Therapeutic usage of anakinra in recurring kawasaki disease

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Abstract

Background: Children under the age of five are affected by Kawasaki disease, a multi-system vasculitis. It is extremely uncommon in babies younger than three months old and is linked to a high incidence of cardiovascular problems that are frequently resistant to therapy. Coronary aneurysms and other cardiovascular problems are more likely to occur in people with this syndrome. Standard therapy is ineffective for 10-20% of patients, and they face an increased risk of cardiovascular issues.

Case Presentation: We are presenting a clinical report of Kawasaki disease detected in accordance with the American Heart Association's guidelines. A 1 year 3month boy, presented with prolonged fever associated with chills and rigors, mouth ulcer, conjunctivitis. He had aspirin and immunoglobulin therapy, as well as a thorough examination. After the IVIG resistant treated with anakinra.

Conclusion: This case report underlines that Kawasaki disease is more common and in children who came with mucocutaneous signs and a persistent fever lasting longer than five days, it should be taken into consideration as a differential diagnosis. To stop the cardiovascular morbidity that comes with this illness, more knowledge about its epidemiology, diagnosis, and treatment is needed. To reduce the cardiovascular risk and to treat IVIG resistance the anakinra is recommended.

Keywords: Anakinra, Aneurysms, Coronary Aneurysms, Fever, Intravenous immunoglobulin, Kawasaki, Rash, Vasculitis

Introduction

Kawasaki illness is among the most prevalent types of vasculitis in children. It usually affects infants and young children, and if left untreated, it can result in long-term cardiovascular disease linked to arterial plaques.[1] It is the primary contributing factor to childhood hereditary cardiovascular disease in affluent countries. Asia possesses the greatest prevalence: approximately one in every 100 children in Japan has the condition by the time they are five years old.[2]The first instance involving an African infant was documented in Ivory Coast in 1981, however two cases involving Caucasian infants were documented in Southern Africa in 1980. Although there have been occasional reports of KD cases in various African countries, primarily in North and West Africa, there is a dearth of epidemiological information for African nations. [3-5].There are various theories that attempt in order to clarify the cause of the illness, but the root cause is still unknown. Epidemiologic evidence indicates that among genetically predisposed individuals, the disease may be caused by an infectious agent.[6]Children under five years old are the target audience for the disease's classic presentation. This implies that there may be an environmental trigger that kids respond to by building an immune system, which then stops the illness from showing symptoms.[7] Among the hypothesised infectious agents are variations of the regular flora brought on by environmental influences like better cleanliness.[8]It is thought that a pathogenetic mechanism involving a regular protein balance pathway causes endothelial damage. Immune system cells in this system attack infectious antigens linked to endothelium cells, which damages host cells.[9] The earliest signs and symptoms include a fever that lasts more than five days, along with rash, conjunctivitis, and adenopathy, among other mucocutaneous symptoms. There are diagnostic standards to diagnose both full and partial illness types. [10]

In roughly ten days, the symptoms go away if no treatment is given. On the other hand, long-term cardiovascular issues could result from the coronary artery lesions. Such as arrhythmias, cardiac failure, and myocardial infarction. Reduction of the prevalence of coronary artery blockages from 25-30% to 3–5% occurs with treatment during the acute period.[11]Currently, intravenous immunoglobulin is advised as a treatment, along with high dosages of acetylsalicylic acid.[10] However, 10–20% of those treated do not respond to regular therapy and are at greater risk of cardiac-related complications. As of right now, there is no recognized procedure for handling the resistant cases. Numerous writers emphasized the part interleukin-1 plays in mediating inflammatory process in Kawasaki disease and proposed targeting IL-1or its binding site for therapeutic purposes. Interleukin antagonist usage in KD patients has been described in scientific literature.[13]

Case presentation

A male infant, aged one and a half, reported having a high-grade fever for nine days, accompanied by chills and rigors, as well as a mouth ulcer that persisted for four days and redness in the eyes. Antibiotics and analgesics were used in the child's initial treatment, but the fever persisted. He arrived at the nursery for more assessment. Upon physical examination, he has conjunctivitis in both eyes, skin rashes, and dental abnormalities.

The results of the investigation revealed low hemoglobin -10.2g/dl[>13.7g/dl], a high platelet count -590 × 109/L[2,50,000-4,50,000], an ESR- 180 mm [<15mm/h];at the end of an hour, and a total WBC count - 12.8 × 109/L[4.5-11 109/L]. An X-ray reveals increased heart size. Urine culture and routine examination came up negative. Even the echocardiogram shown cardiomegaly.

He began receiving treatment on intravenous immunoglobulin 2g × 4 times per day for 5 days. He was then treated with T. Aspirin 75mg 8th hourly. Two days after starting aspirin, his symptoms went away. He received his discharge and continued taking aspirin at the same dosage for a week. He was febrile during his one-week follow-up. For further treatment the child got admitted and treated with Anakinra 1mg/ kilogram/day for eleven days, followed by six weeks.

CRITERIA	MANIFESTATION
FEVER	High spiking and remittent for 9 days
CONJUNCTIVITIS	Eye redness present
MUCOSAL CHANGES	Mouth ulcer present
LYMPHADENOPATHY	Not seen
POLYMORPHOUS RASH	Skin rashes present
EXTREMITY CHANGES	Not seen

Table 1.1 *American Heart Association Diagnostic Criteria which is seen in patient*

the kobayashi score		
Risk factor		*points*
Illness days at diagnosis	*< 4days*	*2*
Serum sodium level	*< 133mmol/l*	*2*
AST	*≥100 IU/l*	*2*
Neutrophil rate	*≥80%*	*2*
CRP	*≥10mg/dl*	*1*
Platelet count	*≤30.0*104/mm^3*	*1*
Age at diagnosis	*≤12 months*	*1*

Table 1.2 *According to the kobayashi score interpretation, the patient shown the score of 5 and diagnosed as IVIG resistant.*

Day	progress	Lab investigation	Treatment
Day 1	9 days of fever, mouth ulcer for 4 days, eye redness, rashes	WBC- 12.8 × 109/L , ESR-180mm /hr, platelet-590 × 109/L, Hemoglobin (10.2g/dl).	Antibiotic therapy(Tazoba-ctum)
Day 5	Persistent Fever diagnosis: Kawasaki Disease	X-Ray- Heart enlarged in size	IVIG Treatment
Day 10	Persistent fever	Echo normal	Low dose aspirin 75mg 8th hourly
Day 12	Fever treated	-	Discharged on same dose of aspirin
After one week	Follow up visit Fever persistent	Echo- Abnormal	Aspirin stopped. Treated with Anakinra 1mg/Kg/day

Table 1.2 *Case Timeline of the patient*

Discussion

The second most typical cause of pediatric vasculitis is Kawasaki disease. Due to the terrible complications appear amid a severe sickness, it is imperative that Kawasaki disease be diagnosed and treated as soon as possible. If left untreated, coronary aneurysms occur in about 20% of cases. Kawasaki disease is primarily diagnosed clinically, by exclusion. The Kawasaki disease can be diagnosed using specific diagnostic criteria. The American Heart Association's guidelines were applied here. Three criteria were used to diagnose Kawasaki disease in this patient. Along with fever lasting no less than five days, the following primary symptoms must be present for Kawasaki disease to be diagnosed: Infections into both conjunctival, usually not purulent, strawberry tongue, dry fissured lips, and injected oropharynx are examples of modifications to the oropharynx's mucosa .alterations in the upper limb and lower limb during the acute phase, such as erythema and/or edema, Rash is mainly polymorphous, truncal, and non-vesicular. Cervical lymphadenopathy, typically unilateral, with a diameter of at least 1.5 cm. Aneurysms in the coronary and peripheral arteries. Beyond these prerequisites, no other established disease mechanism should be used to explain illness. Since early treatment reduces the likelihood of complications, it is essential for Kawasaki disease.

In these situations, one dosage of IV immunoglobulin (two gram/kilogram) plus aspirin (one hundred milligram/kilogram/day) for 14 days, continued by 3-5 mg/kg/day for six weeks, is the recommended course of therapy. Research has demonstrated that IVIG therapy lowers acute inflammation and lowers the incidence of cardiac risk from over 25% in people who are not treated to 1-5% in those who receive treatment. When IVIG is administered within the first 10 days of the illness, the greatest benefits are observed. During the acute phase, high-dose aspirin (80–100 milligram/kilogram/day, divided into 4 doses) is administered orally.
The aspirin is used in higher dose for fever and reduce inflammation during the acute phase and later lower dose is used when the fever subsides used for antiplatelet properties to prevent complications like coronary artery aneurysms. IVIG is used with alongside of aspirin to neutralize autoantibodies.

The patient is subsequently given a low dosage of aspirin (three-five milligram/kilogram/day) for six–eight weeks to test its antiplatelet action, assuming there is no indication of any coronary abnormalities. Through the patient becomes afebrile for between 48 and 72 hours, or up to day 14 of the illness, this dose should be administered. If therapy for Kawasaki disease is started as soon as possible, the prognosis is good. In the US, the average death rate for children affected by the condition is roughly 1%. If a patient is younger than a year old, almost 4% of them will die. Patients one year of age or older have a mortality rate of less than 1%.
After the one week of followup, the patient had a cimplaints of fever on and off. Due to the resistant of IVIG and the cardiovascular abnormalities, the treatment plan modified and started with Anakinra.
Unlike other interleukin antagonist, anakinra acts as a substrate analog of interleukin -1 alpha, interleukin- 1 beta and IL-1, preventing signal transmission through the IL-1 type I receptor. The important function that IL-1α has been demonstrated to play in coronary lesions is notable. Compared to other anti-IL-1 medications, this one has a major benefit due to its early onset effectiveness and brief half-life (4-6 hours). These characteristics limit the consequences in the case of a significant unfavourable incident and enable quick reaction testing. As a result, in clinical settings, the medicine is a tightly controlled treatment.
Anakinra is emerging as a valuable option for treating refractory Kawasaki disease, especially in IVIG-resistant cases, by targeting the IL-1 mediated inflammatory pathway. While more extensive clinical trials are needed, it provides a targeted approach for managing severe inflammation and preventing coronary complications.

Conclusion

Vasculitis in children brought on by Kawasaki disease is horrifying. Any kid exhibiting symptoms of prolonged fever, blisters on the skin, and modified peripheral limbs with puffiness or peeling, lips with cracks, non-purulent corneal inflammation, and lymphadenopathy of the cervical area should be evaluated for Kawasaki disease. The best defense against coronary complications is an early diagnosis, as well as the administration of aspirin and intravenous immunoglobulin. Still the usage of anakinra in Kawasaki disease on trials and there are no accepted regimen. Still in a large population it carried a successful therapeutic outcome.

Abbreviations

IVIG: Intravenous immunoglobulin; WBC: Whiteblood cells, ESR: Erythrocyte sedimentation rate, IL- Interleukin

Accessibility of information and resources: Since no datasets were created or examined for this article, data sharing is not applicable.

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