Medical Expertise

"Development of the European Network in Orphan Cardiovascular Diseases"
„Rozszerzenie Europejskiej Sieci Współpracy ds Sierocych Chorób Kardiologicznych"

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CASE SUMMARY

This report is a remarkable description of a young adult presenting with signs and symptoms consistent with Kawasaki disease. This 19-year-old male was admitted to the Hospital of Lithuanian University of Health Sciences Kaunas Clinics due to fewer (38°C), nausea, vomiting, headache and stomach ache. He was pale and sluggish on admission. Nonexudative, bilateral conjunctivitis, erythema of lips and oral mucosae was found. Resting electrocardiogram showed sinus tachycardia with early repolarization disturbances. Biochemical analysis revealed high rate of inflammatory markers including elevated white blood count, increase in neutrophils concentration, high CRP and elevated platelets count. No particular infectious agent has been detected in the course of differential diagnostics. Cardiac echo study revealed reduced left ventricular ejection fraction (LVEF), posterior wall hypokinesis, tricuspid (TR) and mitral regurgitation (MR). Coronary arteries computed angiography (angioCT) revealed aneurysmal dilatation of the distal part of the left main (LM) with parietal thrombus, dilatation of proximal left anterior descending (LAD) and circumflex (Cx), and nonobstructive aneurysm in the proximal segment of the right coronary artery (RCA). He was treated with intravenous immunoglobulins (IVIG), aspirin and anticoagulants, metilprednisolon, antibiotics and diuretics according to standards. Gradual improvement of the clinical status was observed with reduction of symptoms and laboratory signs of inflammation. Echocardiographic parameters returned to normal. His pharmacological treatment includes aspirin, warfarin, and beta-blocker. After one year follow up he remains asymptomatic, has no chest pain or ST-T segment changes in exercise test, LVEF is normal, angioCT shows persistent aneurysms in left and right coronary arteries without progression. The authors are concerned about the further pharmacological treatment, frequency of follow-up and management of coronary arteries aneurysms.

DISCUSSION

Kawasaki disease (KD) is one of the most common pan-vasculitides in pediatric population [1]. It has extensively been studied in Japan since the 70s. Asian reports an annual incidence

of 112 cases per 100,000 children under age 5 years, whereas American 10 per 100,000 [2,3]. The incidence of KD in adults is unknown. No more than 100 cases of KD in adults have been described, mostly between 18 to 50 years old [4,5].

Clinical manifestations result from the ongoing inflammation of the small and medium sized vessels. The condition is typically self-limiting, lasting for an average of 12 days [6]. Symptoms include prolonging fever, bilateral bulbar conjunctival injection, oral mucous membrane changes, including injected or fissured lips, injected pharynx, or strawberry tongue, peripheral extremity changes, including erythema of palms or soles, edema of hands or feet (acute phase), and periungual desquamation (convalescent phase), polymorphous rash and cervical lymphadenopathy [6]. Following the recommendations of the American Heart Association (AHA) and the American Academy of Pediatrics (AAP) the diagnosis of KD can be made when prolonging, unexplained fever is accompanied by 4 out of 5 abovementioned signs [6]. It is however apparent, that not all of the clinical features are present at a single point in time, and watchful waiting is sometimes necessary before setting the final diagnosis. Biochemical analysis reveals elevation of inflammatory markers, white blood cells and platelets, normocytic anemia, abnormalities in liver and kidney function tests [6].

Cardiac involvement during the acute phase of KD is frequent and include inflammation of the pericardium, myocardium, atrioventricular conduction system, heart valves, and endocardium [7]. Physical examination often reveals hyperdynamic precordium, tachycardia, a gallop rhythm in the setting of anemia, fever, and depressed myocardial contractility secondary to myocarditis. Histological evidence suggests that myocarditis is universal in acute KD [8]. Depressed ventricular contractility is common early in the course of KD and improves rapidly after IVIG therapy. Mild or moderate mitral regurgitation is present in 25% of patients at initial echocardiographic evaluation and diminishes with treatment [9].

The most prominent complication of KD are coronary arteries aneurysms (CAA), which may result in myocardial ischemia, myocardial infarction, or sudden death [10]. CAA can first be detected by echocardiography about seven days after fever onset. It may affect as many as 25 to 43% of children [11,6]. Among patients who develop aneurysms, mortality is highest between 15 and 45 days after onset of KD. The prognosis of CAAs depends on the size and shape of the aneurysm. The best prognosis is associated with small aneurysm size [19].

In all patients with KD, cardiac testing should include echocardiography, electrocardiography, and stress testing. Computed tomographic angiography (CTA) is performed to image the coronary arteries in patients without known aneurysms.

The management of cardiovascular sequelae of KD includes prevention of coronary thrombosis, treatment of patients with myocardial infarction and coronary thrombosis, and in some severe rare cases, cardiac transplantation [6].

Therapeutic regimens used in patients with Kawasaki disease depend on the severity of coronary involvement and include antiplatelet therapy with aspirin or clopidogrel, anticoagulant therapy with warfarin or low-molecular-weight heparin or a combination of anticoagulant and antiplatelet therapy, usually warfarin plus aspirin [6]. In patients with clinical signs of coronary ischemia including reversible ischemia with exertion, coronary artery revascularization intervention should be performed. The type of revascularization depends on the size, location and complexity of CAA. In patients who suffer a myocardial infarction, emergent therapy for reperfusion and revascularization is required.

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EXPERT'S OPINION

This case is an example of KD with its typical long-term complications including coronary arteries aneurysms. Unusually like in this case, KD affects adult patients. Although, the diagnosis is made based upon the presence of classical symptoms, incomplete presentation of KD may also be observed. Vigilance is therefore required not to miss the proper diagnosis. Initiation of appropriate treatment on time may decrease the rate of coronary arteries complications.
Presence of persistent complex coronary arteries aneurysm sized over 6mm and located in proximal segments of right coronary artery, left main, LAD and Cx puts this patient in the high risk of sever coronary complications including ischemia, myocardial infarction or sudden death. Therefore, life-long antiplatelet treatment i.e. aspirin 75mg daily should be recommended. Whether other antiplatelet agent like clopidogrel may be used instead it is a matter of debate. Adding anticoagulants to the treatment regimen seems reasonable taking the size and the complexity of the aneurysm located in the LM bifurcation. Recommended INR ration between 2 and 3. The patient needs to remain in the close follow up. Clinical evaluation with ecg and echocardiography should be recommended every 6 months. Stress test or perfusion evaluation should be scheduled once a year. The patient should be advised to restrict from close contact or high impact sports, however current atherosclerosis prevention recommendations should be delivered to him including regular physical activity. In case of clinically evident myocardial ischemia or observed in stress testing, coronary angiography should be performed. Surgical revascularization seems to be the method of choice in this patient. In case of myocardial infarction emergency coronary angiography should be performed and percutaneous revascularization done.

CONCLUSION

Close follow-up is recommende. Antiplatelet agents with anticoagulants should be prescribed. In case of clinically overt myocardial ischemia coronary angiography and surgical revascularization should be recommended.

REFERENCES

1. Burns JC, Glodé MP. Kawasaki syndrome. Lancet. 2004;364:533
2. Yanagawa H, Nakamura Y, Yashiro M, et al. Incidence survey of Kawasaki Disease in 1997 and 1998 in Japan. Pediatrics. 2005;107:1-4
3. Dillon MJ. Childhood vasculitis. Lupus. 1998;7:259–65
4. Sève P, Stankovic K, Smail A, et al. Adult Kawasaki Disease: report of two cases and literature review. Semin Arthritis Rheum. 2005;34:785–92
5. Gomard-Mennesson E, Landron C, Dauphin C, et al. Kawasaki disease in adults: report of 10 cases. Medicine (Baltimore). 2010;89:149.
6. Newburger JW, Takahashi M, Gerber MA, et al. Diagnosis, treatment, and long-term management of Kawasaki disease: a statement for health professionals from the Committee on Rheumatic Fever, Endocarditis and Kawasaki Disease, Council on Cardiovascular Disease in the Young, American Heart Association. Circulation 2004; 110:2747.
7. Fujiwara H, Hamashima Y. Pathology of the heart in Kawasaki disease. Pediatrics.

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1978;61:100.
8. Yutani C, Go S, Kamiya T, et al. Cardiac biopsy of Kawasaki disease. Arch Pathol Lab Med. 1981;105:470.
9. Moran AM, Newburger JW, Sanders SP, et al. Abnormal myocardial mechanics in Kawasaki disease: rapid response to gamma-globulin. Am Heart J. 2000;139:217.
10. Burns JC, Shike H, Gordon JB, et al. Sequelae of Kawasaki disease in adolescents and young adults. J Am Coll Cardiol. 1996;28:253.
11. Baer AZ, Rubin LG, Shapiro CA, et al. Prevalence of coronary artery lesions on the initial echocardiogram in Kawasaki syndrome. Arch Pediatr Adolesc Med 2006; 160:686.

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