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Pediatric Multisystem Inflammatory Syndrome In Covid -19 Infection: emphasis on Kawasaki Syndrome

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Abstract: *ABSTRACT: BACKGROUND: CoVid-19 presents itself as a cause of SARS and other important pathologies, every day a new sign, symptom or comorbidity related to it is discovered, such as the pediatric multisystem inflammatory syndrome, including the Kawasaki Syndrome that increased its frequency in children in 2020, raising theses that may be related to CoVid-19. Many signs and symptoms of SARS-COV-2 and Kawasaki Syndrome are present in the oropharyngeal region, and the pediatric dentist may lead to the identification and appropriate referral of these pathologies. OBJECTIVE: To alert pediatric dentists to the suspected signs and symptoms of SARS-CoV-2 and Kawasaki Syndrome. METHODOLOGY: systematic searches in articles and books, using the keywords CORONAVIRUS / + / CHILDREN / OR / PEDIATRICS and, SARS / OR / SEVERE ACUTE RESPIRATORY SYNDROME / AND / CHILDREN / OR / PEDIATRICS, KAWASAKI SYNDROME / AND / PEDIATRICS on the platform on platform Virtual Health Bank and MedScape, in open period, in Portuguese and English, visits to collections of university health libraries and non-directive interview with Professor Doctor Aureliano da Silva Guedes with questions related to Kawasaki Syndrome and SARS-COV-2. Being an exploratory-explanatory bibliographic research. CONCLUSION: The pediatric dentist should be alert of the signs and symptoms of SARS-CoV-2 and Kawasaki Syndrome because they are related to the oropharyngeal region, leading to the need for integrated, multidisciplinary and participatory work with national and international institutions, reporting suspect of new signs, symptoms and comorbidities related to CoVid-19 and Kawasaki Syndrome, because the evolution of these pathologies and their implications is not known for the short time between the alert and today.*
KEYWORDS: Severe Acute Respiratory Syndrome; Kawasaki Syndrome; Kawasaki, Disease; SARS-CoV-2; CoVid-19; Pediatric Dentistry; Pediatrics.

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I. Introduction

Acute respiratory infections (ARI) are responsible for high rates of morbidity and mortality worldwide. Children, especially babies, due to a relatively immature immune system, are highly susceptible to the action of respiratory viruses. Although the vast majority of diseases caused by respiratory viruses are self-limited and restricted to the Upper Respiratory Tract (URT), complications and infections of the Lower Respiratory Tract (LRTI), such as bronchiolitis, pneumonia and wheezing, are causes of childhood hospitalizations. Moreover, some acute respiratory infections acquired early can lead to recurrent wheezing and asthma in predisposed individuals and to chronic lung disease[1].

Doctors in France and northern Italy, one of the areas hardest hit by the new coronavirus, reported spikes in cases of a rare inflammatory syndrome in young children that appears similar to that reported in the United States, Britain and Spain, according to a report The Lancet. The condition, "Pediatric Multisystem Inflammatory Syndrome potentially associated with COVID-19", shares symptoms with toxic shock and Kawasaki syndrome. Case reports have raised concerns that COVID-19 could pose a greater risk to children than previously thought[2].

Since SARS-CoV-2 is of concern to all areas of health, with an emphasis on dentistry, especially pediatric dentistry, where in many cases of the signs and symptoms of SARS-CoV-2 have been milder, however new characteristics or related pathologies have been identified with the evolution of studies[2].

In this sense, the objective of this article is to alert pediatric dentists to the suspicious signs and symptoms of SARS-CoV-2-19 and Kawasaki Syndrome in the age groups attended by pediatric dentists.

In the methodology were held systematic searches in articles and books, using the keywords CORONAVIRUS / + / CHILDREN / OR / PEDIATRICS and, SARS / OR / SEVERE ACUTE RESPIRATORY SYNDROME / AND / CHILDREN / OR / PEDIATRICS, KAWASAKI SYNDROME / AND / PEDIATRICS on the platform on platform Virtual Health Bank and MedScape, in open period, in Portuguese and English, visits to collections of university health libraries and non-directive interview with Professor Doctor Aureliano da Silva

Guedes with questions related to Kawasaki Syndrome and SARS-COV-2. Therefore, having the characteristic of an exploratory-explanatory bibliographic research.

II.CoVid-19

Coronavirus belongs to the family Coronaviridae, genus Coronavirus. It presents as human and animal hosts. They are single-stranded RNA viruses, enveloped, helical nucleocapsid, diameter between 100 and 150 nm. Strains of human importance are OC43, 229E, NL63, HKU1 and SARS[1].

CoVid-19 is a potential cause of SARS (Severe Acute Respiratory Syndrome), among other multinflammatory pathologies.

SARS was known in March 2003 when the World Health Organization declared a global alert. The first in humans were described in Guangdong province in China in November 2002, as an acute respiratory disease of unknown cause. In February of the same year it was detected in Hong Kong, and subsequently around the world, reaching 26 countries in 32 regions, totaling 8,096 cases and 774 deaths[3].

Fact that at the end of 2019, emerged as a new strain in the province of Wuhan, China, and history repeats itself as a much more complex pandemic, wath on May 31 it has already reached about 200 countries. However, with signs and symptoms much more complex than in other coronavirus-related SARS, this time called SARS-CoV-2.

The Covid-19 pandemic teaches health professionals every week that the clinical presentation and severity of the disease can be widely varied. The US Centers for Disease Control and Prevention (CDC) recently added new symptoms possibly caused by the new human coronavirus (SARS-CoV-2), responsible for Covid-19. But with each new publication there are more possibilities[4].

III. Covid-19 in children

Research carried out at the Children's Hospital of Wuhan, from January 28 to February 26, 2020, 1391 children were evaluated and tested, 171 (12.3%) were confirmed with SARS-CoV-2, with an average age of 6.7 years . Fever was present in 41.5% of children at any time during the illness. Other signs and symptoms included cough and erythematous pharynx. 27 patients (15.8%) did not show symptoms of infection or characteristics of pneumonia on the radiograph. 12 patients had radiological features of pneumonia, without symptoms of infection. 3 patients required intensive support with invasive mechanical ventilation; all had coexisting conditions (hydronephrosis, leukemia [and were receiving maintenance chemotherapy] and intussusception). 6 patients (3.5%) had lymphopenia (lymphocyte count, <1.2 × 109 per liter). The most common radiological finding was bilateral ground-glass opacity (32.7%). On March 8, 2020, a 10-month-old child with intussusception died four weeks after admission. 21 patients were in stable condition in the wards and 149 were discharged from the hospital[5].

Generally, CoVid-19 may present in pediatric patients: abdominal pain, conjunctivitis, diarrhea, lower and upper limb swelling, emesis, headache localized or disseminated bullous rashes, erythematous tongue, pyrexia ≥ 38ºC (100, 4ºF), cough, among others. However, in addition to the classic signs and symptoms, in some cases, toxic shock syndrome and Kawasaki syndrome are seen as possible immune responses to coronavirus in children, this is still under study, but it is already clear that CoVid infection - 19 can open windows for more of these infections[6].

It is worth mentioning that there were reports, initiated in Brazil, associating yet another possible symptom in children, even if in rare cases, the hematuria. What should be analyzed if there is a relationship with other pathologies or association with other viruses. However, it is noteworthy that, to date, there are no known cases of renal complications in children with COVID-19[7].

The professor Adilia Warris, a specialist in pediatric infectious diseases at the University of Exeter, told the Science Media Center that children so far account for between 1% to 5% of confirmed Covid-19 cases, usually showing milder signs and symptoms than in adults, and deaths are extremely rare[8.]

Several studies carried out in different populations and age groups have shown that a significant proportion of COVID-19 cases were diagnosed without symptoms or with very mild presentations, probably not identified with the current case definition verification criteria. Although asymptomatic or oligosymptomatic, infected infants and children may have a high viral load in the nasopharynx, in addition to fecal elimination of SARS-CoV-2 for longer periods. Moreover, a study in Shenzhen comparing cases identified through symptomatic surveillance and contact tracking, showed that children were at the same risk of being infected as adults. Together, all of this evidence shows that children are susceptible to SARS-CoV-2 infection, often have asymptomatic or mild forms of the disease, represent a substantial source of infection in the community, anticipating that they may be able to play an important role in viral transmission[9].

It is a fact that CoVid-19 has shown new signs and symptoms, as little is known about this pathology and comorbidities (sickle cell anemia, asthma, diabetes, hemoglobinopathies, heart diseases, among others), a situation

that leads to greater attention and immediate sharing of information in order to expand the knowledge of this new strain and its possible geographical adaptations.

The laboratory test of RT-PCR (Reverse Transcription Time Polymerase Chain Reaction) using nasal swab is essential for the diagnosis of SARS-CoV-2. The laboratory test of RT-PCR (Reverse Transcription Time Polymerase Chain Reaction) using nasal swab is essential for the diagnosis of SARS-CoV-2. However, where resources are scarce, pulmonary radiography must be prioritized for imaging diagnosis, where in the areas affected by the sandblasted glass aspect are observed[6].

It is worth mentioning that the most recently diagnosed patients were tested for the qualitative detection of SARS-CoV-2 antibodies (IgM and IgG) using a lateral flow chromatographic immunoassay (NADAL COVID-19 IgG / IgM test, Nal Von Minden, Moers, Germany). Positive for IgM or IgG, or both, it was considered consistent with a previous SARS-CoV-2 infection[10]. Therefore, it is an elective exam to identify if the patient contracted SARS - CoVid-2 at some point, even though he was asymptomatic.

IV.The pediatric multisystemic inflammatory syndrome and Kawasaki syndrome

Pediatric multisystem inflammatory syndromes associated with Severe Acute Respiratory Syndrome Coronavirus 2 are emerging in recent reports that point to evidence that SARS-CoV-2 may be associated with a severe condition, occasionally fatal, of systemic hyperinflammatory disease in the pediatric population[11]. On June 29 in the New England Journal of Medicine, a researcher wrote that he found that about 1,000 children worldwide were diagnosed with pediatric multisystem inflammatory syndromes[12].

Dawn Nolt, associate professor of pediatrics in infectious diseases at Doernbecher Children's Hospital at Oregon University of Science and Health, Portland, Oregon, comments that: "If there is a link between SARS-CoV-2 and these inflammatory syndromes, it may have result of genetic differences / host , changes in the SARS-CoV-2 virus or other factors yet to be determined"[13].

Much has been discussed about whether or not Kawasaki Syndrome is related to CoVid-19. However, the diagnosis of some children with signs and symptoms of Kawasaki Syndrome after infection with Coronavirus is a fact, which leads be suspected that CoVid-19 may to an inflammatory window for Kawasaki Syndrome.

Kawasaki syndrome was described by Kawasaki, in 1967 in Japan, first believed to be benign, however, it was observed that children developed systemic vasculitis, mainly in the coronary arteries, with the appearance of aneurysms, responsible for the disease's morbidity and mortality[14,15]. In 1976, Melish and Hicks described the pathology in Honolulu in Hawaii, then it of which is where it was considered found to be an international pathology[16, 17].

Kawasaki syndrome is an acute childhood vasculitis, which represents the leading cause of heart disease in pediatric patients in developed countries. Most cases occur in children under the age of five. The diagnosis of the classic form of the pathology should be considered in patients with fever for at least five days, who meet at least four of the five clinical criteria of the disease, in the absence of an alternative diagnosis[4].

The main signs and symptoms of Kawasaki Syndrome (SK) reported by Prof Dr Aureliano Guedes of the Federal University of Pará in an interview with the author, consist of: Anemia; Coronary aneurysm in severe cases; Atrial arrhythmia; Anorexia; Coronary arthritis; Bilateral conjunctivitis without secretions; Dysphagia; Abdominal pain; Pain in extremities (hands and feet); Chest pain; Emesis; Erythema of lips; Erythema on the palms of the hands with desquamation; Plantar erythema with desquamation; cutaneous eruption; Polymorphous exanthem; Fever 38º (104.4ºF) to 40ºC (104ºF) persisting for 5 days or more; Pharyngitis; Temporary photophobia; Hyposalivation, Infection of the lower respiratory tract resistant to antibiotic treatment in most cases; Irritation; dry lips and erythematous and may have frissures; Unilateral cervical lymphadenopathy painless of ≥ 1.5 cm .; Mucositis; Nausea; Taste buds prominent in raspberries; Paronychia with desquamation; Rhinorrhea; Tachycardia; Thrombocytosis in severe cases; Vasculitis; among others. It is worth mentioning that death can occur in severe cases, hence the need for a correct diagnosis and immediate treatment [6].

An AHA (American Heart Association) press release noted that Kawasaki Syndrome is the most common cause of heart disease acquired in developed countries, but the condition remains rare[13].

The etiology of Kawasaki Syndrome remains unknown after decades of research, but there is a strong suspicion that there is an infectious trigger, explained Dr. Roshni. “Human coronavirus has been implicated in the past, but not confirmed”[4]. “There is a strong suspicion of the participation of the immune system, probably mediated by bacteria or viruses and, as such, the action of members of the coronavirus family (as well as adenovirus, herpes virus, Epstein-Barr virus and others) has been long time suggested”[18]. Streptococcus, Rickettsia and Candida albicans were also indicated as possible triggering agents[14,15].

It should be noted that in the last 20 years, viruses of the coronavirus family have been proposed as possibly implicated in the pathogenesis of Kawasaki Syndrome. In 2005, a group from New Haven (CT, USA) identified a new coronavirus in humans, called New Haven coronavirus (HCoV-NH), in the respiratory secretions of eight of the 11 children with Kawasaki Syndrome versus one of the 22 case controls tested by RT-PCR [10].

The laboratory alterations reflect the intense inflammatory process that occurs, the blood count shows anemia, leukocytosis, sometimes with marked neutrophilia and left shift, but with eosinophils present, in the second week of evolution it presents marked platelet, coinciding with the appearance of coronary artery disease , increasing the risk of thrombosis; increase in erythrocyte sedimentation rate (ESR), positivity of C-reactive protein and alpha 2-globulin, among others.. When organs are affected, there are obviously changes in the respective exams; in the presence of hepatitis, increased transaminase; pancreas, increased amylase and so on [16].

In the recent cases of Kawasaki Syndrome, Dr. LeCrubier says that: the clinical forms are quite similar to the "classic" Kawasaki Syndrome, however, the clinical presentation in children treated recently is pleomorphic and can be a frustrated form of Kawasaki Syndrome, especially because some patients have coronary dilation. The approximately 20 cases identified in the cardiology and intensive care services at Hospital Necker have certain characteristics: In the few cases described, the manifestations suggestive of Kawasaki Syndrome are observed between the second and the fourth day of fever; The initial presentation is respiratory, hemodynamic, septic or digestive; The initial phase may evoke a cytokine storm, possibly with signs of macrophage activation; The shock is common, whereas left ventricular systolic dysfunction is variable, but sometimes severe; Moderate increase of troponin; Discreet alteration in the electrocardiogram (ECG); SARS-CoV-2 proven infection[18].

Professor Adilia Warris told the Science Media Center: As we do not yet know the entire clinical presentation of Covid-19, we keep open all possibilities that characteristics that cannot be explained by other causes, may be caused by Covid-19 or even a pathogen still unknown[8].

It is a fact that several scientific institutions and Ministries of Health have been warning about Kawasaki Syndrome, which, even though it is a rare pathology, has had higher than normal notifications, exactly now that a SARS-CoV - 19 pandemic is being experienced. It is noted that in Belgium, Spain, USA, France, England, Italy, among others have identified cases of Kawasaki disease.

Treatment should be started as soon as possible, with acetylsalicylic acid at a dose of 50 to 80 mg / kg / day in the acute phase, followed by 3 to 5 mg / kg / day, and intravenous administration of immunoglobulin in a single dose of 2 g / kg. Response to treatment is usually very good, with fever elimination in a few hours[18].

The prevalence of anomalies in the coronary arteries has been shown to depend on the dose of immunoglobulins and not acetylsalicylic acid, since treatment with intravenous immunoglobulin reduces the frequency of coronary aneurysms to less than 5%. The administration of immunoglobulins should be early, ideally in the first week of the disease; however, if there are signs of persistent inflammation, treatment may continue even after the first week. In therapeutic failure after immunoglobulin infusion, defined as persistence or relapse of fever 36 hours after the end of the infusion, a second or even third infusion cycle can be performed[18].

Corticosteroids have long been contraindicated in Kawasaki Syndrome, but recent data show that corticosteroid therapy can be recommended currently in case of initial therapeutic failure with the use of immunoglobulin. Acetylsalicylic acid is administered in the anti-inflammatory dose in the acute phase and in the antiplatelet dose during the subacute phase. In the absence of cardiac complications, maintenance is performed at a low dose until the erythrocyte sedimentation rate and platelet count are normalized[18].

In children with anomalies of the coronary arteries, treatment is continued until the complete regression of the coronary aneurysms or for life if the aneurysms persist. In the case of a giant aneurysm, it may be necessary to do anticoagulation with vitamin K or heparin and, in some cases, surgical intervention (bypass surgery or transplantation)[18].

V.Conclusion

The pediatric dentist should be aware of the signals and symptoms of SARS-CoV-2 and its various manifestations, since some signals and symptoms are related to buccals problems such as dysgeusia, erythematous tongue emesis and anosmia. Besides that the main forms of contamination are related to saliva, production of aerosols with possible viral particles, etc. very present in dental offices

Signs of Kawasaki Syndrome that should be observed by the pediatric dentist are: hyposialia, dry and erythematous lips (may have fissures), mucositis, prominent taste buds (in raspberries), unilateral cervical lymphadenopathy ≥ 1.5 cm and fever.

Pediatric dentistry must work in an integrated, multidisciplinary and participatory manner with the main national and international institutions, reporting any suspicions of new signs and symptoms related to CoVid-19, since there is still no knowledge all of the evolution of this pathology, and related comorbidities, for the short time between the alert and today.

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