SERIJA SLUČAJEVA

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PERIPHERAL NERVE SHEATH TUMORS: CLINICAL AND EPIDEMIOLOGICAL CHARACTERISTICS – A RETROSPECTIVE ANALYSIS OF 46 PATIENTS

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SAŽETAK

Uvod/Cilj: Tumori omotača perifernih nerava (PNST) predstavljaju raznoliku grupu neoplazmi koje nastaju iz Švanovih ćelija i fibroblasta perifernih nerava. Njihova heterogena priroda i varijabilna povezanost sa sindromima neurofibromatoze (NF) zahtevaju sveobuhvatno razumevanje njihovih epidemioloških i kliničkih karakteristika. Cilj ove studije je bio da se analiziraju kliničke i epidemiološke karakteristike osoba sa tumorom omotača perifernih nerava (PNST) kod kojih je dijagnoza postavljena tokom poslednjih pet godina.
Metode: U ovoj studiji, sprovedena je retrospektivna analiza 46 pacijenata sa histološki potvrđenim tumorima omotača perifernih nerava. Svi ispitanici uključeni su u studiju u vremenskom periodu od 1. januara 2020. do 1. januara 2025. Iz istorija bolesti ovih pacijenata prikupljeni su svi neophodni podaci. Procenjeni su demografski podaci, tip tumora, anatomska lokalizacija, prisustvo neurofibromatoze, vreme od pojave simptoma do operacije i kliničke manifestacije.
Rezultati: Švanomi su bili najčešći tip tumora (73,9%), a zatim maligni tumori omotača perifernih nerava (MPNST) (15,2%) i neurofibromi (10,9%). Najčešća lokalizacija tumora bili su gornji ekstremiteti. Neurofibromatoza tip 1 (NF1) je bila prisutna kod 19,6% pacijenata.
Zaključak: Tumori omotača perifernih nerava su pretežno benigni i najčešće se nalaze na gornjim ekstremitetima. Neurofibromatoza ostaje važan faktor rizika, posebno kod pacijenata sa višestrukim lezijama.

Ključne reči: Tumori omotača perifernih nerava, Švanom, Neurofibromatoza tip 1, MPNST

Uvod

Tumori perifernih nervnih omotača (PNN) predstavljaju heterogenu grupu lezija koje uključuju benigne oblike - najčešće švanome i neurofibrome - i maligne oblike poznate kao maligni tumori perifernih nervnih omotača (MPNN). Iako retki, ovi tumori zahtevaju značajnu kliničku pažnju zbog svog potencijalnog maligniteta, lokalne agresivnosti i povezanosti sa genetskim sindromima kao što je neurofibromatoza tipa 1 (NF1) (1–3).

Epidemiološke studije su pokazale da se PNN najčešće javljaju na gornjim ekstremitetima, posebno pogađajući živce kao što su srednji, ulnarni i radijalni živac (4). Iako ređi, MPNN predstavljaju najveću kliničku pretnju i često su povezani sa NF1 (5,6).

Metod

Ova serija slučajeva je obuhvatila 46 pacijenata sa histološki potvrđenim tumorima perifernih nervnih omotača (PNNN), identifikovanim iz baze podataka patologije jednog tercijarnog centra

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CASE SERIES

PERIPHERAL NERVE SHEATH TUMORS: CLINICAL AND EPIDEMIOLOGICAL CHARACTERISTICS – A RETROSPECTIVE CASE SERIES OF 46 PATIENTS

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SUMMARY

Introduction/Aim: Peripheral nerve sheath tumors (PNSTs) represent a diverse group of neoplasms arising from Schwann cells and fibroblasts of peripheral nerves. Their heterogeneous nature and variable association with neurofibromatosis (NF) syndromes necessitate a comprehensive understanding of their epidemiological and clinical profiles. The aim of this study was to analyze the clinical and epidemiological characteristics of persons with peripheral nerve sheath tumors (PNSTs) diagnosed during the last five years.
Methods: In this stusy, the retrospective analysis of 46 patients with histologically confirmed peripheral nerve sheath tumors was conducted. All subjects were included in the study in the period from January 1st, 2020 to January 1st, 2025. All necessary data were collected from the medical records of these patients. Demographic data, tumor type, anatomical location, presence of neurofibromatosis, time from symptom onset to surgery, and clinical manifestations were evaluated.
Results: Schwannomas were the most common tumor type (73.9%), followed by malignant peripheral nerve sheath tumors (MPNSTs) (15.2%) and neurofibromas (10.9%). The most frequent tumor localization was the upper extremities. Neurofibromatosis type 1 (NF1) was present in 19.6% of patients.
Conclusion: Peripheral nerve sheath tumors are predominantly benign and most commonly located in the upper extremities. Neurofibromatosis remains an important risk factor, particularly in patients with multiple lesions.

Keywords: peripheral nerve sheath tumors, Schwannoma, Neurofibromatosis type 1, MPNST

Introduction

Hearing is the sense that allows us to perceive soPeripheral Nerve Sheath Tumors (PNSTs) represent a heterogeneous group of lesions that include benign forms - most commonly schwannomas and neurofibromas - and malignant forms known as malignant peripheral nerve sheath tumors (MPNSTs). Although rare, these tumors warrant significant clinical attention due to their potential malignancy, local aggressiveness, and association with genetic syndromes such as neurofibromatosis type 1 (NF1) (1–3).

Epidemiological studies have shown that PNSTs most frequently occur in the upper extremities, particularly affecting nerves such as the median, ulnar, and radial nerves (4). Although less common, MPNSTs pose the greatest clinical threat and are frequently associated with NF1 (5,6).

za negu, Neurohirurške klinike Univerzitetskog Kliničkog Centra Srbije. Analizirana je baza podataka Neurohirurške klinike za poslednjih pet godina (2020-2024. godine). Za svakog pacijenta prikupljeni su podaci o polu, starosti, tipu tumora, anatomskoj lokaciji, simptomima koji se javljaju, prisustvu NF1/NF2 i vremenskom intervalu od pojave simptoma do hirurške intervencije.

U statističkoj analizi podataka izračunata je srednja vrednost i standardna devijacija (SD) za numeričke varijable, a za kategorijalne varijable frekvencije i procenti.

Rezultati

Ova serija slučajeva je obuhvatila 46 ispitanika sa tumorima omotača perifernih nerava. Od toga, 22 (47,8%) ispitanika su bile žene, a 24 (52,1%) muškarci. Što se tiče anatomske distribucije (slika 1), većina pacijenata je imala tumor lociran na gornjim ekstremitetima (58,7%), a zatim na donjim (34,78%). Tumori u predelu glave i vrata primećeni su kod 6,5% ispitanika, dok kod ispitanika nije pronađen tumor u predelu trupa.

Što se tiče tipova tumora (slika 2), švanomi su bili najčešće primećeni i to kod 34 od 46 ispitanika (73,9%). Neurofibromi su identifikovani kod 5 pacijenata (10,9%), a maligni tumori perifernih nervnih omotača kod 7 pacijenata (15,2%).

Najčešća klinička manifestacija tumora omotača perifernih nerava (slika 3) je bilo prisustvo opipljive mase, prijavljene kod 71,7% pacijenata. Bol je bio prisutan u 52,2% slučajeva, zatim senzorni deficiti u 28,3% i motorna slabost kod 10,9% pacijenata.

Što se tiče neurofibromatoze, kod 9 pacijenata (19,6%) je dijagnostikovana neurofibromatoza tipa 1 (NF1), a kod jednog pacijenta (2,2%) neurofibromatoza tipa 2 (NF2).

Prosečno vreme od pojave simptoma do hirurške intervencije za ovih 46 pacijenata je bilo 3,10±3,64 godine.

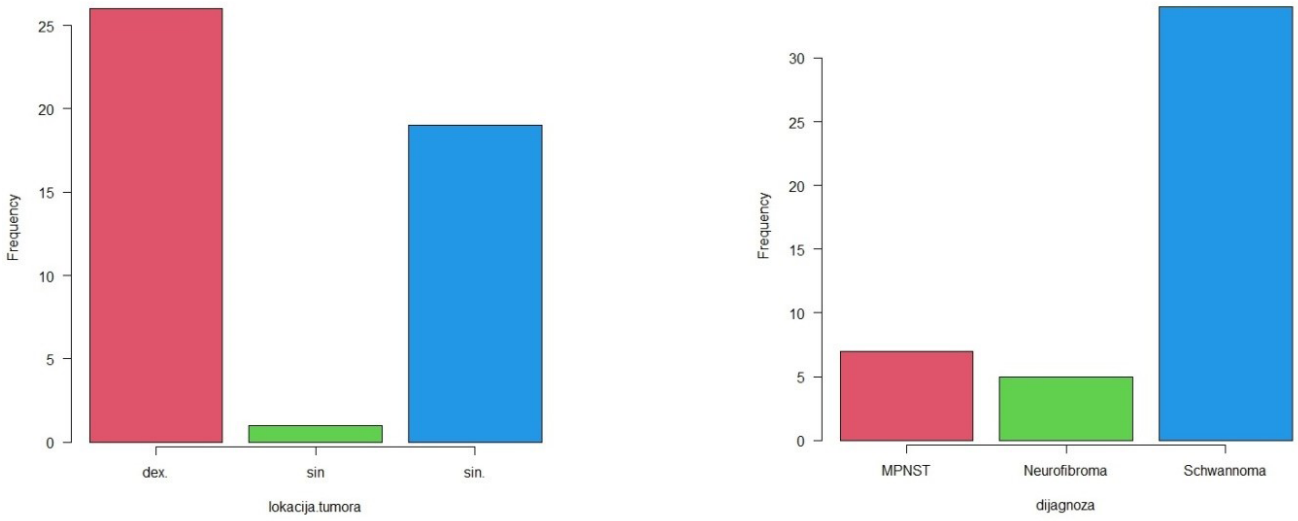
Diskusija

Ova studija predstavlja jednu od retkih domaćih retrospektivnih analiza tumora perifernih nervnih omotača, pružajući vredne uvide u njihovu distribuciju, kliničku prezentaciju i povezanost sa neurofibromatozom. Naši rezultati su u skladu sa većinom prethodnih istraživanja sprovedenih u Evropi i Severnoj Americi.

Prevalencija i distribucija tumora

Najčešći tip tumora kod naših ispitanika je bio švanom (73,9%), što je u skladu sa podacima koje su objavili *Sandberg* i dr., koji su identifikovali švanome kao dominantne benigne tumore perifernih nerava tokom perioda od 22 godine u Švedskoj (1). Pored toga, naša studija je pokazala da se ovi tumori češće nalaze na gornjim ekstremitetima (58,7%), što se i očekuje s obzirom na veću gustinu perifernih nerava i veću dostupnost za otkrivanje i dijagnozu u ovom regionu (2).

S druge strane, MPNST su činili 15,2% svih slučajeva – što predstavlja veći udeo u poređenju sa većim epidemiološkim istraživanjima kao što je SEER (*Surveillance Epidemiology and Results*), gde je učestalost incidencija ovih maligniteta bila



Slika 1. Tumori prema anatomskoj lokalizaciji i dijagnozi

Methods

The case series included 46 patients with histologically confirmed peripheral nerve sheath tumors (PNSTs), identified from the pathology database of a tertiary care center, the Clinic of Neurosurgery of the Univeristy Clinical Center of Serbia. The electronic database of the Clinic of Neurosurgery was analyzed for the last five years (2020-2024). For each patient, data were collected on sex, age, tumor type, anatomical location, presenting symptoms, presence of NF1/NF2, and the time interval from the symptom onset to surgical intervention.

In the statistical analysis of data, the mean value and standard deviation (SD) were calculated for numerical variables, and frequencies and percentages for categorical variables.

Results

This case series included 46 subjects with peripheral nerve sheath tumors. Of these, 22 (47.8%) were women and 24 (52.1%) were men. According to anatomical distribution (Figure 1), the majority of patients had a tumor located in the upper extremities (58.7%), followed by the lower extremities (34.8%). Tumors in the head and neck region were observed in 6.5% of subjects, while no tumors were found in the trunk region.

As far as tumor types are concerned (Figure 2), schwannomas were the most common tumors and they were observed in 34, out of 46 patients (73.9%). Neurofibromas were identified in 5 patients (10.9%), and malignant peripheral nerve sheath tumors (MPNST) in 7 patients (15.2%).

The most common clinical manifestation of peripheral nerve sheath tumors (Figure 3) was the presence of a palpable mass, reported in 71.7% of patients. Pain was present in 52.2% of cases, followed by sensory deficits in 28.3% and motor weakness in 10.9% of patients.

As far as neurofibromatosis is concerned, 9 patients (19.6%) were diagnosed with neurofibromatosis type 1 (NF1), and one patient (2.2%) with neurofibromatosis type 2 (NF2).

The average time from the onset of symptoms to the surgical intervention for these 46 patients was 3.10±3.64 years.

Discussion

This study represents one of the few domestic retrospective analyses of peripheral nerve sheath tumors (PNSTs), offering valuable insights into their distribution, clinical presentation, and association with neurofibromatosis. Our results are consistent with the majority of previous studies conducted in Europe and North America.

Prevalence and Tumor Distribution

The most prevalent tumor type in our subjects was schwannoma (73.9%), which is in line with data reported by Sandberg et al, who identified schwannomas as the dominant benign peripheral nerve tumors over a 22-year period in Sweden (1). Additionally, our study shows that these tumors are more commonly located in the upper extremities (58.7%), which is expected given the

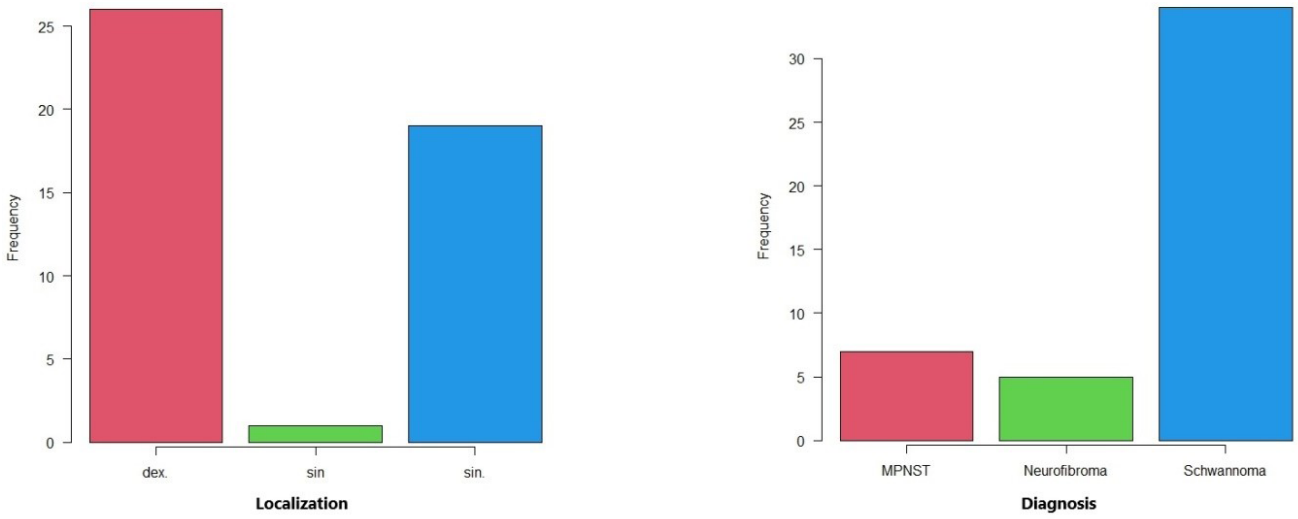
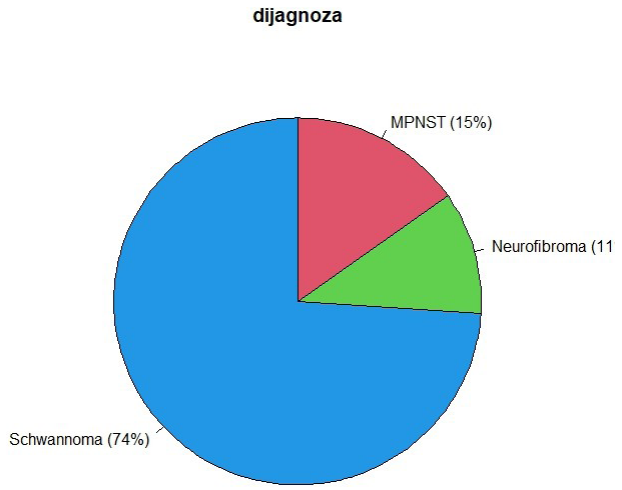
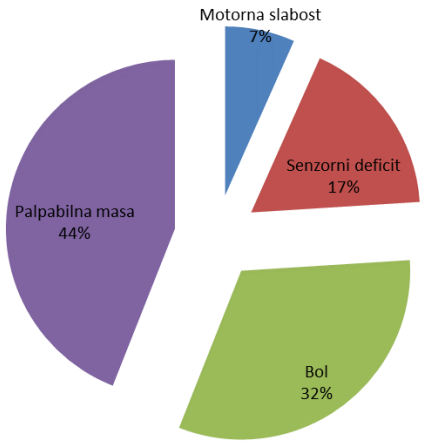


Figure 1. Tumors by anatomical region and diagnosis



Slika 2. Distribucija pacijenata sa kliničkim manifestacijama tumora omotača perifernih nerava prema tipu tumora



Slika 3. Distribucija pacijenata sa kliničkim manifestacijama tumora omotača perifernih nerava prema kliničkoj manifestaciji

znatno niža (manje od 0,1% svih sarkoma mekih tkiva) (3,4). Ova neslaganja mogu biti rezultat pristrasnosti u izboru ispitanika za uključivanje u istraživanje svojstvenu tercijarnom centru za negu ili ograničen vremenski obim studije.

Klinička prezentacija i dijagnostički izazovi

Najčešće kliničke manifestacije naših ispitanika u našoj kohorti bile su palpabilna masa i bol, što se poklapa sa nalazima drugih studija (2,5). Međutim, senzorni i motorni deficiti su bili ređi, što ukazuje na to da su mnogi benigni tumori dijagnostikovani u kasnijoj fazi, često nakon što dostignu značajnu veličinu.

Primetno je da je prosečno vreme od pojave simptoma do hirurške intervencije bilo približno 3 godine, što ističe podmuklu prirodu kliničke progresije i verovatna kašnjenja u postavljanju dijagnoze. Ovo zapažanje je u skladu sa nalazima *Amirijana* i sar., koji su takođe istakli da MPNST često ostaju nedijagnostikovani dok ne postanu značajni ili ne proizvedu neurološke deficite (3).

Neurofibromatoza kao faktor rizika

Približno 20% pacijenata u našoj kohorti imalo je potvrđenu neurofibromatozu tipa 1 (NF1), što je u skladu sa prethodnim kliničkim serijama koje su izveštavale o učestalosti NF1 kod 15–25% pacijenata sa tumorima perifernih nerava (6). Važno je naglasiti da su pacijenti sa NF1 pokazali povećan rizik od višestrukih tumora, što je u našoj studiji dokazano slučajevima koji uključuju višestruke švanome ili kombinacije švanoma i neurofibroma.

Iznenađujuće, u našem istraživanju nijedan slučaj MPNST u našem uzorku nije bio povezan ni sa NF1 ni sa NF2, što je u suprotnosti sa nalazima iz većih serija slučajeva (npr. SEER i brazilske studije), gde je NF1 identifikovan kao glavni faktor rizika za malignu transformaciju benignih lezija (3,7). Ovaj nalaz se može pripisati malom broju ispitanika uključenih u našu studiju, ali takođe pokreće mogućnost nepoznatih patogenih mehanizama koji leže u osnovi sporadičnih MPNST.

Uporedni podaci i kontekst zdravstvene zaštite

Studije iz Brazila koje analiziraju lečenje u okviru javnog zdravstvenog sektora ukazuju na to da je hirurško lečenje tumora perifernih nerava finansijski zahtevno i da postoje značajne razlike u pristupu dijagnostičkim i terapijskim resursima (7,8). Iako nije direktno procenjeno u našoj studiji, produženo vreme do operacije ukazuje na potencijalne sistemske prepreke ranoj dijagnozi – kritično područje za poboljšanje sistema zdravstvene zaštite.

Štaviše, istraživanja koja se bave socioekonomskim i rasnim razlikama u preživljavanju MPNST ističu značajnu heterogenost u pristupu lečenju i ishodima, čak i unutar zemalja sa visokim prihodima (9). Ovi uvidi su ključni za oblikovanje strategija javnog zdravlja i planiranje specijalizovanih centara za tumore nerva.

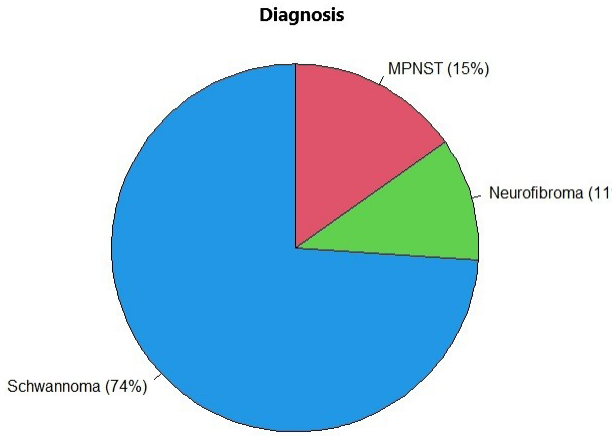


Figure 2. Distribution of patients with clinical manifestations of peripheral nerve tumors by type of tumor

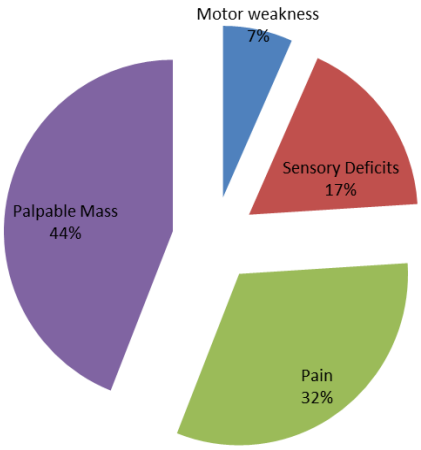


Figure 3. Distribution of patients with clinical manifestations of peripheral nerve tumor by clinical manifestation

higher density of peripheral nerves and the greater accessibility for detection and diagnosis in this region (2).

On the other hand, MPNSTs accounted for 15.2% of all cases - representing a higher proportion compared to larger epidemiological datasets such as SEER (Surveillance Epidemiology and Results), where the incidence of these malignancies is considerably lower (less than 0.1% of all soft tissue sarcomas) (3,4). This discrepancy may reflect sample selection bias inherent to a tertiary care center or the limited temporal scope of the study.

Clinical Presentation and Diagnostic Challenges

The most frequent clinical manifestations in our cohort were palpable mass and pain, which is consistent with the findings from other studies (2,5). However, sensory and motor deficits were less common, suggesting that many benign tumors were diagnosed at a later stage, often after reaching significant size.

It was observed that the mean duration from symptom onset to surgical intervention was approximately 3 years, highlighting the insidious nature of clinical progression and likely delays in diagnostic evaluation. This observation is consistent with the findings of Amirian et al, who also reported that MPNSTs often remain undiagnosed until they become sizable or produce neurological deficits (3).

Neurofibromatosis as a Risk Factor

Approximately 20% of patients in our cohort had confirmed neurofibromatosis type 1 (NF1), which is consistent with prior clinical series reporting NF1 prevalence in 15–25% of patients with peripheral nerve tumors (6). It is important to emphasize that patients with NF1 exhibited an increased risk for multiple tumors, as evidenced in our study by cases involving multiple schwannomas or combinations of schwannomas and neurofibromas.

Surprisingly, in our study, no MPNST cases in our sample were associated with either NF1 or NF2, which contrasts with findings from larger series (e.g. SEER and Brazilian studies), where NF1 is identified as a major risk factor for malignant transformation of benign lesions (3,7). This finding may be attributed to the small number of subjects included in our study, but also raises the possibility of unknown pathogenic mechanisms underlying sporadic MPNSTs.

Comparative Data and Healthcare Context

Studies from Brazil analyzing treatment within the public healthcare sector indicate that surgical management of peripheral nerve tumors is financially demanding and that significant disparities exist in access to diagnostic and therapeutic resources (7,8). Although not directly assessed in our study, the prolonged time to surgery suggests potential systemic barriers to early diagnosis—a

Ograničenja studije

Glavno ograničenje studije je retrospektivni dizajn i mali broj ispitanika, što ograničava generalizaciju rezultata. Nedostatak multivarijantne analize i molekularnih podataka dodatno smanjuje dublje razumevanje patogeneze tumora.

Preporuke za buduća istraživanja

Buduća istraživanja treba da obuhvate veće, multicentrične prospektivne studije koje uključuju molekularne biomarkere, praćenje recidiva, poređenje sporadičnih i sindromskih oblika tumora, kao i analizu troškova i dostupnosti lečenja.

Zaključak

Tumori perifernog nervnog omotača su retki, ali klinički značajni entiteti. Švanomi su najčešći i pretežno su benigni, dok MPNST predstavljaju maligni oblik sa potencijalno lošom prognozom. Povezanost sa NF1 ostaje klinički važna, posebno zbog povećanog rizika od višestrukih lezija. Neophodna su dalja detaljnija istraživanja u ovoj oblasti.

Konflikt interesa

Autori su izjavili da nema konflikta interesa.

Etičko odobrenje

Studija je odobrena od strane Etičkog odbora naše katedre i sprovedena je u skladu sa Helsinškom deklaracijom i njenim amandmanima. Porodica je dala informisani pristanak.

Etička izjava

Retrospektivna studija, koja analizira podatke u periodu koji prethodi početku istraživanja, a u skladu sa odredbama Zakona o zaštiti podataka o ličnosti Republike Srbije, sa uvidom u dokumentaciju tokom istraživanja, u skladu sa članom 3 ovog Zakona nameće potrebu da se precizno definiše mogućnost korišćenja ovih medicinskih podataka iz dokumentacije. U skladu sa Pravilnikom Univerzitetskog Kliničkog Centra Srbije, pacijent daje saglasnost za učešće u retrospektivnim studijama potpisivanjem saglasnosti za hospitalizaciju i prateće lečenje. Svi pacijenti su potpisali saglasnost za medicinsko lečenje i učešće u bilo kojoj vrsti studija.

Finansiranje

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critical area for healthcare system improvement.

Furthermore, research addressing socioeconomic and racial disparities in MPNST survival highlights significant heterogeneity in treatment access and outcomes, even within high-income countries (9). These insights are crucial for shaping public health strategies and planning for specialized nerve tumor centers.

Study Limitations

The main limitation of this study is its retrospective design and the small number of subjects, which may limit the generalizability of findings. The lack of multivariate analysis and molecular data additionally reduces a deeper understanding of tumor pathogenesis.

Recommendations for Future Research

Future research should include larger, multicenter prospective studies that include molecular biomarkers, tracking of recurrence rates, comparative analysis of sporadic and syndromic tumor forms, as well as the analysis of costs and availability of treatment.

Conclusion

Peripheral nerve sheath tumors are rare but clinically significant entities. Schwannomas are the most common and are predominantly benign, whereas MPNSTs represent the malignant form with potentially poor prognosis. The association with NF1 remains clinically important, particularly due to the increased risk of multiple lesions. More detailed research is needed in this field.

Competing interests

The authors declared no competing interests.

Ethical Approval

The study was approved by the local Ethics Committee of our University Department and was performed in accordance with the Helsinki declaration and its amendments. Informed consent was obtained from the family.

Ethical statement

Retrospective study, which analyzes data in the period preceding the beginning of the research, and in accordance with the provisions of the Law on the Protection of Personal Data in the Republic of Serbia, with the insight into the documentation provided for in this research, and according to Article 3 of this Law, imposes the need to precisely define the possibility of using this medical data from the documentation. In accordance with the Regulations of the University Clinical Center of Serbia, the patient gives his consent to participate in retrospective studies by signing his consent to hospitalization and accompanying treatment. All patients have signed their consent for medical treatment and participation in any type of studies.

Competing interests

Authors declare no conflicts of interest.

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