatment.

Authors' contributions

Ana Lara Milian Prates: Validation, Writing – review & editing
Giovana Nascimento Antocheviez: Conceptualization, Investigação
Ricardo Silva dos Santos: Project administration
Samir Ale Bark: Validation, Writing – review & editing
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Joel Lavinsky: Data curation, Writing – original draft
Artur Koerig Schuster: Validation, Writing – review & editing
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