

Case Report

Incomplete Kawasaki disease: The usefulness of BCG reactivation as a diagnostic tool

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ABSTRACT

Kawasaki disease (KD) is an extremely rare condition in infants younger than 3 months old. Cardiovascular complications are unfortunately most common in young infants and it is in this age group, incomplete Kawasaki disease (IKD) is more frequently reported. Because IKD is a diagnostic dilemma, any sign that could help early diagnosis, such as BCG reactivation is useful. Here we report on an infant less than 3 months old with IKD wherein, BCG reactivation helped us in making the diagnosis. In this article, we highlight the usefulness of this sign for early diagnosis of IKD, especially in countries where BCG vaccination is still part of the immunization schedule.

Key words: Kawasaki disease, incomplete Kawasaki disease, BCG reactivation, infants.

INTRODUCTION

Kawasaki disease (KD) formerly known as mucocutaneous lymph node syndrome or infantile polyarteritis nodosa, is an acute febrile vasculitis of childhood first described by Dr. Tomisaku

Kawasaki in Japan in 1967 [1]. Since then it has been described widely in America, Europe, and Asia [2]. Approximately 20% of untreated patients develop coronary artery abnormalities, and it has replaced rheumatic fever as the leading cause of acquired heart disease in children in the United States and Japan [1]. KD occurs in young children, with a yearly incidence of 80 to 90 per 100,000 children younger than 5 years in Japan and 10 per 100,000 children younger than 5 years in the United States [2]. The cause of KD is unknown, but epidemiologic data suggest that the mechanism involves an immune response to a predisposing infection in genetically predisposed people [3]. The diagnostic criteria for the classic case of KD include fever persisting at least for 5 days and presence of 4 principal features which include: (i) changes in extremities which may be acute such as erythema of palms and soles and edema of hands and feet or sub-acute such as periungual peeling of fingers and toes, (ii) polymorphous exanthema. (iii) bilateral bulbar conjunctival injection without exudates, (iv) changes in lips and oral cavity including erythema, lip cracking, strawberry tongue and

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diffuse injection of oral and pharyngeal mucosa, (v) cervical lymphadenopathy (more than 1.5cm in diameter), usually unilateral. In addition to these features, exclusion of other diseases with similar findings is mandatory [4]. There is no specific diagnostic test or pathognomonic clinical feature. This difficulty in diagnosis is further compounded with increasing reports of incomplete Kawasaki disease (IKD) [5]. Cardiovascular complications are most common in young infants and unfortunately it is in this age group, IKD is more frequently reported [4]. Isolated cases of the usefulness of reactivation of the Calmette-Guerin Bacillus (BCG) inoculation scar in the diagnosis of KD has been described in the literature [6,7,8,9].

We hereby present a young case of IKD wherein this sign aided us in making the diagnosis.

CASE REPORT

A 75 days old Indian male infant was admitted to our Pediatric ward with the complaint of high grade fever and a non-bloody diarrhea for 3 days. He was born at our hospital by normal spontaneous vaginal delivery after an uneventful pregnancy. His immunizations including BCG, given at birth, were up to date. The rest of his medical history was insignificant.

On physical examination, the boy was well looking despite his high fever (39 degree centigrade) and with no other significant findings except for a mild hyperemia of the oropharynx. Complete blood count (CBC) revealed hemoglobin (Hb) level of 9.3g/dl, white blood count (WBC) of 14,500/mm³, and platelet count of 292,000/mm³. A urine analysis showed pyuria. After samples for blood, urine and stool cultures were taken, he was started on parenteral ceftriaxone 75mg/kg, for the diagnosis of urinary tract infection.

His fever continued despite the antibiotic

treatment. At the 4th day of admission (7th day of fever), his WBC raised to 19,700/mm³, with neutrophils of 40%, lymphocytes of 44%, monocytes of 10% and eosinophils of 6%, platelets increased to 823,000/mm³. Hb was 9.8g/dl and erythrocyte sedimentation rate (ESR) was 77 mm in the 1st hour. His blood, urine and stool cultures remained sterile. At his 9th day of fever, his platelet count increased to 903,000/mm³ and he was noticed to have more marked erythema of the oropharynx and mildly erythematous lips. He also developed marked erythema, induration and crusting at his left upper-arm that is corresponded to the area of his BCG vaccination (Figures 1 & 2). The rest of his investigations including renal and electrolyte panel, calcium, liver function test and serum albumin were normal. Echocardiography done on the 9th day of fever was normal and an abdominal ultrasonography revealed no abnormality, in particular there was no hydrops of the gall bladder.

The inflammation of the BCG scar and the daily continuing fever with erythema of the oropharynx and red lips led us to think of the presumptive diagnosis of IKD. On the 9th day of fever, he was started on intravenous immunoglobulins (IVIG) 2 gram/kg over 12 hours infusion and low dose aspirin 5mg/kg per day and the antibiotics were discontinued. His fever subsided dramatically after the IVIG and the erythema over the BCG scar disappeared over 3 days. Subsequent CBC at 3 weeks of fever demonstrated reduction in the WBC to 13,000/mm³, increased Hb to 10.8g/dl and decreased platelets to 605,000/mm³. After 6 week, his CBC was normal with WBC of 10,200/mm³, Hb of 11.2g/dl, platelets of 400,000/mm³ and ESR of 15mm in the 1st hour. Repeated echocardiograms at the 2nd and 6th weeks were normal. Convalescent phase was unremarkable and aspirin therapy was continued for 8 weeks.

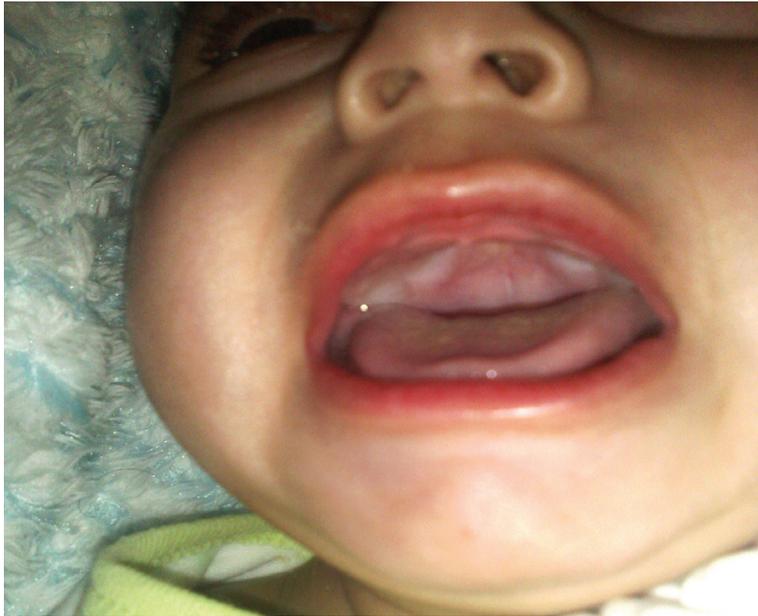


Figure 1- Erythema of the oropharynx and lips, one of the classical signs of Kawasaki disease.



Figure 2- Marked erythema and induration involving the BCG scar in an infant with Kawasaki disease.

DISCUSSION

KD affects primarily young children, with 80% of patients under the age of 4 years and with the peak incidence at 9 to 11 months of age [2]. Although there are reports of KD presenting at the neonatal period [10], it is extremely rare in infants younger than 3 months old. In one Japanese series, only 1.7% of patients were younger than 3 months [11]. Lee et al found 11 (3.8%) out of 291 cases of KD, were 3 months old or

younger, and they found 10 out of the 11 had atypical presentations [12]. In infants, the atypical presentations (longer duration of illness before diagnosis, lower incidence of conjunctivitis, rash and extremity changes and lower C-reactive protein), are common [10]. Infants usually have fewer of the accepted criteria, and the most common findings are fever (100%) and oral mucosal changes (72%) [12]. In this young age, coronary artery involvement – more rapid and severe coronary

artery disease- is more common than in older patients [12,13]. Delayed diagnosis of KD is a significant risk factor for the development of coronary artery abnormalities [14]. In 1987, Sonobe and Kawasaki [15] stated that, the presence of fewer than four of the principal clinical features accompanying fever and the presence of coronary artery aneurysms allows the diagnosis of atypical incomplete KD (IKD). IKD cases are being recognized with increasing frequency [16], with an incidence of 10 to 45% [17]. Early diagnosis of KD is extremely important, since coronary artery aneurysms occur as a sequela of the vasculitis in 15 to 25% of untreated patients, and treatment, in the 1st 10 days of illness, with 2 grams/kg of IVIG reduces the prevalence of coronary abnormalities to 2 -4 % [18]. Therefore, any clinical finding that could lead to early diagnosis is worth taking into consideration. Non-cardiac features known to be associated with KD include: extreme irritability, aseptic meningitis, pneumonitis, arthritis and arthralgia, sterile pyuria, elevated liver transaminases, uveitis, otitis media, hydropic gall bladder and reactivation of the BCG site. BCG reactivation and hydrops of the gall bladder (in 15% of patients) are relatively specific for KD, and

provide stronger support for the diagnosis of IKD [6]. The local inflammatory reactivation of the BCG vaccination site was first highlighted in the Japanese literature as a specific early sign of KD [19]. This phenomenon has been hypothetically ascribed to cross-reactivity between mycobacterial heat shock protein (HSP) 65 and a human homologue HSP 63 [8,20].

Our patient had persistent fever despite antibiotic treatment. During the first days of the fever he had no feature suggestive of KD except mild hyperemia of oropharynx. Later he developed the BCG reactivation which led us to suspect IKD. This in addition to his persistent fever, increased acute phase reactants and sterile pyuria which is seen in 33% of KD patients [4]. With the use of IVIG, prompt resolution of his symptoms occurred without any squeal involving coronary arteries.

In conclusion, this case report highlights the importance of reactivation of BCG as an early sign suggestive of atypical Kawasaki Disease, especially in countries where BCG vaccination is still a part of the immunization schedule, as in Sudan and Saudi Arabia.

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