

The relationship between nasopharyngeal tonsil size and laboratory markers in children infected with HIV

Relação entre tamanho da tonsila faríngea e marcadores laboratoriais em crianças infectadas por HIV

Abstract

Purpose: The enlargement of nasopharyngeal tonsils, which leads to nasal obstruction and subsequent mouth breathing, can be caused by the presence of HIV. The aim of this research was to study nasopharyngeal tonsil sizes in HIV-infected children ranging from 6 to 13 years and to relate these findings to CD4+ T-cell counts and viral loads.

Methods: Sixty children with HIV (mean age: 9 years and 8 months), infected by vertical transmission, had the sizes of their nasopharynx measured using lateral cephalometric radiographs, specifically focusing on the anatomical areas occupied by the nasopharyngeal tonsils. The children's medical records were analyzed to assess information about TCD4+ lymphocyte count (%) and viral loads (\log_{10}).

Results: The mean value for the nasopharyngeal tonsil size percentage was $70.37\% \pm 14.07\%$. All of the children showed moderate or accentuated hypertrophy of nasopharyngeal tonsils. The average percentage of CD4+ T-cells among the 60 HIV-infected children was $35.01\% \pm 10.76\%$, whereas the mean value for the viral load was $3.35 \pm 1.08 \log_{10}$.

Conclusion: There was no association between the size percentages of the nasopharyngeal tonsils (calculated against overall nasopharynx sizes) and CD4+ T-cell percentage ($r = -0.0136$; $P = 0.298$) or the viral load \log_{10} ($r = -0.033$; $P = 0.805$).

Key words: HIV; pediatric AIDS; adenoids; lateral cephalometric radiograph

Resumo

Objetivo: A presença do HIV na tonsila faríngea pode causar seu aumento de volume, ocasionando obstrução nasal e, conseqüentemente, respiração bucal. O objetivo deste trabalho foi avaliar o tamanho da tonsila faríngea em crianças infectadas pelo HIV por transmissão vertical, de 6 a 13 anos de idade, relacionando-a com a contagem de células T-CD4+ e carga viral (\log_{10}).

Metodologia: Sessenta crianças HIV positivo (idade média: 9 anos e 8 meses), infectadas por transmissão vertical, tiveram o tamanho da tonsila faríngea mensurado na radiografia cefalométrica lateral da face. Os prontuários das crianças foram analisados para buscar os dados de contagem de linfócitos T-CD4+ (%) e carga viral (\log_{10}).

Resultados: A média do tamanho da tonsila faríngea foi de $70,37\% \pm 14,07\%$. As crianças apresentaram hipertrofia da tonsila faríngea considerada moderada ou acentuada. A porcentagem média de linfócitos T-CD4+ nas 60 crianças foi de $35,01\% \pm 10,76\%$ e a média da carga viral foi de $3,35 \pm 1,08 \log_{10}$.

Conclusão: Não foi comprovada relação entre o tamanho da tonsila faríngea com a porcentagem de linfócitos T-CD4+ ($r = -0,0136$; $P = 0,298$) e com a carga viral ($r = -0,033$; $P = 0,805$).

Palavras-chave: HIV; AIDS pediátrica; adenóide; radiografia cefalométrica lateral

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Introduction

The nasopharyngeal lymphoid tissue contributes to the chronic replication of HIV-1 (1). HIV-1-infected cells were found in the lymphoepithelium of the nasopharyngeal tonsil invaginations. These tissues serve as a reservoir and a vehicle for virus dissemination. A child's nasopharyngeal tonsil has a greater number of lymphocytes than adult tonsils (2).

The nasopharyngeal tonsillar tissue, a secondary lymphoid tissue, reveals the stage of immunodeficiency of HIV-infected patients and can also provide additional information about the evolution and response of the affected patients to their treatment (3). A large increase in the amount of nasopharyngeal tonsillar tissue can be found in magnetic resonance images of HIV-infected adults, especially when they are compared to those of healthy people (4). A study of lateral radiographs of the nasopharynx in HIV-infected and non-infected children using the adenoid-nasopharyngeal (AN) ratio showed a correlation between the increase in tonsillar tissue and the different stages of the disease (5).

The increase of the nasopharyngeal tonsil size due to the presence of HIV may reduce nasal flow, obstruct the upper respiratory tract and lead to mixed or orally-substituted breathing patterns. During examination of breathing function, patients' lips and jaw postures are verified and an overall assessment is conducted to determine lip competence (6). Furthermore, oral breathing may cause breathing complications such as pneumonia, which is considered one of the main causes of mortality in HIV-infected children (7-9).

The aim of this research was to study nasopharyngeal tonsil sizes in HIV-infected children ranging from 6 to 13 years in age to relate these findings to CD4+ T-cell counts (%) and viral loads – VL (\log_{10}).

Methodology

This research was approved by the Institutional Committee for Ethics in Research with Human Beings. A descriptive transversal study with 60 children with HIV who were infected by vertical transmission (ages 6 to 14 years old) was conducted in the Infectology Section of Joana de Gusmão Children Hospital (HIJG) in Florianópolis, Santa Catarina, Brazil. Children with past history of tonsillectomies, cleft lips or cleft palates were excluded. After an interview was conducted and the procedures to be accomplished were explained, all children participated in the research under the free informed consent of their parents and/or legal representatives.

Clinical diagnosis

A pediatrician and a dentist were responsible for the clinical examination of the children. When necessary, patients were submitted for a radiographic examination. The clinical indication for a radiographic evaluation involved patients presenting with mouth breathing (6,9) and was based on the following criteria:

- a) Alterations of behavior during the daytime: uneasiness, bad humor, impatience, disturbances, lack of concentration in daily activities, hyperactivity, aggressiveness, fatigue and sleepiness during the day, all of which may be suggestive of mouth breathing.
- b) Collected data showing occurrences of allergic rhinitis, sinusitis, bronchitis, constant colds, tonsillitis and reports on increases in the size of the nasopharyngeal tonsils.
- c) Collected data showing nocturnal behaviors, such as night mouth breathing, snoring, sleeping position, enuresis and excessive slobbering on the pillow.

Methods of radiographic analysis

The children were submitted for a lateral cephalometric radiographic examination (J. Morita Veraview®, Kyoto, Japan) at the dental radiographic service. The radiographs were obtained following the recommended patterns and were automatically processed (Processor REVELL®, São Paulo, SP, Brazil).

Two examiners, specialists in dentomaxillofacial radiology, were allocated to perform the evaluation of the radiographic images (agreement value of 95% and an intra-examiner error value of 5%). The radiographs were numbered and masked by another professional before analysis.

Pictures of anatomical structures of interest were transferred to an acetate paper with the aid of masks, allowing the subsequent identification of reference points and the construction of lines and planes to analyze the nasopharyngeal space (10). After the manual tracing was done, the radiographs were scanned (Scanner HP Scanjet 4C/T®, São Paulo, Brazil), and the images were transferred to a cephalometric analysis software. To identify the degree of obstruction of the aerial tract in the lateral view and to determine the nasopharyngeal space occupied by the nasopharyngeal tonsil, a measurement of the adenoid percentage was utilized, according to previous studies (11-13). The total nasopharyngeal size was obtained through the calculation of a trapezoid area. The four sides of the trapezoid are represented by four planes: the *Palate Plane (PP)*, which goes through the anterior nasal spine (ANS) and posterior nasal spine (PNS); the *Sphenoid Plane (SP)* that goes through the basio point (Ba) and the sphenoid bone adjacent plane; the plane *PAA* that goes through the most anterior point of the Atlas Vertebra (AA); and the *Pterygomaxillary Plane (PtmP)*, a space perpendicular to the palate area that goes through the PPtm/PNS (Fig. 1). The nasopharyngeal plane was determined mathematically using the nasopharyngeal depth, the nasopharyngeal height, and the angle formed between the sphenoid and the palate planes, as shown in Figure 1. The aerial portion was measured using a polar planimetric compensation, whereas the plane occupied by the nasopharyngeal tonsil was obtained by subtracting the aerial portion from the total nasopharyngeal area. A modified software (Radiocef, developed by Radiomemory®, Belo Horizonte – MG, Brazil), which showed the calculation of this percentage of obstruction of the nasopharyngeal tonsil, was used to perform the analysis. A nasopharyngeal tonsil obstructing less than half of the nasopharyngeal

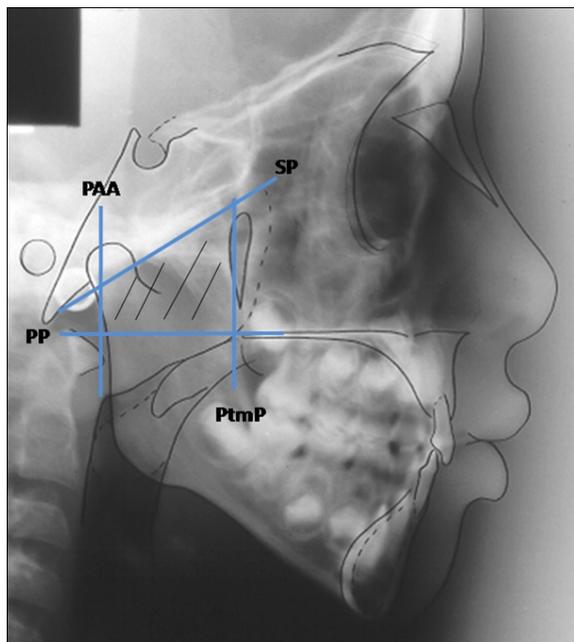


Fig. 1. Planes that define the trapezoid for calculation of the nasopharyngeal area: palate plane (PP), sphenoid plane (SP), plane going through AA (PAA) and pterygomaxillary plane (PtmP).

space ($\leq 50\%$) was considered to be *normal sized*; a tonsil obstructing between 50% and 75% of the nasopharyngeal space was considered *moderate sized*; and a tonsil obstructing more than 75% of such space was considered *enlarged* (8).

Data from medical records

Based on an analysis of the children's records, medicinal intake values and both absolute and relative counts of TCD4+ lymphocytes and VL (\log_{10}) were obtained. The results obtained were submitted to descriptive statistical analyses involving a chi-squared test (t), and Pearson's correlation.

Results

In the total sample consisting of 60 HIV-infected children, 33 were female (55%) and 27 were male (45%). Their ages ranged from 5 years and 1 month to 13 years and 7 months (average age: 9 years and 8 months). According to radiographic analyses, 5 children (8.3%) presented normal percentage values for their nasopharyngeal areas obstructed by nasopharyngeal tonsils (below 50%), 34 (56.7%) presented moderate obstruction of the nasopharynx (from 50% to 75%), and 21 (35%) presented increased obstruction (above 75%).

The results of the VL (\log_{10}) and TCD4+ lymphocytes counts (%) are shown in Table 1. The average percentage of TCD4+ lymphocytes was $35.01\% \pm 10.76$ and the VL algorithm was 3.25 ± 1.08 .

Pearson's correlation showed no correlation between the TCD4+ lymphocyte count and the percentage of obstruction of the nasopharyngeal area by the nasopharyngeal tonsil ($r=0.136$; $P=0.298$). Similarly, no correlation was found between the VL \log_{10} and the percentage of obstruction of the nasopharynx by the nasopharyngeal tonsil ($r=0.033$; $P=0.805$).

Fifty eight children (96.7% of the children in the studied sample) were under some type of therapeutic plan. The great majority utilized an association of Zidovudin (AZT), Didanosine (ddI) and Sulphametoxazol + Trimetoprim (SMX + TMT or Bactrim). Two children lacked any clinical indication to utilize a therapeutic plan, because they presented with non-detectable VL counts and adequate CD4+ lymphocyte counts.

Discussion

The dentist plays an important role in the treatment of HIV-infected patients, which includes the maintenance of a good oral health and assistance in improving their overall quality of life. It is essential that the dentist be able to recognize all of the manifestations of HIV/AIDS that can affect patients (14).

An increase in the size of the nasopharyngeal tonsil can result in an alteration of breathing dynamics, which makes breathing through the nose more difficult, causes a decrease in nasal air flow, and results in patients' adoption of temporary or definitive substitute breathing methods, such as through the mouth (1,9,15-21).

Almost 91.7% of the children in this study showed an obstructed nasopharyngeal space by the nasopharyngeal tonsil of greater than 50%, which corresponds to a moderate or increased obstruction. Nasal obstruction and mouth breathing, as discussed in Nishimura & Suzuki (22) and Kobayashi et al. (23), can cause snoring, nocturnal slobbering, hypotonicity of the upper lip, ogival-shaped hard palates, narrow nostrils, and tension of the mentalis muscles.

HIV-infected children present with a greater occurrence of upper respiratory tract infections and repetitive colds that can, despite being temporary, also be responsible for nasal obstruction and may contribute to changes in the assessment of nasal air flow (19). Yousem et al. (4) and Benito et al. (5) detected an increase in nasopharyngeal tonsil sizes in HIV-infected patients.

Table 1. Descriptive analysis of age, percentage of nasopharyngeal area obstructed by nasopharyngeal tonsil (PT), TCD4+ lymphocytes count and VL \log_{10} in HIV infected children.

Characteristics	Minimum	Maximum	Average	Pattern deviation
AGE	6.10	13.60	9.69	1.92
% of PT Occupation	29.07	99.45	70.37	14.07
Viral Load \log_{10}	1.90	5.36	3.25	1.08
TCD4+ Lymphocytes (%)	7.00	56.02	35.01	10.76

In the present study, no correlation was seen between the percentage of obstruction of the nasopharyngeal area by the nasopharyngeal tonsil and TCD4+ lymphocyte counts or VL counts. These findings are in agreement with the results obtained by Yousem et al. (4).

With regard to the clinical stage of HIV, as well as to the level of immunodeficiency, it was found that the children in the present study were well controlled with the utilization of anti-retroviral medicine and presented an average TCD4+ lymphocyte count of 35% and an average VL log₁₀ of 3.25%. These values are considered ideal clinical presentations without symptoms, which specifically involve a relative TCD4+ lymphocyte count above 25% and a VL log₁₀ below 2.00 (24). All but two (3.3%) children were taking medicines and showing a positive treatment acceptance. Furthermore, the increase in the size of the nasopharyngeal tonsil may be considered a physiological function of their ages. Therefore, the size increase of the nasopharyngeal tonsil may simply be a response of the immune system to the HIV infection stimulus, as sometimes happens with other diseases. The results may be a reflection of the positive treatment acceptance, represented here by the responsibility of the caretaker and the good conditions of the children who comprised the sample.

Considering the role of the nasopharyngeal tonsil as a lymphoid tissue and a reservoir site for HIV, the clinical and radiographic evaluation of the tonsil can be utilized as a clinical criterion for the evaluation of disease progression. This evaluation constitutes a possible means of an early identification of the infection in patients during clinically latent periods. Although this study does not show a correlation between the increased nasopharyngeal tonsil sizes with the TCD4+ lymphocyte and VL log₁₀ counts, the authors believe that radiographic analyses of the nasopharyngeal tonsils may represent an effective criterion for the evaluation of disease progression, because it provides easy access, sufficient acceptance by the patients, and simple technical execution.

Conclusions

The study findings reveal the following conclusions:

- HIV-infected children presented moderate-to-large increases in their nasopharyngeal tonsil sizes.
- No correlation was established between the increased sizes of the nasopharyngeal tonsils and the TCD4+ lymphocytes (%) or VL (log₁₀) counts.

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