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Features of the clinical course of streptococcal and Epstein-Barr virus tonsillopharyngitis in children at the present stage

Introduction. Acute tonsillopharyngitis is an inflammatory process of the pharyngeal mucosa, which also involves the tonsil tissue, caused by various microorganisms. This disease is widespread among the population, especially among children, accounting for 1.3% of all outpatient visits. Early etiologic diagnosis is key for optimized treatment in childhood, which will avoid the irrational use of antibacterial therapy.

The aim of the study. To study the features of the clinical course of streptococcal and Epstein-Barr virus tonsillopharyngitis in children to optimize treatment.

Materials and methods. We examined 103 children of different ages with acute tonsillopharyngitis who were treated in the infectious boxed wards No. 1 and No. 2 of the Chernivtsi Regional Children's Clinical Hospital during 2017–2019 and 2022–2023. The first (I) group consisted of 63 patients with Epstein-Barr virus acute tonsillopharyngitis (EBV ATP), and the second (II) group consisted of 40 children with the presence of BGSA in smear-prints/bacteriological culture – the group of streptococcal acute tonsillopharyngitis (sATP). The severity of acute tonsillopharyngitis was assessed by the constellation principle.

Results and discussions. During inpatient treatment, patients with Epstein-Barr virus acute tonsillopharyngitis complained of sore throat, discomfort when swallowing, the presence of dyspeptic manifestations, and persistent lymphadenopathy for a longer period of time. In particular, on the 5th day of hospitalization, these indicators were recorded with the following severity, which was assessed according to the constellation principle: sore throat ≥ 2 points, sore throat discomfort ≥ 2 points, dyspeptic manifestations ≥ 1.5 points, lymphadenopathy ≥ 2 points. In children with streptococcal tonsillitis, clinical symptoms such as intoxication and headache were more pronounced.

Conclusions.

1. Preservation of sore throat ≥ 2 points (sensitivity 68.2%), sore throat discomfort ≥ 2 points (sensitivity 68.2%), dyspeptic manifestations ≥ 1.5 points (odds ratio 25.8%), lymphadenopathy ≥ 2 points (odds ratio 5.1%) on the 5th day of inpatient treatment with high sensitivity and probable risk are in favor of Epstein-Barr virus tonsillitis.

2. The predominance of severe symptoms of intoxication ≥ 3.5 points (specificity 66.7%, odds ratio 5.1%) and headache ≥ 1.5 points (specificity 94.9%, odds ratio 12.9%) in patients with acute tonsillopharyngitis was more typical for streptococcal tonsillopharyngitis.

Key words: children, acute tonsillopharyngitis, group A beta-hemolytic streptococcus, Epstein-Barr virus.

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Особливості клінічного перебігу стрептококового та Епштейн-Барр-вірусного тонзилофарингіту у дітей в сучасних умовах

Вступ. Гострий тонзилофарингіт – це запальний процес слизової оболонки глотки, який також охоплює тканину мигдаликів, спричинений різними мікроорганізмами. Дане захворювання широко розповсюджене серед населення, особливо дитячого віку, складаючи 1,3% усіх амбулаторних звернень. Рання етіологічна діагностика є ключовою для проведення оптимізованого лікування у дитячому віці, що дозволить уникнути нераціонального використання антибактеріальної терапії.

Мета дослідження. Вивчити особливості клінічного перебігу стрептококового та Епштейн-Барр вірусного тонзилофарингіту в дітей для оптимізації лікування.

Матеріали та методи. Обстежено 103 дітей різного віку, хворих на гострий тонзилофарингіт, які знаходилися на стаціонарному лікуванні інфекційних боксованих відділень №1 та №2 ОКНП «Чернівецька обласна дитяча клінічна лікарня» впродовж 2017-2019 рр. та 2022-2023рр. Першу (І) з них утворили 63 хворих на Епштейн-Барр вірусний гострий тонзилофарингіт (ЕБВ ГТФ), а другу (ІІ) сформувало 40 дітей із наявністю у мазках-відбитках/бактеріологічному засіві БГСА – група стрептококового гострого тонзилофарингіту (сГТФ). Оцінку тяжкості перебігу гострого тонзилофарингіту оцінювали за констеляційним принципом.

Результати та обговорення. Впродовж стаціонарного лікування пацієнти з Епштейн-Барр вірусним гострим тонзилофарингітом триваліше скаржилася на біль в горлі, дискомфорт при ковтанні, наявність диспепсичних проявів, збереження лімфаденопатії. Зокрема, на 5-ту добу перебування в госпіталі дані показники реєструвалися з наступною виразністю, яка оцінювалася за констеляційним принципом: біль в горлі ≥ 2 балів, дискомфорт в горлі ≥ 2 балів, диспептичні прояви ≥ 1,5 бала, лімфаденопатія ≥ 2 балів. У дітей зі стрептококовим тонзилітом більш виразними були такі клінічні симптоми, як інтоксикація та головний біль.

Висновки. Збереження на 5-ту добу стаціонарного лікування болю в горлі ≥ 2 балів (чутливість 68,2%), дискомфорту в горлі ≥ 2 балів (чутливість 68,2%), диспептичних проявів ≥ 1,5 бала (відношення шансів 25,8%) лімфаденопатії ≥ 2 балів (відношення шансів 5,1%) із високою чутливістю та вірогідним ризиком свідчать на користь Епштейн-Барр вірусного тонзиліту. Переважання у хворого на гострий тонзилофарингіт виразних симптомів інтоксикації ≥ 3,5 бала (специфічність 66,7%, відношення шансів 5,1%) та головного болю ≥ 1,5 балів (специфічність 94,9%, відношення шансів 12,9%) було характернішим для стрептококового тонзилофарингіту.

Ключові слова: діти, гострий тонзилофарингіт, бета гемолітичний стрептокок групи А, Епштейн-Барр вірус.

Introduction. Every year, a significant number of cases of upper respiratory tract infections (URTIs) are reported, especially among children. One of the most common manifestations of URTIs is acute tonsillopharyngitis (ATP), an inflammatory disease of the pharyngeal mucosa and tonsils, an important aspect of successful treatment of which is differential diagnosis to identify the etiologic factor [1–3]. Early etiologic diagnosis is an important component of successful treatment, as it can prevent the irrational use of antibiotics, which in turn will have a positive impact on the problem of antibiotic resistance in the population. The global growth of antibiotic resistance poses a significant threat, reducing the effectiveness of empirical antibiotics in situations where they are really needed [4–6].

The vast majority of cases of ATP are caused by viruses, such as adenoviruses, cytomegaloviruses, rhinoviruses, and Epstein-Barr virus. Bacterial genesis accounts for a much smaller share in the structure of the incidence, but is no less important. The bacterial pathogen that most often causes ATP in children is group A beta-hemolytic streptococcus [7–10]. This pathogen is quite dangerous due to the possible subsequent occurrence of complications, namely acute rheumatic fever, post-streptococcal glomerulonephritis, and others.

Frequent manifestations of acute tonsillitis are the sudden onset of characteristic clinical symptoms, such as pain and discomfort in the throat (with or without difficulty swallowing), enlargement and hyperemia of the tonsils (with possible plaque), enlargement of the cervical lymph nodes, fever, and general malaise [11–14].

The differential diagnosis of BGSA tonsillitis is based on clinical symptoms, blood tests, rapid antigen tests, and tonsil culture. Blood tests do not have significant diagnostic value in making a diagnosis. The method of bacterial culture of tonsil material is characterized by greater specific sensitivity compared to rapid tests. In turn, a significant advantage of the latter is the speed of execution (5–10 minutes), which significantly speeds up the diagnosis with the subsequent prescription of rational treatment [15–16].

A significant disadvantage of rapid tests is the high cost of equipment and, accordingly, the lack of state support for this type of testing. In Ukraine, the method of bacterial culture from the tonsils is in demand, but in the early stages of diagnosis, this examination has no diagnostic value due to the long wait for test results.

The diagnosis of acute tonsillitis remains predominantly clinical, and distinguishing viral infection from bacterial infection is still a difficult issue. Thus, clinical diagnostic approaches, especially in resource-limited settings, remain relevant and allow, based on the results of diagnostic tests, to use clinical experience in optimizing the etiotropic treatment of children with GTF. Monitoring of the totality of symptoms of the disease, reflecting the severity of its course, seems to be a rather promising additional component in the diagnostic process [17].

The aim of the study. To study the features of the clinical course of streptococcal and Epstein-Barr virus tonsillopharyngitis in children to optimize treatment.

Materials and methods. To achieve the aim of the study, a cohort of 103 children of different ages with acute tonsillopharyngitis who were inpatients during 2017–2019 and 2022–2023 was comprehensively examined on the basis of infectious boxed departments No. 1 and No. 2 of the Chernivtsi Regional Children's Clinical Hospital.

The average age of the patients was 7.18±0.42 years, 50.5% of boys (n=52) and 49.5% of girls (n=51), respectively (P<0.001). The age distribution of the group of examined patients showed a predominance of children of preschool and early school age (59.2%), in early childhood, ATP was recorded in 20.3% of cases and in adolescence – in 20.5%.

All children underwent a comprehensive examination, among which the group-forming feature was the presence or absence of β-hemolytic group A streptococcus (BHSA) in smear-prints or inoculation from the tonsillar surface. To confirm the Epstein-Barr viral etiology of acute tonsillopharyngitis, serological testing by enzyme-linked immunosorbent assay for IgM and IgG to VCA EBV was used. Based on this analysis, two clinical observation groups were formed. The first (I) was formed by 63 patients with Epstein-Barr virus acute tonsillopharyngitis (EBV ATP), and the second (II) was formed by 40 children with the presence of BGSA in smear-prints/bacterial culture – the group of streptococcal acute tonsillopharyngitis (sATP).

When patients were admitted to an infectious diseases hospital, the severity of acute tonsillopharyngitis was assessed according to the constellation principle in such a way that as the severity of the course of ATP increased, the sum of the points of the scale for assessing the severity of acute tonsillopharyngitis developed by us increased.

The study results were analyzed by biostatistics and clinical epidemiology. Statistical analysis of the results was performed using Statistica-v.7.0 (StatSoft, USA) and Excel XP for Windows.

Results and discussions. In the current episode of acute tonsillopharyngitis, patients with EBV GTF were admitted to the hospital on average 4.84+0.46 days after the onset of the disease, patients with streptococcal ATP – 3.56+0.57 (min – 1 day, max – 21 days) (P>0.05). A burdened epidemiologic history in the form of contact with

patients with acute tonsillopharyngitis in clinical group I occurred in 6.4% of children, and in group II – in 17.5% of observations (P>0.05).

Upon admission to the infectious diseases hospital, the general condition of patients in clinical groups I and II was moderate in the vast majority of cases – 98.41% and 97.5% (P>0.05).

A common symptom of the onset of acute tonsillopharyngitis in both groups was an increase in body temperature, so in clinical group I it reached 2.43 points, in clinical group II – 3.54 points. Febrile body temperature (38.5–39 C) at the onset of the disease with high sensitivity (69.3%) and a positive predictive value of 62.7% indicated streptococcal tonsillitis.

It is believed that pain and discomfort in the throat in children with Epstein-Barr viral ATP are more pronounced than in other etiologic factors. In the analysis of the dynamics of sore throat severity in children during 7 days of inpatient treatment, a significant difference was found on days 5–7. Thus, in children with EBV acute tonsillopharyngitis, the severity of pain was higher on day 5 – 2.21+0.97 points, and in patients with sATP – 1.74+0.71 points (P<0.05), on day 6 – 1.85+0.8 points and 1.38+0.54 points (P<0.05), respectively, on day 7 – 1.75+0.77 points and 1.13+0.34 points (P<0.05), respectively.

In our study, the above indicators in the first days did not differ significantly in the comparison groups, but on day 5, with the same sensitivity, 68.2% indicated EBV infection. The risk of EBV tonsillitis increased by 1.5% in the severity of sore throat ≥ 2 points and by 1.7% in the presence of sore throat discomfort with a severity of ≥ 2 points.

Dyspeptic manifestations in children of clinical group I were more pronounced, especially in the first 4 days of inpatient treatment compared with the cohort of patients of clinical group II. Thus, in children with EBV ATP, the above indicator on day 1 was 1.83+1.06 points, and in patients with sATP – 1.23+0.48 points (P<0.05), on day 2 – 1.57+0.73 points and 1, 1+0.31 (P<0.05), respectively, on day 3 – 1.41+0.56 points and 1.01+0.01 points, respectively (P<0.05), on day 4 – 1.22+0.46 points and 1.0+0.01 points, respectively (P<0.05). The greater severity of dyspepsia in children with Epstein-Barr virus tonsillitis is probably due to the pathogen's tropism to the gastrointestinal tract and liver and spleen damage. It should also be noted that the severity of dyspeptic manifestations ≥ 1.5 points on day 5 of treatment with a specificity of 99%, a positive predictive value of 95.4% indicated in favor of EBV ATP, and the risk of development in the presence of this symptom increased by 25.8%.

The severity of lymphadenopathy ≥ 2 points on the 5th day of hospitalization with a specificity of 87.1%, a positive predictive value of 76.8% indicated in favor of EBV ATP, and the risk of development in the presence of this symptom increased in 5.1%.

The above clinical characteristics of ATP in children suggest that the presence of pathognomonic symptoms of the disease with a certain severity (in points), or their combination, allows an alternative solution to the issue of infection caused by BGSA or other pathogens.

The manifestations of intoxication syndrome on the first day of hospitalization and during 6 days of inpatient treatment were significantly more pronounced in representatives of clinical group II.

Thus, the presence of signs of intoxication with high sensitivity (71.8%), specificity (66.7%), and the predictive value of a positive result of 68.3% testified in favor of sATP. The risk of infection caused by this pathogen in the presence of an intoxication syndrome with a severity of ≥ 3.5 points was 5.1%. The presence of a headache ≥ 1.5 points with a high specificity (94.9%) and a positive predictive value of 89% indicated in favor of streptococcal tonsillitis.

Our study found that children with Epstein-Barr viral tonsillopharyngitis were characterized by longer-lasting complaints of pain and discomfort in the throat, the presence of dyspeptic symptoms, and lymphadenopathy on the fifth day of inpatient treatment. Similar results are reported in the works of other authors, where EBV infection was associated with prolonged tonsillar symptoms, as well as systemic manifestations of lymphatic system involvement [Takács et al., 2023; do Nascimento P, 2020].

In contrast, in the group of patients with streptococcal tonsillopharyngitis, pronounced symptoms of intoxication, an increase in body temperature above 38.5 °C, and headache dominated. A similar clinical picture is described in studies by J. Pallon et al., where high temperature, absence of cough, and presence of tonsillar exudate are identified as the most informative markers of bacterial etiology [Pallon et al., 2021; Seeley A et al., 2021].

It is important to note that no single symptom can serve as a reliable criterion for differentiating between bacterial and viral tonsillopharyngitis. However, the use of a combination of clinical signs and their severity in points (constellation principle), as demonstrated in our work, increases the accuracy of diagnosis. This approach is consistent with modern clinical scales (Centor, FeverPAIN), which are also based on a combination of several symptoms [Pallon et al., 2021, Sykes EA et al., 2020].

Table 1

Shows the dynamics of intoxication syndrome (in points) in acute tonsillopharyngitis in children of comparison groups (M+m)

Days of inpatient treatment	The groups of patients		P
	Group I – EBV ATP	Group II – sATP	
1 day	3.11±0.99	3.77±0.54	**P<0.05**
2 day	2.46±0.99	3.44±0.59	**P<0.05**
3 day	1.94±0.88	2.85±0.54	**P<0.05**
4 day	1.54±0.78	2.62±0.67	**P<0.05**
5 day	1.32±0.62	2.1±0.68	**P<0.05**
6 day	1.18±0.49	1.85±0.54	**P<0.05**
7 day	1.14±0.44	1.29±0.46	P>0.05

Notes: P – Student's t-test; EBV ATP – Epstein-Barr virus acute tonsillopharyngitis; sATP – streptococcal acute tonsillopharyngitis

Conclusions

1. Preservation on the 5th day of inpatient treatment of sore throat ≥ 2 points (sensitivity 68.2%, odds ratio 1.5%), sore throat discomfort ≥ 2 points (sensitivity 68.2%, odds ratio 1.7%), dyspeptic manifestations ≥ 1, 5 points (sensitivity 20.7%, odds ratio 25.8%) lymphadenopathy ≥ 2 points (sensitivity 20.7%, odds ratio 5.1%) with high sensitivity and probable risk are in favor of the Epstein-Bar for viral tonsillitis.

2. The predominance of severe symptoms of intoxication ≥ 3.5 points (specificity 66.7%, odds ratio 5.1%) and headache ≥ 1.5 points (specificity 94.9%, odds ratio 12.9%) in a patient with acute tonsillopharyngitis was more typical for streptococcal tonsillopharyngitis.

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Personal contribution of the author:

Horbatiuk I.B. – idea, aim of the study, study design, manuscript preparation, literature search, funds collection;
Horbatiuk Ir.B. – idea, purpose, data interpretation, manuscript preparation, literature search.

REFERENCES

1. Kocher JJ, Selby TD. Antibiotics for sore throat. Am Fam Physician. 2014 Jul;90(1):23-4.
2. Putto A. Febrile exudative tonsillitis: viral or streptococcal? Pediatrics. 1987 Jul;80(1):6-12.
3. Berner R, editor. DGPI Handbuch. Stuttgart: Georg Thieme Verlag; 2018. doi:10.1055/b-006-160379.
4. Shirley WP, Woolley AL, Wiatrak BJ. Pharyngitis and Adenotonsillar Disease. In: Cummings Otolaryngology - Head and Neck Surgery. Elsevier; 2010. p. 2782-802. doi:10.1016/B978-0-323-05283-2.00197-X.
5. Morgan DG, Niederman JC, Miller G, Smith HW, Dowaliby JM. Site of Epstein-Barr virus replication in the oropharynx. Lancet. 1979 Dec;2(8153):1154-7. doi:10.1016/S0140-6736(79)92384-5.
6. Kobayashi R, Takeuchi H, Sasaki M, Hasegawa M, Hirai K. Detection of Epstein-Barr virus infection in the epithelial cells and lymphocytes of non-neoplastic tonsils by in situ hybridization and in situ PCR. Arch Virol. 1998;143(4):803-13. doi:10.1007/s007050050332.
7. Roughan JE, Thorley-Lawson DA. The intersection of Epstein-Barr virus with the germinal center. J Virol. 2009 Apr;83(8):3968-76. doi:10.1128/JVI.02609-08.
8. Chiappini E, et al. Analysis of different recommendations from international guidelines for the management of acute pharyngitis in adults and children. Clin Ther. 2011 Jan;33(1):48-58. doi:10.1016/j.clinthera.2011.02.001.
9. Koloskova OK, Bezrukov LO, Ivanova LA, Horbatiuk IB, Horbatiuk IrB. Optimization of clinical diagnosis and treatment of acute tonsillopharyngitis in children. Arch Balk Med Union. 2019 Mar;54(1):51-6. doi:10.31688/ABMU.2019.54.1.07.
10. Krüger K, Töpfner N, Berner R, Windfuhr J, Oltrogge JH. Sore throat. Dtsch Arztebl Int. 2021 Mar;doi:10.3238/arztebl.m2021.0121.
11. Hasegawa K, Tsugawa Y, Cohen A, Camargo CA. Infectious disease-related emergency department visits among children in the US. Pediatr Infect Dis J. 2015 Jul;34(7):681-5. doi:10.1097/INF.0000000000000704.
12. Mitchell RB, et al. Clinical practice guideline: Tonsillectomy in children (update) – executive summary. Otolaryngol Head Neck Surg. 2019 Feb;160(2):187-205. doi:10.1177/0194599818807917.
13. Patel PD, Alghareeb R, Hussain A, Maheshwari MV, Khalid N. The association of Epstein-Barr virus with cancer. Cureus. 2022 Jun;doi:10.7759/cureus.26314.
14. Shi T, Huang L, Tian J. Prevalence of Epstein-Barr viral DNA among children at a single hospital in Suzhou, China. J Pediatr (Rio J). 2022 Mar;98(2):142-6. doi:10.1016/j.jped.2021.05.006.
15. Smatti MK, Al-Sadeq DW, Ali NH, Pintus G, Abou-Saleh H, Nasrallah GK. Epstein–Barr virus epidemiology, serology, and genetic variability of LMP-1 oncogene among healthy population: an update. Front Oncol. 2018 Jun;8:211. doi:10.3389/fonc.2018.00211.
16. Guerrero-Ramos A, Patel M, Kadakia K, Haque T. Performance of the Architect EBV antibody panel for determination of Epstein-Barr virus infection stage in immunocompetent adolescents and young adults with clinical suspicion of infectious mononucleosis. Clin Vaccine Immunol. 2014 Jun;21(6):817-23. doi:10.1128/CVI.00754-13.
17. Dunmire SK, Verghese PS, Balfour HH. Primary Epstein-Barr virus infection. J Clin Virol. 2018 May;102:84-92. doi:10.1016/j.jcv.2018.03.001.
18. Regoli M, Chiappini E, Bonsignori F, Galli L, de Martino M. Update on the management of acute pharyngitis in children. Ital J Pediatr. 2011;37(1):10. doi:10.1186/1824-7288-37-10.
19. Takács T, Kendelényi R, Varga Z, Szűcs Á, Kónya J, Bányai K, et al. Clinical and laboratory characteristics of primary Epstein-Barr virus infection in children. Front Pediatr. 2023;11:1168796. doi:10.3389/fped.2023.1168796.
20. do Nascimento P, Medeiros I, Falcão R, Stransky B, de Souza J. A decision tree to improve identification of pathogenic mutations in clinical practice. BMC Med Inf Decis Mak. 2020;20(1). DOIhttps://doi.org/10.1186/s12911-020-1060-0
21. Pallon J, de With K, Lemiengre MB, Verbakel JY. Clinical prediction rules for differentiating streptococcal from viral pharyngitis in children and adults: A systematic review. BMJ Open. 2021;11(3):e043845. doi:10.1136/bmjopen-2020-043845.
22. Seeley A, Fanshawe T, Voysey M, Hay A, Moore M, Hayward G. Diagnostic accuracy of Fever-PAIN and centor criteria for bacterial throat infection in adults with sore throat: a secondary analysis of a randomised controlled trial. BJGP Open. 2021;5:BJGPO20210122. doi: 10.3399/BJGPO.2021.0122.
23. Sykes EA, Wu V, Beyea MM, Simpson MTW, Beyea JA. Pharyngitis: Approach to diagnosis and treatment. Can Fam Physician. 2020 Apr;66(4):251-257. PMID: 32273409; PMCID: PMC7145142.

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