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CLINICAL VIGNETTE

Complete Adult-Onset Kawasaki Disease: Case Report

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Introduction

Kawasaki disease (KD), also known as mucocutaneous lymph node syndrome, is a medium vessel vasculitis that typically occurs in children of East Asian descent under 5-years-old. Dr. Tomisaku Kawasaki first described kidney disease in 1967 from clinical observation of 50 patients in Japan.[1] KD is a clinical diagnosis based on at least 5 days of fever and 4 out of 5 of the following features: bilateral conjunctival injection, polymorphous rash, nonpurulent cervical lymphadenopathy, mucocutaneous changes of lips and oral cavity, indurative edema of extremities and membranous desquamation from fingertips.[1] 'Complete' KD occurs when all the diagnostic criteria are met. Mortality is from coronary artery aneurysms, which is an uncommon yet fatal in KD. In Japan, there are 264.8 cases of KD per 100,000 children under 5 years old. In the United States, the incidence is 18.1 per 100,000.[2] KD rarely occurs in adults, with only approximately 100 documented cases of adult-onset KD in 2015.[3] Due to its rarity in populations over the age of 5, Kawasaki Disease is often overlooked in the differential diagnosis in our patient population. We present a case of adult onset Kawasaki disease.

Case Description

A 20-year-old Caucasian woman with a distant medical history of childhood rashes of unknown significance presents to the hospital with 10 days of fever and 8 days of widespread rash. She had first presented to an outside hospital several days prior with an evolving widespread rash and cervical lymphadenopathy. At that time, patient was presumptively diagnosed with bacterial pharyngitis and was discharged with a course of doxycycline and clindamycin. She had no improvement in her symptoms and presented to our hospital.

In the ED, the patient's vital signs were significant for a temperature of 38.1 and a heart rate of 118. Physical exam was significant for cervical lymphadenopathy, patchy bilateral diffuse erythematous rash, bilateral conjunctival injection, cracked lips, oral mucositis, and periungual desquamation. The rash had started on hands and feet and progressed centrally to the trunk over two weeks. In the emergency department, patient was given prednisone 60 mg, IV fluids and broad spectrum antibiotics. Internal Medicine and Dermatology were called to assess the patient. Initial laboratory tests were unremarkable including CBC and Basic Chemistry Panel. Infectious disease studies returned negative, including HIV, EBV, Parvovirus B19, Rickettsial, RPR, Mycoplasma, Quantiferon Gold. ESR was elevated at 54 mm/hr (ref. range: <25 mm/hr), and CRP was elevated at 7.2 mg/dL (ref. range: <0.8 mg/dL). Outside hospital tests were negative for strep throat and influenza. Skin biopsy revealed presence of spongiosis, perivascular eosinophils and plasma cells. Given the clinical presentation, diagnostic criteria and discussion with consultants, a diagnosis of adult-onset Kawasaki disease was made 1 day after initial presentation.

The patient was treated with high dose aspirin (650 mg QID, 4 total doses) and IVIG (2 g/kg, 1 dose), and corticosteroids were discontinued. IVIG infusion was well tolerated and she reported significant reduction in maculopapular rash, resolution of conjunctival injection, and improvement in mucositis. Echocardiogram 12 days after symptom onset was normal. The patient was discharged 3 days after admission, on daily aspirin 325 mg. Follow up CT Angiography showed no evidence of coronary aneurysms.

Discussion

Kawasaki disease is a clinical diagnosis without specific diagnostic lab tests. Adult-onset KD is much rarer than childhood-onset, and therefore lacks an established standard of diagnosis and treatment. Diagnosis of adult-onset KD is often made with the childrens's clinical criteria. However, the presentation in adults often differs from that in children. In both children and adults, KD typically presents with fever, desquamation, conjunctivitis, injected pharynx, and strawberry tongue. However, adults more commonly present with cervical adenopathy (93% versus 15% in children), abnormal liver function tests (65% versus 10%), arthralgia (61% versus 24-38%). Conversely, children more commonly present with thrombocytosis (100% versus 55% in adults), meningitis (34% versus 10%), and coronary aneurysms (20% versus 5%).[4]

KD has several proposed triggers and causes. Given that KD rarely occurs in patients under 6 months old and adults, it is likely related to an immune reaction to an infectious agent which maternal and adult immunity normally protects.[5] A review of the epidemiology of KD may provide insight into the etiology of both childhood and adult-onset KD. In the United States, KD has an incidence of 18.1 per 100,000 children <5 years old compared to Japan's 264.8 per 100,000.[2] There is

likely a genetic predisposition to KD given that children of Japanese descent in Hawaii are more likely to be afflicted with KD, with an incidence similar to Japan (approx. 200 per 100,000).[2] Adult-onset KD is much rarer, with approximately 100 cases described in literature in 2015.[2] Adult-onset KD appears to be associated with HIV infection, further suggesting an immunological factor.[3] Interestingly, KD's geographic predilection and timing of outbreaks has also been explained by a widespread environmental antigen that is carried by tropospheric winds.[6-8]

With no specific lab tests available, KD is difficult to diagnose when the clinical presentation of the patient is equivocal. Perhaps, by understanding the changes in laboratory values and identifying possible biomarkers for KD, diagnoses can be made more swiftly and treatment could be initiated. Within the first 10 days of symptoms, CRP and bands will peak. In the next 11 to 20 days, platelet, lymphocyte, and eosinophil counts will peak.[9] Additionally, when comparing acute KD patients and febrile controls, several biomarkers (including A1AT, ALT, ANC, CRP, ESR, fibrinogen, GGT, platelet count) were able to diagnose 81-96% of KD patients.[10]

Coronary artery aneurysm is a feared fatal complication of KD. On the 10th day of disease, lymphocytes and macrophages infiltrate the arterial wall leading to inflammation of all layers of the artery and eventual dilation. Activation of monocytes and macrophages causes release of inflammatory cytokines and growth factors like tumor necrosis factor (TNF-alpha), interferon (INF-gamma), interleukin (IL-6), vascular endothelial growth factors (VEGF) and platelet derived growth factor (PDGF). These inflammatory and growth factors induce migration of leukocytes and proliferation of smooth muscle cells. Aneurysms occur after the 12th day of disease, due to damage that has occurred to the tunica intima and smooth muscle cells of tunica media. Non-laminar blood flow in the aneurysms allow for thrombi formation and can lead to myocardial ischemia.[11]

Treatment of KD within the first 10 days after onset of fever has shown to reduce the rate of coronary aneurysms from 25% to 5%.[12] First line treatment is a single infusion of IVIG (2g/kg over 10 h) plus aspirin 30-50mg/kg/day during the acute phase of disease. After fever and inflammatory symptoms have resolved, aspirin dosage should be lowered to 3-5 mg/kg/day and continued until aneurysms resolve. However, if giant aneurysms are present (>8 mm) the addition of warfarin is recommended. For patients who are IVIG-resistant (20% of cases), corticosteroids can be considered in addition to a concurrent second infusion of IVIG.[13]

Conclusion

In conclusion, a definitive etiology of KD is still unknown and a topic of much discussion. Better understanding of KD presentation and triggers in adults needs further investigation given relative rarity compared to childhood cases. Development of diagnostic algorithms in adults would facilitate timely diagnosis and treatment. This case illustrates the importance of including adult-onset KD on the differential diagnosis in adults presenting with prolonged fever and mucocutaneous symptoms. Additionally, it also further demonstrates the effectiveness of IVIG and aspirin in treating adult-onset KD and the importance of close monitoring for possible cardiac manifestations.

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