Revista Científica Escola de Saúde Pública do Ceará Paulo Marcelo Martins Rodrigues
1808-7329 (1809-0893)

ORIGINAL ARTICLE
Public / Collective Health

CASE REPORT: INCOMPLETE KAWASAKI DISEASE IN AN INFANT WITH PNEUMONIA

RELATO DE CASO: DOENÇA DE KAWASAKI INCOMPLETA EM LACTENTE COM PNEUMONIA

REPORTE DE CASO: ENFERMEDAD DE KAWASAKI INCOMPLETA EN UN LACTENTE CON NEUMONÍA

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ABSTRACT
To report a case of incomplete Kawasaki Disease (KD) with concomitant infection - pneumonia - in infant who was admitted to a secondary hospital of the Unified Health System in the pediatric ward in Fortaleza, Ceará. It is a cross-sectional observational study with descriptive and retrospective elements carried out in January 2024, through electronic medical record review. The assistant team was responsible for the study and used the literature found in UpToDate and MEDLINE as a reference base. It was demonstrated that concomitant infection does not exclude the diagnosis of incomplete KD and that treatment is instituted late - approximately 22.4 days after the onset of fever. The presence of infection did not alter the response to therapy. Incomplete KD must be considered in patients with prolonged febrile illness in an attempt to institute therapy and avoid complications.
Keywords: *Fever; Pneumonia; Mucocutaneous Lymph Node Syndrome; Vasculitis*.

RESUMO
Relatar caso de Doença de Kawasaki (DK) incompleta com infecção concomitante - pneumonia - em lactente que esteve internada em hospital secundário do Sistema Único de Saúde na ala pediátrica em Fortaleza, Ceará. É um estudo observacional do tipo transversal, com elementos descritivos e retrospectivos, realizado em janeiro de 2024, por meio da revisão de prontuário eletrônico. A equipe assistente foi a responsável pelo estudo e teve como base de referencial a literatura que consta no UpToDate e MEDLINE. Evidenciou-se que infecção concomitante não exclui o diagnóstico da DK incompleta e que o tratamento é instituído tardiamente - cerca de 22,4 dias do início da febre. A presença da infecção não alterou a resposta à terapêutica. A DK incompleta deve ser lembrada em pacientes com doença febril prolongada na tentativa de instituir a terapêutica e evitar complicações.
Descritores: *Febre; Pneumonia; Síndrome de Linfonodos Mucocutâneos; Vasculite*.

RESUMEN
Comunicar un caso de Enfermedad de Kawasaki (EK) incompleta con infección concomitante – neumonía – en un lactante internado en un hospital secundario del Sistema Único de Salud en el pabellón de pediatría de Fortaleza, Ceará. Es un estudio observacional transversal con elementos descriptivos y retrospectivos realizado en enero de 2024, mediante revisión de historias clínicas electrónicas. El equipo asistente fue responsable del estudio y se basó en la literatura encontrada en UpToDate y MEDLINE. Se demostró que la infección concomitante no excluye el diagnóstico de EK incompleta y que el tratamiento se inicia tarde - aproximadamente 22,4 días después del inicio de la fiebre. La presencia de infección no alteró la respuesta al tratamiento. La EK incompleta debe considerarse en pacientes con enfer medad febril prolongada en un intento de instaurar el tratamiento adecuado y evitar complicaciones.
Descriptores: *Fiebre; Neumonía; Síndrome Mucocutáneo Linfonodular; Vasculitis*.

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INTRODUCTION

Kawasaki disease (KD) - formerly called monocutaneous lymph node syndrome - is a systemic necrotizing vasculitis and is one of the most common vasculitis in childhood[1]. Commonly, it is an acute, self-limiting, benign disease. However, complications such as coronary artery involvement - aneurysms, stenosis or dilations - can lead to significant morbidity and even mortality[2].

The etiology of KD is unknown. There are several theories that have been proposed based on pathological, epidemiological, and demographic data. The possibility of being triggered by an asymptomatic or non-vasculitic infection in most children, but resulting in KD in genetically predisposed children, fits well with the epidemiological data. However, the role of a possible environmental trigger in genetically predisposed individuals cannot be ruled out either[3].

Children with suspected Kawasaki disease who do not meet the diagnostic criteria for KD may have incomplete or atypical Kawasaki disease, which is also susceptible to the risks of cardiovascular sequelae. It is also noteworthy that the presence of a concomitant infection does not exclude the diagnosis of this disease[4]. While the recognition of complete KD is clinical, in the diagnosis of incomplete KD, the child meets some clinical criteria and presents alterations in laboratory or echocardiographic tests. It is noteworthy that early diagnosis and the implementation of appropriate therapy reduce the risk of complications[6].

The present study aims to report a case of incomplete Kawasaki disease with concomitant infection - pneumonia - in an infant who was admitted to a secondary hospital of the Unified Health System (SUS), in the pediatric ward in Fortaleza, Ceará, Brazil.

METHODS

This is an observational, cross-sectional, retrospective study, with descriptive elements, which was developed in a secondary hospital of the SUS in the pediatric ward. It was carried out in January 2024 in a secondary hospital of the Unified Health System (SUS), through the review of the electronic medical record of a patient who was hospitalized for community-acquired pneumonia (CAP), and was later diagnosed with incomplete Kawasaki Disease.

The information was organized in a standard format and the data were compiled for descriptive analysis. The data of the described case were correlated with the data found in the scientific literature, by means of a review of the UpToDate and MEDLINE databases, using the keywords "Incomplete Kawasaki disease", "infants", "complications", "pneumonia", published in the last twenty-five years.

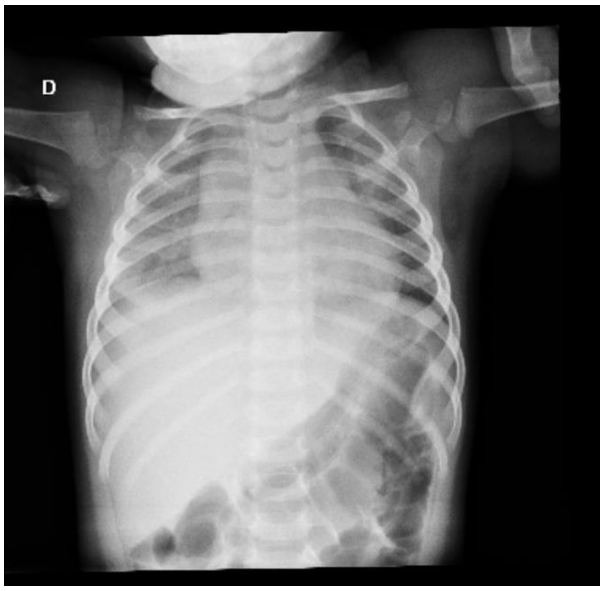
The research complied with the norms defined in Resolution No. 466 of December 2012, of the National Health Council/Ministry of Health, which regulated research involving human beings and ensured the rights and duties that concern the scientific community, the research subjects and the State. The project was submitted for analysis by the Research Ethics Committee (REC) of the hospital in question after the consent of those responsible for carrying out the research, through the Free and Informed Consent Form, and was approved by the IRB in question. Opinion number: 6.625.803.

RESULTS

A 1-year-old female infant developed fever, hyaline nasal runny nose, productive cluster cough with associated vomiting and diarrhea - without hematochezia or mucus -, having used symptomatic medication, without improvement. She progressed, in four days, with the symptoms described and significant hyporexia remaining. The mother reported having offered, on her own, oral antibiotic therapy, but the patient did not accept medication, presenting episodes of emesis. The patient reported having sought emergency medical care and was in a regular general condition - but with maintenance of clinical and hemodynamic stability - and complementary tests that showed leukocytosis - 19700/mm³ - at the expense of segmented patients, with a left deviation of 4%. In addition, a chest X-ray showed a discrete perihilar opacity on the right, with a normal cardiac area and free costophrenic sinuses. Hospital admission was chosen due to suspicion of community-acquired pneumonia (CAP).

The patient was referred to a secondary hospital for continued treatment with parenteral antibiotic therapy with ceftriaxone. On admission, the patient was in a regular general condition and had slightly decreased auscultation in the right hemithorax, but without signs of respiratory distress and remained eupneic on room air. The infant progressed with regular general condition, fever, irritability, severe hyporexia, drowsiness and tachycardia, and the sepsis protocol was opened, measurements were taken, laboratory tests were requested, according to the protocol of the service, and oxacillin was associated with the therapy in the face of a possible pulmonary infection by *Staphylococcus aureus*, since the admission chest X-ray revealed that the right pleural effusion was questioned.

Image 1: Chest X-ray in AP with involvement of the base and middle third of the right hemithorax. The image reinforces that a concomitant infection, especially pulmonary infection, does not exclude the diagnosis of KD.



Source: Authored by the authors.

The patient progressed with improvement of the general condition, partial acceptance of the diet and resolution of sleepiness. However, she maintained daily fever

peaks and irritability, despite the use of antimicrobials for more than 72 hours. In this context, new laboratory tests were requested, which showed significant improvement in the infectious and inflammatory tests, respectively, leukocytes and CRP falling. It is also noteworthy that the patient underwent chest ultrasonography, which showed minimal pleural effusion, anechoic and homogeneous, with a liquid lamina thickness of 0.5 cm, bilateral.

On the 10th day of the patient's daily fever, the hypothesis of incomplete Kawasaki disease was raised, since the child had fever for at least 5 days, anemia for age, leukocytes with a value greater than 15000/mm³, pyruvic transaminase (TGP) greater than 50, platelets above 450000/mm³ and albumin below 3g/dl. The patient did not meet the criteria for complete Kawasaki Disease, since she only had a fever for more than 5 days, mild edema in the extremities and lip dryness with fissures - previously attributed to the septic condition of the patient with hypoalbuminemia and significant dehydration.

It is important to note that the minor underwent a viral panel collected at admission, which was negative for SARS-CoV-2, Influenza A and Influenza B. In this context, Acetylsalicylic Acid (ASA) was started at an antiplatelet dose (4mg/kg/day), intravenous immunoglobulin (IVIG) - 2g/kg/day - and oxacillin was discontinued.

The infant also had an isolated febrile episode during IVIG infusion, but with resolution of the fever after the end of the infusion. In addition, the patient evolved in good general condition, with resolution of irritability and maintaining a food intake pattern similar to that of the patient, according to the mother. The patient underwent transthoracic echocardiography (TT-ECHO) while still in the acute phase of the disease - day 14 - with no changes in the coronary arteries, with a Z score lower than 2.

After 72 hours of IVIG infusion, the infant progressed with laboratory improvement of the three series of blood counts, improvement of albumin and normalization of the transaminase value. It is noteworthy that the patient completed a 7-day regimen of parenteral antibiotic therapy with Ceftriaxone for CAP and collected two blood cultures during hospitalization, both of which were without bacterial growth.

Table 1: Absolute platelet count and its relationship with the onset of fever. One of the laboratory criteria for diagnosing incomplete KD is significant platelet disease - above 450 thousand.

Absolute platelet value and its relationship with the onset of fever

Days after the onset of fever	Platelets
Day 9°	729000
Day 12°	1293000
Day 14°	1077000

Source: Authored by the authors.

Still in the hospital and on the 17th day after the onset of fever, the patient presented desquamation of the extremities.

Image 2: Desquamation at the extremities of the upper limb. Manifestation present in the subacute phase of KD.

Source: Authored by the authors.

Image 3: Desquamation at the extremities of the lower limb. Manifestation present in the subacute phase of KD.

Source: Authored by the authors.

The patient was discharged from the hospital with instructions to return to the General Pediatrics outpatient clinic, undergo two control ECHO-TT at 2 weeks and 6-8 weeks after diagnostic suspicion, and should maintain daily use of ASA in antiplatelet dose until the third control ECHO-TT. In addition, she was referred to a specialized outpatient clinic with a pediatric rheumatologist for clinical follow-up.

DISCUSSION

Kawasaki disease (KD) - formerly called monocutaneous lymph node syndrome - is a systemic necrotizing vasculitis and is one of the most common vasculitis in

childhood1. It affects medium-sized vessels, mainly affecting children under five years of age[4].

Commonly, it is an acute, self-limiting, benign disease. However, complications such as coronary artery involvement - aneurysms, stenosis or dilations - can lead to significant morbidity and even mortality[2].

The etiology of KD remains unknown, although there are several theories about the role of an infectious trigger that may trigger the disease4. In addition, there is no laboratory test that can identify the affected patients, and the diagnosis of classic KD is established by clinical criteria, and the child must have fever for at least five days and at least four of the five clinical characteristics: polymorphous rash, changes in the extremities, involvement of the mucosa of the lips and oral cavity, bilateral nonpurulent conjunctivitis and unilateral cervical lymphadenopathy[4].

KD has three evolutionary phases: acute, subacute and convalescent. The acute phase lasts until the 14th day and is usually the febrile period in which almost all clinical manifestations are present. The subacute phase lasts 2-4 weeks, with a decrease or disappearance of the main alterations and the beginning of skin desquamation. The convalescence phase, on the other hand, corresponds to a period of more than 4 weeks, and is characterized by the disappearance of acute alterations and normalization of laboratory tests[5].

While the recognition of complete KD is clinical, in the diagnosis of incomplete or atypical KD, the patient meets some clinical criteria and presents alterations in laboratory or echocardiographic tests[4].

If incomplete KD is suspected, the patient must have fever for at least 5 days, associated with at least 2 compatible criteria: C-reactive protein greater than or equal to 3mg/dl or ESR greater than or equal to 40mm/h associated with a suggestive change in the echocardiogram or the presence of at least three of the following criteria: anemia for age, platelet greater than or equal to 450000/mm³, albumin less than or equal to 3g/dl, increased TGP, leukocytes greater than or equal to 15000 and presence of sterile pyuria - greater than or equal to 10 leukocytes per field[2].

It is important to emphasize that the patient in the present study did not meet the criteria for complete Kawasaki disease, since she only had fever for more than 5 days, mild edema in the extremities, and lip dryness with fissures - findings that were attributed to the current infectious context. The pneumonia presented by the patient evolved with pleural effusion, which was detected by chest ultrasound, which showed minimal pleural effusion, anechoic and homogeneous, with a liquid lamina thickness of 0.5 cm, bilateral.

However, the minor had fever for more than 5 days, anemia for her age, leukocytes with a value greater than 15000/mm³, pyruvic transaminase (TGP) greater than 50, platelets above 450000/mm³ and albumin below 3g/dl, findings compatible with incomplete KD. Of the laboratory criteria needed to diagnose incomplete KD, the patient only did not have sterile pyuria.

It is important to emphasize that a concomitant infection does not exclude the diagnosis of this disease. As studies have shown, about 33% of children with KD had at least one confirmed infection at diagnosis6, with lung infections being relevant[7].

A study conducted in India showed that about 1.83% of the children – sample space (N) of 602 patients – had pulmonary involvement, with the first sign of KD being observed on average 14.5 days after the onset of symptoms. The patients in this study had persistent fever despite the use of antimicrobials, thrombocytosis, increased erythrocyte sedimentation rate and C-reactive protein, and the diagnosis was made late, approximately 22.4 days after the onset of fever[8], which makes evident the diagnostic challenge in incomplete KD associated with infectious involvement.

The study also reported the presence of parenchymal consolidation on chest X-rays in all patients. In addition, pleural effusion was observed in six, empyema in three, and pneumothorax in three patients[8].

The reported case is consistent with the description in the literature, since the patient did indeed have a concomitant infection - pneumonia with mild bilateral pleural effusion. In addition, the diagnostic suspicion for incomplete KD of the patient only occurred on the 10th day of symptom onset.

The primary complications of KD are cardiac sequelae, including dilatation, aneurysm, and/or stenosis in the coronary arteries. However, other cardiac sequelae may occur, including reduced ventricular function, valvular regurgitation, and pericardial effusion. Acute myocardial infarction is the leading cause of death in KD. Considering the involvement of medium-sized vessels, vascular alterations can also occur in the other vessels, causing renal dysfunction, gastrointestinal manifestations, and sensorineural hearing loss, for example. In some cases, shock and macrophage activation syndrome may also occur[2]. Children affected by incomplete KD are also susceptible to the risks of cardiovascular sequelae[9].

Both children affected by complete and incomplete KD should be treated in the same way, since a review of nearly 16,000 cases recorded in the 17th Japanese National KD Survey found that 16.1% of children with coronary artery (CA) abnormalities had incomplete KD[9].

Therefore, initial therapy with intravenous immunoglobulin (IVIG) given as a single infusion over 8 to 12 hours should be initiated. Published guidelines also include antiplatelet aspirin as the initial treatment of KD, thereby reducing the risk of complications. It is also noteworthy that the risk of resistance to IVIG should also be determined before the initiation of therapy[10,11].

It is noteworthy that the presence of infection did not alter the response to treatment with intravenous immunoglobulin in patients diagnosed with KD, since approximately 83% of the sick children had resolution of fever after a dose of IVIG associated with the administration of aspirin[6].

In addition, a study published in 1999 showed that the incidence of coronary aneurysms increases by about three times when the diagnosis is made late and treatment is started after the 10th day of the disease[12].

The challenge of diagnosing incomplete KD can also affect the mental health of patients and their parents, since the delay in clinical suspicion and the prolongation of hospitalization affect the psychosocial well-being of caregivers, causing anguish and anxiety[13].

This is in line with what is recommended by Public Health, since diagnostic suspicion and the institution of appropriate treatment in cases of prolonged fever that are characterized as incomplete KD reduce health problems. Both the problems related to morbidities and comorbidities resulting from the complications of this disease and the personal, social, environmental and cultural aspects of each individual in the health-disease process.

CONCLUSION

It is noteworthy that the limitation of this study is the fact that data are still scarce in the literature associating typical and incomplete Kawasaki disease with concomitant infection. This fact reinforces the importance of this article, in order to disseminate scientific content and alert health professionals, especially pediatricians, about this possible differential diagnosis, reducing health problems and consequently impacting public health.

Thus, considering the absence of the typical characteristics of the typical disease and the difficulty of establishing the diagnosis in patients with incomplete Kawasaki disease and pulmonary disease, this disease should be suspected in a patient with prolonged fever, in order to establish an early diagnosis, appropriate therapy and, consequently, reduce the complications resulting from this vasculitis.

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