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Analysis of patients with recurrent laryngeal papillomatosis of the ENT Pediatric Department of the Medical University of Warsaw in the last 15 years (2009-2024)

Analiza pacjentów Kliniki Otolaryngologii Dziecięcej WUM z nawracającą brodawczakowatością krtani w ostatnich 15 latach (2009-2024)

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KEYWORDS:

recurrent laryngeal papillomatosis, hoarseness, HPV virus, children, diagnostics

SUMMARY

Introduction. Recurrent laryngeal papillomatosis in children is a disease of viral etiology caused by the human papillomavirus HPV type 6 and/or type 11. Clinical symptoms of laryngeal papillomatosis include hoarseness, aphonia, dyspnea with varying degrees of severity. Treatment consists in the surgical removal of lesions that narrow the lumen of the airways. The disease has an unpredictable course, Prognostic factors could not be identified.

Aim. The aim of the study is to draw attention to recurrent laryngeal papillomatosis in children, which is a very serious disease that devastates the life of the child and the family, and manifests itself in potentially harmless clinical symptoms that are often underestimated.

Material and methods. We analyzed the medical histories of children treated in the ENT Pediatric Department of the Medical University in Warsaw due to recurrent laryngeal papillomatosis over the last 15 years.

Results. Finally, we found that the disease is adversely affected by any delay in diagnosis and initiation of treatment relative to the appearance of the first clinical manifestations.

Conclusions:

1. Persistent hoarseness requires visualization of the vocal folds.
2. Voice change in children may be a symptom of laryngeal papillomas.
3. Laryngeal papillomas can occur in children of any age.
4. The onset of the disease at the age of less than 1 year is associated with an aggressive course of the disease.
5. Diffuse papillary lesions in the larynx are associated with a more aggressive course of the disease.
6. Lesions limited to 1 or 2 places in the larynx are associated with a mild course of the disease.

SŁOWA KLUCZOWE:

nawracająca brodawczakowatość krtani, chrypka, HPV wirus, dzieci, diagnostyka

STRESZCZENIE

Wstęp. Nawracająca brodawczakowatość krtani u dzieci jest chorobą o etiologii wirusowej, wywołowaną przez wirusa brodawczaka ludzkiego HPV typu 6 i/lub typu 11. Do klinicznych objawów brodawczakowatości krtani zalicza się: chrypkę, bezgłos oraz duszność o różnym stopniu nasilenia. Leczenie polega na chirurgicznym usunięciu zmian zwięzających światło dróg oddechowych. Nie udało się zidentyfikować czynników prognostycznych mających wpływ na przebieg choroby, który jest nieprzewidywalny.

Cel pracy. Celem pracy jest zwrócenie uwagi na nawracającą brodawczakowatość krtani u dzieci, która jest chorobą bardzo poważną, rujną życie dziecka i jego rodziny, a objawiającą się pierwotnie potencjalnie mało poważnymi objawami klinicznymi, które często są bagatelizowane.

Materiał i metody. Przeanalizowano historię chorób dzieci leczonych w ciągu ostatnich 15 lat w Klinice Otolaryngologii Dziecięcej Warszawskiego Uniwersytetu Medycznego z powodu nawracającej brodawczakowatości krtani.

Wyniki. Stwierdziliśmy, że na przebieg choroby prawdopodobnie niekorzystnie wpływa każde opóźnienie w rozpoznaniu i rozpoczęciu leczenia w stosunku do pojawienia się pierwszych objawów klinicznych.

Wnioski:

1. Każda utrzymująca się chrypka wymaga badania krtani z uwidocznieniem fałdów głosowych.
2. Zmieniony głos u dzieci może być objawem brodawczaków krtani.
3. Brodawczaki krtani mogą pojawić u dzieci w każdym wieku.
4. Początek choroby w wieku poniżej 1 roku wiąże się z agresywnym przebiegiem choroby.
5. Rozlane zmiany brodawkowe w krtani wiążą się z bardziej agresywnym przebiegiem choroby.
6. Zmiany ograniczone do 1 lub 2 miejsc w krtani wiążą się z łagodnym przebiegiem choroby.

INTRODUCTIONS

Recurrent laryngeal papillomatosis is a disease of viral etiology caused by the human papillomavirus HPV. In children type 6 and/or type 11 are identified in the respiratory tract. The disease involves the formation of numerous papillary nodules infiltrating the mucous membrane of the respiratory tract, which narrows their lumen. Most often are located in the glottis (vocal folds, anterior commissure), laryngeal vestibule and in subglottic area. In rare cases, lesions spread to the trachea and bronchi. Occasionally, there are single lesions in the mucous membrane of the mouth or throat, which usually disappear spontaneously. Changes in the respiratory tract occur cyclically. The disease has an unpredictable course, the frequency of relapses, the length of remission periods and the degree of airway obstruction vary greatly in individual patients (1-3). It was not possible to identify prognostic factors influencing the course of the disease. There is currently no certain evidence as to the mode of infection. It is believed that the risk of developing the disease increases in children of mothers with a history of HPV infection (the same types of virus are found in condyloma acuminata). The disease most often occurs in children over 2 years of age; diagnosis is usually made between 2-6 years of age (1-3). Childhood papillomas, unlike adult papillomas, do not undergo neoplastic transformation. They tend to undergo spontaneous involution during puberty.

Clinical symptoms of laryngeal papillomatosis include primarily phonation disorders: hoarseness, aphonia, voiceless crying. As the changes gradually narrow the airway, dyspnea occurs with varying degrees of severity and progression (1-4).

Treatment is aimed at clearing the airways by removing papillomatous lesions. The standard of care is the surgical removal of papillomas that narrow the respiratory tract under general anesthesia, the so-called papillotomy. Treatment methods are being sought to reduce the number of disease relapses and extend remission periods (1-4).

The disease is very disabling and its course is difficult to predict. This is associated with multiple hospital stays, subsequent general anesthesia for surgery and restrictions in the everyday life of children and their families (interruptions in education, social isolation). Additionally, each subsequent surgery with the respiratory mucosa causes scarring, which manifests itself in chronic hoarseness, voice disorders.

AIM

The aim of the study is to draw attention to recurrent laryngeal papillomatosis in children, which is a very serious disease that devastates the life of the child and family and manifests itself in potentially harmless clinical symptoms that are often underestimated.

MATERIAL AND METHODS

The medical histories of children treated in the Department of Pediatric Otolaryngology of the Medical University of Warsaw due to recurrent laryngeal papillomatosis over the last 15 years, i.e. from 2009 to 2024, were analyzed. The clinical symptoms occurring in the above-mentioned patients were analyzed, age of onset of first symptoms; age of diagnosis and type of HPV virus causing the disease. Attention was paid to the location and local characteristics of changes in the respiratory tract. The number of surgical interventions was also analyzed.

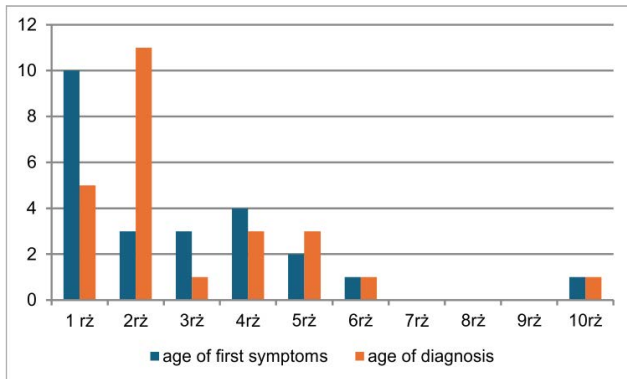


Fig. 1. Age of onset of first symptoms and age of diagnosis

RESULTS

Currently, 24 children remain under care of the Paediatric Otolaryngology Clinic of the Medical University of Warsaw due to recurrent laryngeal papillomatosis: 8 boys and 16 girls. Children are aged from 11 months to 10 years.

We analysed the age at which the children first came to the clinic and were diagnosed with laryngeal papillomatosis and the moment when the first clinical symptoms appeared. Most children came to the clinic at 2 years of age and there were 12 out of 24; in 5 children the disease was diagnosed by 1 year of age; in 3 at 4 years of age, 3 at 5 years of age and 1 child each at 3, 6 and 10 years of age. An interview with the parents showed that the first symptoms in the children occurred much earlier. In 10 children the first symptoms appeared in the first year of life, in another 3 children in the second year, in 3 in the third year, in 4 children in the fourth year, in the fifth year in 2 children and in one child in the sixth and tenth year. Figure 1 shows the age of the children at the onset of the first symptoms and the date of diagnosis.

The main symptom presented by our patients with laryngeal papillomas is hoarseness or aphonia. In the youngest children from 1-6 months of age, the first symptom was a voiceless cry; the parent reported not hearing their child cry. In older children, hoarseness. Another symptom occurring in the course of recurrent laryngeal papillomatosis in our patients was dyspnoea, which was presented by 5 children. From the parents' reports, the dyspnoea initially occurred only on exertion and the child became more fatigued during feeding or crying. Three children were treated for acute laryngitis. The lack of therapeutic effect and persistent dyspnoea with features of respiratory failure led to qualification for urgent airway control. Directoscopy diagnosed laryngeal papillomas.

All children with the above-mentioned symptoms underwent fiberoptic laryngoscopy and, if lesions were present, laryngotracheoscopy of the airways under general anaesthesia. Lesions found in the larynx were removed simultaneously during the procedure. Tissue material was sent for histopathological examination and human papilloma virus typing. The histopathological examination yielded the result: Squamous cell papilloma. Virus typing identified the

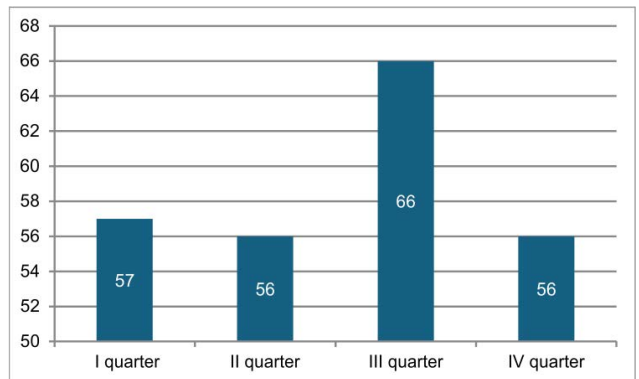


Fig. 2. Time of the year and amount of surgery

HPV type: in 4 cases type 11, in 18 cases type HPV-6 and in 2 children HPV-11 and HPV-6 simultaneously.

During the surgery the extent of the changes was assessed. Single exophytic lesions were found in 12 children mainly on the vocal folds. These were children with the first clinical symptoms at the age of: 2, 3, 4, 5, 6 and 10 years old. They were diagnosed with hoarseness of varying degrees, slight aphonia, and no shortness of breath. Children required surgical intervention no more than 1-2 times a year. In total, 48 papillotomies were performed in these 12 children. The total number of papillotomies in our patients during the above-mentioned 15 years was 235, which means that the remaining 12 children required 187 surgical interventions. In the remaining 12 children diffuse lesions were initially found: in the anterior commissure and the anterior third of the both vocal folds, and in some children in the subglottic area. These children presented with a changed voice, depending on age: hoarseness or soundless crying and always varying degrees of dyspnoea. The severity of shortness of breath ranged from that occurring during exercise, crying or feeding, to dyspnoea at rest with activation of additional respiratory muscles, to respiratory failure in 3 children.

The analysis also included the time of year when children undergo surgery due to the increase of hoarseness or respiratory symptoms; this distribution shown figure 2. Slightly more children undergo surgery in the summer.

The interview also included questions about the birth and the mother's illnesses. 20 babies out of 24 were born by natural childbirth, 2 by caesarean section. The babies were born from term pregnancies, i.e. from the 38th week of gestation. The babies did not present respiratory distress at birth and did not require respiratory support or intubation. 15 mothers had HVP testing before pregnancy and were not found to be infected. 1 mum was found to have HPV type 32 without symptoms of disease. The remaining 8 mothers had tests after diagnosis in their children and were not found to have the virus. 18 of the 24 children have siblings, older and younger, none of whom were diagnosed with papillomaviruses.

In 10 children symptoms were present from birth. The parents of all these children reported that they had

never heard their baby cry loudly. In 5 children, the diagnosis was made in first year of life when the symptoms included dyspnoea. In 2 children, shortness of breath occurred already in the 1st and 2nd month of life, which resulted in quick diagnosis. Three children appeared in the hospital with symptoms of severe shortness of breath with activation of additional respiratory muscles or respiratory failure, and the first symptoms of dysphonia occurred in them at the age of 1. Another 5 children from this group came to the clinic at the age of 2 due to worsening symptoms. The delay in diagnosis from the onset of the first symptoms was 8-26 months, respectively. To this day, all the above-mentioned children have required from 15 to over 40 surgical interventions each child, from 3 to 10 a year. In 9 children, the diagnosis was made at 3, 4, 5, 6 and 10 years of age. These children presented hoarseness with minimal shortness of breath, and symptoms appeared no more than 2 months before they were reported to the hospital and diagnosed. These children required 1-3 papillotomy procedures, no more than 1 time a year.

In 18 children HPV type 6 was found, in 4 children HPV 11 type 11 and in 2 HPV types 6 and 11 together. In 2 children who required tracheostomy: in one HPV type 6 was recognized and in 1 type 11. They were diagnosed with the first clinical symptoms aphonia and dyspnea, which occurred before 1 year of age. To date 30 and 21 surgical interventions have been performed in these children. 2 children with type 11 were girls diagnosed at the age of 2 and 10, who reported hoarseness without shortness of breath. Exophytic lesions located on the vocal fold were found in them. They required 1 and 5 surgical interventions, respectively, no more often than 1 x per year. 2 girls with HPV type 6/11 were diagnosed on the basis of hoarseness at 2 and 4 years of age. They required 2 and 5 interventions, respectively.

DISCUSSION

Recurrent laryngeal papillomatosis is a viral disease. The route of infection and the age at which it occurs are difficult to determine. Only 1 mother of our child with laryngeal papillomas was a carrier of HPV virus and the type of virus did not correspond to the type of child diagnosed; HPV 32 type in the mother and HPV 6 type in the child (1).

The moment of infection is also difficult to determine. According to the analysis of the cases of our patients, the disease was often diagnosed in the youngest patients approximately 1 year later after the first symptoms appeared. The main symptom, hoarseness, is often underestimated. In children who are developing speech and start babbling, hoarseness is often unnoticeable because the caregiver does not know any other voice the child makes. The reason for earlier reporting was only shortness of breath or breathing disorders that occurred in 5 children under 1 year of age, but they were also preceded by various types of dysphonia. Diagnosis made in children at the age of 2 years

or older is often related to the child's entry into preschool education and the staff's attention to the child's changed voice in relation to others in the group. From the analysis of this work, as well as from the information contained in numerous publications, it seems that the early age of onset of the disease – the appearance below 1 year of age and perhaps a delay in diagnosis and treatment may affect the course of the disease and the frequency of surgery. Of the 24 children 10 first symptoms appeared at the age of 1, but only 5 of them reported to the clinic at that time because they experienced shortness of breath or respiratory failure. Another 5 came in the second year of life. To this day these children have required the highest number of surgery with a frequency of several times a year (1-6).

This study noted that the type of changes in the airway influences the course of the disease. Twelve children (50%) with single, exophytic lesions limited in the larynx to 1 or 2 locations required fewer surgical interventions only 48 (21%) out of 235 performed in all patients. The frequency of these interventions was also lower: 1-2 times per year. They were children over 2 years old. Another 12 children (50%) with diffuse lesions involving numerous structures of the glottis, subglottis or supraglottis required numerous and frequent interventions. They underwent 187 papillotomies, which constitutes 79% of all interventions in our patients. This group was dominated by children under and up to 2 years of age.

The type of HPV virus 6 or 11 in our group of patients was not associated with a different course of the disease. The children did not have worse symptoms depending on the type of virus and did not require more surgical interventions. Only 2 children required tracheostomy due to the course of the disease; one with HPV type 11 and 1 with type 6. In both of them the first symptoms appeared before the age of 1 year and treatment was started immediately (7-9).

CONCLUSIONS

1. Any hoarseness that persists after the acute respiratory tract infection has been cured requires an assessment of the larynx with visibility of the vocal folds, e.g. fiberoscopy.
2. Voice change in children in the form of hoarseness, aphonia, and silent crying may be a symptom of laryngeal papillomas.
3. Laryngeal papillomas can occur in children of any age.
4. The onset of the disease at the age of less than 1 year is associated with an aggressive course of the disease.
5. Disseminated papillomatous lesions in the larynx are associated with a more aggressive course of the disease.
6. Changes limited to one max 2 places in the larynx are associated with a mild course of the disease.

**CONFLICT OF INTEREST
KONFLIKT INTERESÓW**

None
Brak konfliktu interesów

**CORESPONDENCE
ADRES DO KORESPONDENCJI**

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REFERENCES/PIŚMIENNICTWO

1. Derkay CS, Wiatrak B: Recurrent respiratory papillomatosis: a review. *Laryngoscope* 2008; 118(7): 1236-1247.
2. Silva L, Gonçalves CP, Fernandes AM et al.: Laryngeal papillomatosis in children: The impact of late recognition over evolution. *J Med Virol* 2015; 87(8): 1413-1417.
3. Tasca RA, Clarke RW: Recurrent respiratory papillomatosis. *Arch Dis Child* 2006; 91: 689-691.
4. Boo WH, Rajan P, Ching SM, Lee PY: Juvenile recurrent respiratory papillomatosis: A rare masquerade of asthma. *Malays Fam Physician* 2015; 10(2): 45-48.
5. Harris AT, Atkinson H, Vaughan C et al.: Presentation of laryngeal papilloma in childhood: The Leeds experience. *Int J Clin Pract* 2012; 66(2): 183-184.
6. Zacharisen MC, Conley SF: Recurrent respiratory papillomatosis in children: Masquerader of common respiratory diseases. *Pediatrics* 2006; 118: 1925-1931.
7. Wiatrak BJ, Wiatrak DW, Broker TR, Lewis L: Recurrent respiratory papillomatosis: a longitudinal study comparing severity associated with human papilloma viral types 6 and 11 and other risk factors in a large pediatric population. *Laryngoscope* 2004; 114: 1-23.
8. Buchinsky FJ, Valentino WL, Ruskay N et al.: Age at diagnosis, but not HPV type, is strongly associated with clinical course in recurrent respiratory papillomatosis. *PLoS One* 2019; 14: e0216697.
9. Matinhira N, Soko ND, Bandason T et al.: Human papillomavirus types causing recurrent respiratory papillomatosis in Zimbabwe. *Int J Pediatr Otorhinolaryngol* 2019; 116: 147-152.