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CHALLENGES IN PREOPERATIVE DIAGNOSIS OF GLOSSOPHARYNGEAL NERVE SCHWANNOMA: OWN FINDINGS ANALYSIS

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Abstract. Challenges in preoperative diagnosis of glossopharyngeal nerve schwannoma: own findings analysis. Skobska O.E., Sirko A.H., Zemskova O.V., Lisianyi O.M., Popovych I.O., Malyi R.R. *Medical history, disease onset, clinical symptoms, and results of neuroimaging of 14 glossopharyngeal schwannoma patients, who were examined and treated in the Subtentorial Neurooncology Department of the State Institution, Romodanov Institute of Neurosurgery of the NAMS of Ukraine (8 patients) and the Neurosurgery Department No. 2 of the Municipal Enterprise, Mechnikov Dnipropetrovsk Regional Clinical Hospital of Dnipropetrovsk Regional Council (6 patients) in 2018 to 2021 have been analyzed in details. The study inclusion criteria were as follows: patient's age over 18, presence of unilateral primary glossopharyngeal nerve schwannoma. Our study showed that most of clinical signs and symptoms of the glossopharyngeal nerve schwannoma are associated with otolaryngological disorders (such as hearing loss, tinnitus, hoarseness, or dizziness) or cerebellar disorders (such as ataxia, nystagmus, or dizziness). Neuroimaging cerebellopontine angle tumors diagnosis must include brain computed tomography (with mandatory assessment of the state of jugular foramen and internal auditory canal) and IV contrast brain magnetic resonance tomography and inclusion of high-resolution sequences, gradient echo (3D CISS, DRIVE, TRUFFI, B-FFE) with the aim of better visualization and differentiation of various cerebellopontine angle cranial nerves. The study demonstrates the complexity of a reliable preoperative diagnosis when using standard diagnostic tools. Preoperative jugular foramen and cerebellopontine angle tumors diagnosis should be based on a systematic approach and include a comparison of results of comprehensive clinical and instrumental examination and neuroimaging studies.*

Резюме. Проблемні питання діагностики шваноми язикоглоткового нерва на доопераційному етапі: аналіз власних спостережень. Скобська О.Є., Сірко А.Г., Земскова О.В., Лісяний О.М., Попович І.О., Малий Р.Р. *Метою роботи є детальний аналіз анамнезу, дебюту захворювання, клінічних симптомів і результатів нейровізуалізації 14 пацієнтів з язикоглотковими шваномами, які перебували на обстеженні та лікуванні у відділенні субтенторіальної нейроонкології Державної установи «Інститут нейрохірургії ім. акад. А.П. Ромоданова НАМН України» (8 пацієнтів) і відділенні нейрохірургії № 2 КП «Дніпропетровська обласна клінічна лікарня ім. І.І. Мечникова» ДОС (6 пацієнтів) у період 2018-2021 рр. Критерії включення пацієнтів у*

дослідження: вік пацієнтів старше 18 років, наявність однобічної первинної шваноми язикоглоткового нерва. Як показало наше дослідження, більшість клінічних ознак і симптомів язиоглоткових шваном пов'язана з отоларингологічними порушеннями (такими як втрата слуху, шум у вухах, охриплість голосу, запаморочення); з мозочковими порушеннями (такими як атаксія, ністагм, запаморочення). Нейровізуалізаційна діагностика пухлин, що розташовані в ділянці мостомозочкового кута, повинна обов'язково включати спіральну комп'ютерну томографію головного мозку (з обов'язковою оцінкою стану яремного отвору та внутрішнього слухового проходу) та магнітно-резонансну томографію головного мозку з внутрішньовенним підсиленням та включенням послідовностей з високою роздільною здатністю, градієнтного ехо (3D CISS, DRIVE, TRUFFI, B-FFE) з метою кращої візуалізації та диференціації різних черепних нервів у мостомозочковому куті. Результати дослідження демонструють труднощі в постановці достовірного діагнозу на доопераційному етапі стандартним діагностичним комплексом. Діагностика пухлин яремного отвору й мостомозочкового кута на доопераційному етапі повинна базуватися на системному підході і включати зіставлення результатів комплексу клініко-інструментального обстеження та нейровізуалізаційних методів досліджень.

Schwannomas account for approximately 7% to 10% of all primary intracranial tumors. 2.9% to 4% of tumors originating from the jugular foramen (JF) are cranial nerve (CN) IX, X, and XI schwannomas. CN pair IX schwannomas are the second in terms of occurrence and can extension intra- and extracranially [3, 8].

Clinical picture of glossopharyngeal schwannoma (GPS) and vestibular schwannoma (VS) is characterized by a similar set of clinical symptoms of lesions and irritation of both cerebellopontine angle (CPA) and caudal group of CNs. Difficulties in differential preoperative diagnosis are caused not only by the VS but also by other intra- and extracranial tumors (in particular, JF paraganglioma) [3, 9].

Reliable diagnosis as early as the preoperative stage makes it possible to determine a rational treatment strategy, first of all, of surgical intervention (selection of optimal surgical approach and surgery stages) [10].

Availability of reliable information on the origin of schwannoma allows minimizing the risk of iatrogenic intraoperative CN damage and postoperative neurological deficit in order to maintain a high quality of patient's life.

All of the above is of practical and scientific interest in terms of methodology; therefore, we consider it necessary to make detailed analysis of the medical history, clinical manifestations, and neuroimaging features of the GPS based on our own clinical experience in comparison with literature data.

Study purpose. Analyze the features of preoperative clinical course of the GPS based on the study of medical history, clinical and instrumental examination, and neuroimaging results.

MATERIALS AND METHODS OF RESEARCH

We made a retrospective analysis of examination and surgical treatment of 249 patients with code D 33.3 according to the 10th revision of the International Classification of Diseases (WHO, 2007) treated in the Subtentorial Neurooncology Department of the State Institution, Romodanov Institute of Neurosurgery of the NAMS of Ukraine (183 patients) and the Neurosurgery Department No. 2 of the Municipal enterprise, Dnipropetrovsk Regional Clinical Hospital of Dnipropetrovsk Regional Council (66 patients) in 2018 to 2021.

Study inclusion criteria were patients' age over 18, availability of unilateral primary MRI data, no prior surgery or radiation treatment, availability of preoperative intravenous paramagnetic contrast MRI data, histological diagnosis verification.

Study exclusion criteria were the following: age under 18, other CN schwannomas, including type II neurofibromatosis due to peculiarities of etiopathogenesis and clinical symptoms, no intravenous paramagnetic contrast MRI data, no histological verification.

Our work involved a retrospective analysis of examination and surgical treatment of 14 patients who met the study inclusion criteria.

The GPS was ultimately diagnosed based on a comprehensive assessment of clinical and instrumental otoneurological examination and neuroimaging studies, intraoperative information, and pathomorphological studies. Preoperatively, 3 (21.4%) patients were diagnosed with the GPS; 4 (28.6%) had caudal CN group schwannomas with no reference to a particular nerve; 1 (7.1%) patient presumably had a glioma, namely a pilocytic astrocytoma; 5 (35.7%) patients were diagnosed with the VS (based on the MRI data); 1 (7.1%) patient had paraganglioma. Other patients were diagnosed with a CPA tumor subject to further intraoperative clarification. In most cases, it was possible to clearly visualize the CN from which the tumor originated intraoperatively. However, sometimes large tumor size did not allow determining the initial tumor growth site, even intraoperatively [5].

Histological surgical material examination in all 14 cases confirmed plexiform or cellular histological subtype, I degree of anaplasia schwannoma. When visualized, as in histological verification, the GPS's morphological structure and signal are similar to those of the VS. Therefore, all schwannomas have

similar histostructure, which does not allow determining particular CN where the tumor originates from. Histologically, caudal CN group schwannomas do not differ from VS but have different arrangement of fascicular and reticular structures and degeneratively dystrophic secondary changes in the stroma.

In our series, the main clinical group accounted for 5.6% of the total number of the studied schwannomas, which corresponds to the literature data on GPS occurrence among all intracranial schwannomas.

Today, the JF schwannomas are often classified similarly to jugular glomus tumors using the methods developed by Kaye and Pellet [6,7]. Samii and Tatagiba (1996) modified this classification [8] and proposed to distinguish types A, B, C, and D depending on predominant tumor extension. In our study, tumors had the following breakdown: 6 (42.9%) cases, type A (tumor predominantly located in the CPA with minimal extension to the JF) (Fig. 1); 2 (14.3%) cases, type B (tumor mainly located in the jugular foramen with intracranial extension); 6 (42.9%) cases, type D (dumb bell form with significant extra- and intracranial extension). There were no type C (mainly extracranial tumor with extension to the JF) tumors in our study. Among all GPS cases, up to 2% are type C tumors 2% 11].
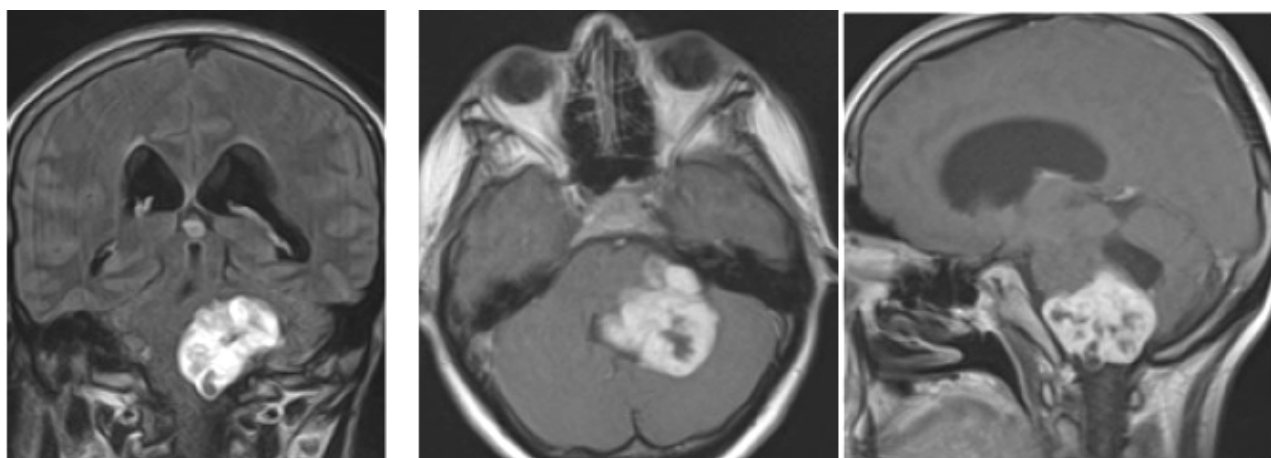

Fig. 1. MRI of JF schwannoma. Type A

Preoperatively, standard demographic (patient's age and gender) and metric (tumor size) data and medical history (disease duration, symptoms onset time and sequence, prehospital clinical course peculiarities) were collected from all patients.

All patients underwent general clinical, laboratory, and cliniconeurological studies in order to assess preoperative GPS course.

A comprehensive clinical and instrumental otoneurological examination was carried out before and 4-10 days after the surgery (depending on patient's condition severity and level of consciousness) and included assessment of complaints, standard otolaryngological examination (anterior and posterior rhinoscopy, otoscopy, pharyngoscopy), qualitative assessment of CN innervation (CN I , V, VII, X, IX, and XII), assessment of the function of auditory and vestibular analyzers. Hearing function was assessed using the Gardner-Robertson scale (GRS), facial nerve (FN) function impairment (preservation) was assessed using the House-Brackmann scale (HBS).

Audiometric studies were performed using a serial MA-51 audiometer (Germany) based on applicable standards.

Neuroophthalmological examination included fundus state examination (presence and severity of retinal vascular changes, signs of hypertension), oculomotor, pupillary innervation, and determination of optic nerve pathway damage.

Brain MRI was performed using Intera 1.5 TI tomograph (Philips, Netherlands) in T1 and T2 modes, slice thickness 5 mm, step 5 mm, with intravenous paramagnetic contrast.

Average postoperative period duration was 16 bed-days. All patients were discharged for follow-up in medical institutions at their place of residence in satisfactory condition.

8 (57.1%) patients underwent subtotal tumor removal, 3 (21.4%) patients had total removal and 3 (21.4%) had partial removal.

The data was processed and analyzed using STATISTICA 10 (StatSoft® Inc., USA, license No. STA862D175437Q) and SPSS 17.0 (IBM, USA). Differences were considered statistically significant at $p<0.05$ [1].

Written informed consent was obtained from all patients to conduct the study, in accordance with the Declaration of Helsinki of the World Medical

Association regarding ethical principles of scientific medical research with human participation (1964-2008), the EEC Directive 86/609 on human participation in biomedical studies, and the Order of the Ministry of Health of Ukraine No. 690 23/09/2009, as amended.

RESULTS AND DISCUSSION

In the presented group of patients, female patients predominated: 9 (64.3%). Average patient's age was 46.4 [33.5; 66.5]. The average age of men was 44.8 [35; 59]; women – 50.8 [32; 61]). The difference between the average age of men and women was not statistically significant (p=0.17).

Medical history ranged widely from 1 month to 12 years, and averaged 37 [12; 54] months, which is explained by the lack of patients' alertness after hearing impairment/loss in the absence of new symptoms. The vast majority of patients had a long asymptomatic period with large tumor size. This is consistent with the literature data – clinical symptoms of the GPS may not appear until the tumor reaches a sufficiently large size and they vary from mild to severe and can develop over several years [4,12]. A common feature of this series is the onset of the disease characterized by one-sided ear noise, followed by hearing loss on the same side.

A defining attribute in the majority of the 12 patients studied (85.7%) was the detection of large and very large tumors – over 35 mm and 51 mm in one of the linear dimensions, respectively. An interesting fact is that there was a clinical and radiological dissociation with a length of medical history less than 2 years in all cases. This may probably be due to the peculiarity of the anatomical location of JF schwannomas (particularly, GPS) and possible greater caudal group of CN resistance, which allows such tumors to grow asymptomatically for a relatively long time.

In all cases, the tumors intensively accumulated paramagnetics, while the presence of a cystic component in a tumor increased the heterogeneity of its contrasting. Note that in our study, tumors with cystic areas prevailed (8 (57.1%) patients).

No tumor lateralization was determined (p=0.27); 8 patients had right-sided tumors and 6 had left-sided tumors.

2 (14.3%) patients had initial fundus congestion, with a medical history of more than 5 years and a gigantic tumor.

Hearing impairment of varying severity and sensorineural nature on the affected side was diagnosed preoperatively in all patients. Before the surgery, patients had the following score according to GRS: class I, 1 patient; class II, 2 patients; class III, 4 patients; class IV, 4 patients; class V,

3 patients. It is noteworthy that 11 (78.6%) patients had hearing impairment corresponding to *socially useless* hearing.

12 (85.7%) patients had one-sided subjective ear noise on the affected side as one of the most common symptoms accompanying sensorineural hearing loss.

Maintaining the anatomical and functional integrity of the FN during tumor removal is a challenging task. Preoperatively, the FN function was preserved in 10 (71.4%) patients, while 4 (28.6%) patients had grade II HBS deficiency.

4 (28.6%) patients had neurological deficit expressed in decrease/loss of taste on the anterior 2/3 of the tongue on the affected side. 5 (35.7%) patients had trigeminal nerve dysfunction.

All patients had preoperative spontaneous small and medium amplitude, clonic, and rhythmic nystagmus and static coordination disorders of varying severity.

Only 4 (28.6%) patients had caudal CN group damage symptoms; these patients had both dysphagia and dysphonia and 1 (7.1%) patient also had dysarthria. Common clinical finding of our series was the presence of CPA CN lesion symptoms in all cases.

Clinical GPS symptoms are non-specific and may include hearing loss or impairment, tinnitus on the affected side, dizziness, static coordination disorders, headache, nystagmus, velopharyngeal and facial hypesthesia, depending on initial growth and the primary direction of tumor extension to the CPA. Many researchers note that if the GPS spreads to the CPA, it is difficult to differentiate such tumor from the VS while JF schwannomas to the VS ratio is 1 to 24 [3, 12-14].

Our study showed that most of clinical signs and symptoms of the GPS are associated with otolaryngological disorders (such as hearing loss, tinnitus, hoarseness, or dizziness) or cerebellar disorders (such as ataxia, nystagmus, or dizziness).

MRI data showed that in 4 (28.6%) cases, a tumor was surrounded by moderately pronounced perifocal edema. On the other hand, the vast majority of patients (11 (78.6%)) had compressed stem structures, cerebellum, and IV ventricle, which correlated with the tumor size. Moreover, 6 (42.9%) patients had radiological signs of occlusive hydrocephalus.

In one case, it was impossible to exclude process extension to the internal auditory canal; however, in none of the cases the MRI data indicated internal auditory canal expansion on the affected side.

Only in a small number of cases (4 (28.6%)) the primary diagnosis' MRI protocols included sequences allowing a detailed assessment of the caudal and CPA CNS (high-resolution protocols, gradient echo, etc.).

In all cases, the degree of tumor extension to the JF was determined; however, a detailed assessment of the latter, as well as impact on other nearby bone structures, including internal auditory canal, petrous part of the temporal bone, and clivus (the presence of destruction, expansion, pressure atrophy, sclerosis, etc.), only based on MRI data was difficult and required inclusion of multislice spiral computed tomography (MSCT) in the examination protocol (Fig. 2).
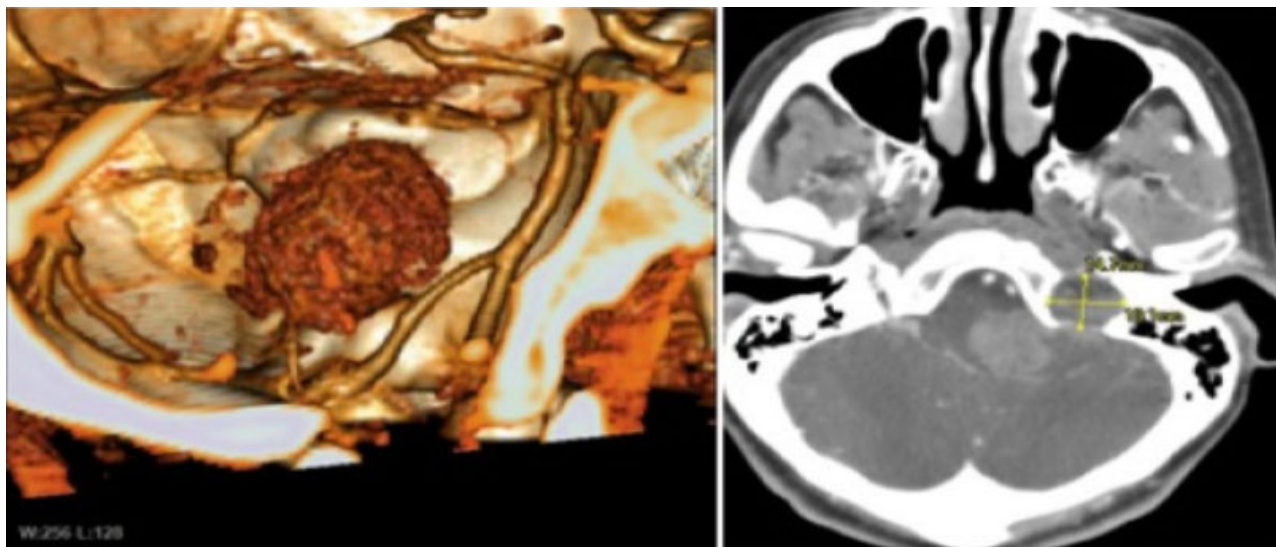

Fig. 2. CT-angiography image of JF schwannoma (Type D) with destruction of JF

A characteristic symptom of JF schwannomas is the JF expansion, while maintaining the clarity of its contours, often with a "ring" of sclerosis, clearly visualized on CT in the bone window mode. However, this feature cannot be considered pathognomonic for GPS, as there may be no JF expansion in case of types A and C JF schwannomas by Samii (1996) [8].

Adding high-resolution gradient echo sequences (3D CISS, DRIVE, TRUFFI, B-FFE) to standard MRI protocol allows detailed visualization of relationship between the tumor and nearby CNs, which is extremely important when the tumor is suspected to originate from the JF.

Literature review and our own observations suggest that the GPSs do not have exclusively pathognomonic visualizing symptoms.

Differential diagnosis of glomus tumors is difficult as well. For such tumors, the *"salt and pepper"* sign, caused by the presence of large vessels in the tumor (hypointense pepper-shaped areas alternate with hyperintense salt-shaped areas due to slow blood flow or subacute hemorrhages), is pathognomonic [2].

Determination of the main axis of tumor growth allows differentiation between JF schwannomas and paragangliomas. JF schwannoma is characterized by a supramedial growth axis along the adjacent CN in the brainstem direction, while paragangliomas typically have supralateral axis towards the bottom of the tympanic cavity [4].

Thus, one of the most important conditions of effective differential diagnosis of the CPA and JF tumors and rational choice of treatment tactics is a multidisciplinary team approach based on the analysis of comparison of a set of clinical and instrumental otoneurological examinations, neuroimaging studies, and intraoperative diagnosis.

This is especially important in the surgery of hard-to-reach (anatomically complex) CN tumors, such as VS and GPS. The choice of the volume of tumor removal and surgical approach affects the functional preservation of the vestibulocochlear nerve. GPS causes hearing loss due to indirect mechanisms in contrast to VS, which increases the possibility of hearing restoration [2].

Determination of the CN where the schwannoma originated from makes it possible to adequately plan surgical intervention and predict the treatment outcome. Therefore, the determination of a specific clinical profile of symptoms for a specific tumor type requires further study of a larger cohort of patients.

CONCLUSIONS

1. In most cases, there are no specific signs of glossopharyngeal lesion during preoperative examination.

2. A variety of clinical manifestations of the disease and a long asymptomatic period create objective difficulties for differential (correct) preoperative diagnosis of glossopharyngeal nerve schwannoma.

3. Comprehensive clinical and instrumental otoneurological examination is an obligatory stage in clinical local protocol of medical care for cerebellopontine angle or jugular foramen tumor patients, preoperatively, postoperatively, and during the follow-up.

4. Neuroimaging cerebellopontine angle tumors diagnosis must include brain computed tomography (with mandatory assessment of the state of jugular foramen and internal auditory canal) and intravenous contrast brain magnetic resonance tomography and inclusion of high-resolution sequences, gradient echo (3D CISS, DRIVE, TRUFFI, B-FFE) with the aim of better visualization and differentiation of various cranial nerves of cerebellopontine angle.

5. Preoperative comparison of topographic and anatomical radiological characteristics with a detailed otoneurological examination will significantly help neurosurgeons in treatment method, surgical approach and scope planning.

Conflict of interests. The authors declare no conflict of interest.

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