A CASE OF KAWASAKI DISEASE SHOCK SYNDROME WITH CONCOMITANT *PANTOEA SPP* SEPSIS

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ABSTRACT

Kawasaki disease (KD) is a common systemic vasculitis of childhood involving medium sized arteries that may result in life-threatening coronary artery abnormalities [1]. Children with Kawasaki disease generally do not develop shock however, in some patients a more intense inflammatory response may lead to shock syndrome [2]. This is a case of a seven-year-old male who presented with neck pain, fever, rash, and with clinical signs of poor perfusion and shock. 2D-echocardiography showed dilated coronary arteries, and he was managed as a case of Kawasaki Disease Shock Syndrome (KDSS).

CASE REPORT

K.A.C. is a seven-year-old male who initially presented with unilateral neck pain and came at our institution due to increase in sleeping time. He was apparently well until five days prior to admission when he complained of sudden onset right sided neck pain which was tender to touch. There was no history of trauma or associated symptoms such as fever, cough, colds, headache, or vomiting. No consult was done, and no medications were taken.

Four days prior to admission, there was noted persistence of the right sided neck pain now accompanied by swelling and limitation of movement. He also had fever with a maximum temperature of 39.4oC. He was then brought to a Rural Health Unit and was assessed to have Mumps vs Musculoskeletal Pain. He was given mefenamic acid which provided temporary relief of pain and resolution of fever. Three days prior to admission, there was persistence of symptoms which prompted consult with a private pediatrician. Urinalysis showed pyuria, the assessment was urinary tract infection, for which he was given Cefixime. Two days prior to admission, there was persistence of symptoms now accompanied by erythematous maculopapular rashes on the neck which progressively involved the chest and face. They sought consult with their pediatrician wherein a complete blood count (CBC) was done which showed thrombocytopenia with a platelet count of 146 x 109/L. He was assessed to have dengue fever and was advised CBC monitoring. One day prior to admission, patient had persistence of intermittent fever and right sided neck pain, accompanied by progression of erythematous maculopapular rashes coalescing into plaques now involving the trunk and extremities. There was also erythema and swelling of bilateral hands and drying of the lips. He also had decreased appetite, generalized body weakness, episodes of shortness of breath,

easy fatigability, and occasional non-productive cough. The patient was again seen by his private pediatrician and a complete blood count was done with normal results. He was assessed to have Kawasaki Disease and he was given Cetirizine and Prednisone. On the day of admission, the patient was noted to be drowsy with increase in sleeping time hence consult was done in our institution and was subsequently admitted.

Upon further history, it is noted that the patient usually plays with animals and insects at the mini garden in front of their home, and the patient had a history of thorn pricks within the past month from this admission.

Upon admission, the patient was awake, weak looking, stretcher-borne, and in cardiorespiratory distress. He was hypotensive with a blood pressure of 80/50, tachycardic with a heart rate of 160 beats per minute, tachypneic with a respiratory rate of 35 cycles per minute, afebrile at 37.4oC, and with desaturation at 93% on room air. He had bilateral conjunctival erythema, dry lips, alar flaring, neck stiffness, and swelling of the right lateral neck. Chest examination showed symmetric chest expansion, with noted subcostal and intercostal retractions, clear breath sounds, adynamic precordium, tachycardic, with regular rhythm, and with no murmur. Abdominal examination showed flat abdomen, nondistended, with normoactive bowel sounds, and with direct tenderness over the epigastric area, no organomegaly noted. He had cool extremities, prolonged capillary refill time of 4 seconds, and poor pulses. Upon examination of the skin, there was noted erythematous to hyperpigmented maculopapular rash coalescing into plaques on the trunk and extremities.

The admitting impression was toxic shock syndrome r/o Kawasaki disease, COVID suspect, r/o multisystemic inflammation in children. Fluid resuscitation was initiated accordingly, and vasopressors were started. Blood culture revealed moderate growth of Pantoea spp. He was given appropriate antibiotics, completed Meropenem for 14 days, Amikacin for 7 days, and Vancomycin for 7 days. He was persistently in respiratory distress which eventually led to necessitating ventilatory support and referral to Pediatric Intensive Care. The patient was subsequently referred to the service of Cardiology for 2D-Echocardiogram which revealed dilation of bilateral coronary arteries. He was assessed to have Kawasaki disease shock syndrome hence intravenous immune globulin and Aspirin were initiated. The patient showed significant improvement thereafter and was discharged improved and stable on the 16th hospital day. He came in for follow up check up after 1 week, asymptomatic with reported good appetite and activity. A repeat 2D Echocardiography showed residual bilateral coronary artery aneurysm.

DISCUSSION

Kawasaki disease (KD), formerly known as mucocutaneous lymph node syndrome and infantile polyarteritis nodosa, is an acute febrile illness of childhood seen worldwide, with the highest incidence occurring in Asian children younger than 5

years old [6]. KD in older children is usually prominent among males, with observed delays in diagnosis, presenting with additional signs and symptoms, and a substantial incidence of coronary artery abnormalities [2].

Our patient initially presented with a four-day history of fever associated with right sided neck swelling and pain, erythematous to hyperpigmented maculopapular rash coalescing into plaques, bilateral hand edema and erythema, dry lips, and bilateral conjunctival erythema. He had three of the five principal criteria of Kawasaki disease which are: (1) bilateral nonexudative conjunctival injection with limbal sparing; (2) erythema of the oral and pharyngeal mucosa with strawberry tongue and red, cracked lips; (3) edema (induration) and erythema of the hands and feet; (4) rash of various forms (maculopapular, erythema multiforme, scarlatiniform or less often psoriatic-like, urticarial or micropustular); and (5) nonsuppurative cervical lymphadenopathy, usually unilateral with node size >1.5cm. Also, in KD, fever is characteristically high spiking (> 38oC), remitting, and unresponsive to antipyretics. He also presented with clinical signs of poor perfusion which is rarely seen in Kawasaki disease. He was hypotensive, tachycardic, tachypneic, with poor pulses, prolonged capillary refill time of 4 seconds, and with cool extremities. He also presented with persistent respiratory distress which eventually necessitated ventilatory support. A chest x-ray showed reticulonodular densities and ground glass pneumonic opacities on both lungs. On further work up, laboratories showed: leukocytosis with a white blood cell count of 20.5 x 109/L, thrombocytopenia with a platelet count of 110 x109/L but then developed thrombocytosis with a platelet count of 933 x109/L, elevated inflammatory markers such as C-reactive protein (210.5 mg/L, 21 times elevated), Procalcitonin (36.950 ug/L, 73.9 times elevated), and Erythrocyte sedimentation rate (60 mm/hr, 6 times elevated). With these findings, the patient was admitted and managed as a case of toxic shock syndrome.

KDSS is often misdiagnosed as toxic shock syndrome (TSS) or septic shock as their clinical pictures are similar. Both present with fever, rash, hypotension, multi-system involvement and desquamation. Laboratory studies are then essential to differentiate the two groups. KDSS may present with significantly lower albumin levels indicating a possible correlation between albumin and increased vascular permeability [7]. Thrombocytosis is a characteristic finding in KDSS, whereas thrombocytopenia is more common in other types of shock [3]. The most important difference is the presence of echocardiographic abnormalities, such as valvulitis (mitral or tricuspid regurgitation) and coronary artery lesions in the KDSS group [4].

Another differential diagnosis for this case is the multisystem inflammatory syndrome in children (MIS-C). These findings are consistent with the World Health Organization case definition of MIS-C: (1) age 0-19; (2) fever for □ 3 days; (3) clinical signs of multisystem involvement (rash, bilateral nonpurulent conjunctivitis, or

mucocutaneous inflammation signs, hypotension or shock, cardiac dysfunction, evidence of coagulopathy, acute gastrointestinal symptoms); and (4) elevated markers of inflammation. However, MIS-C was ruled out because our patient had a blood culture growth of Pantoea spp and there was no proven evidence of SARS-CoV-2 infection or exposure.

On further work-up, the blood culture revealed presence of moderate growth of Pantoea spp., hence toxic shock syndrome is more less likely. Pantoea spp is a gram-negative aerobic bacillus that belongs to the family Enterobacteriaceae. It is primarily an environmental and agricultural organism that inhabits plants, soil, and water [9]. Human infections caused by Pantoea spp are most often associated with wound infection with plant material or hospital acquired due to contamination of medical equipment and fluids. The source of these infections is due to thorn pricks, infected parenteral fluids, and indwelling catheters [10]. It commonly results in soft tissue or bone/joint infection and has a predilection for the lungs, with rare cases in pediatric patients of septicemia with respiratory failure [11]. Infections may be life-threatening, especially in young patients with pneumonia. Management mainly depends on antimicrobial susceptibility upon blood culture. In our patient, the sepsis caused by Pantoea spp may just have been an isolated infection but we cannot totally rule out that this could have triggered the Kawasaki disease shock syndrome our patient had.

On the sixth hospital day, the patient was referred to Cardiology for 2D echocardiography. Harada scoring was done with which the patient fulfilled six out of the seven criteria namely: white blood cell count >12,000/mm3 (20.1 x 109/L), platelet count less than 350,000/mm3 (110 x 109/L), C-reactive protein >3+ (210mg/L), hematocrit <35 (31), albumin <3.5 g/dL (2.3g/dL), age <12 years old, and male sex. The patient was then started on intravenous immune globulin. On the eighth hospital day, 2D Echocardiogram was done which revealed bilateral coronary artery aneurysm, hence a confirmed diagnosis of Kawasaki disease shock syndrome. Other cardiovascular findings are myocarditis (50-70%), pericarditis with pericardial effusion (25%), systemic arterial aneurysms (2%), valvular disease, mild aortic root dilatation and myocardial infarcts (1%) [14].

Kawasaki disease shock syndrome is defined as hemodynamic instability during the acute phase of the disease. KDSS is considered a rare disease around the world. The incidence rate of KDSS varied from 2.60%to 6.95% in children in Western countries. In contrast, a study in China reported a lower incidence rate of 1.23% [15]. Kanegaye et al found KDSS in 13 (7%) of 187 KD patients and in the study of Gamez-Gonzalez et al., of 214 patients with KD, 11 (5%) met the definition for KDSS. In our institution, there has been no recorded case of KDSS for the past 20 years. The cause of KDSS is unknown but capillary leakage due to vasculitis, myocardial dysfunction, and cytokine dysregulation are thought to be responsible [16]. The clinical manifestations of KDSS are atypical. It can rapidly develop into shock, and often with strong inflammatory responses which could

lead to coronary artery disease and multiple organ dysfunctions. The patients are hypotensive and would show signs and symptoms of poor perfusion.

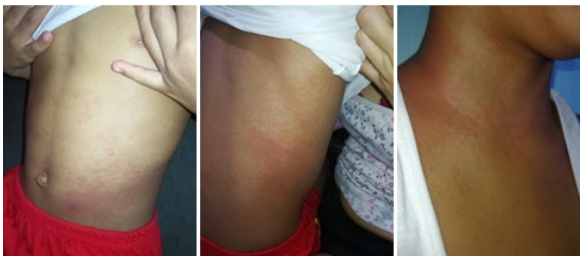
A thorough clinical evaluation of a patient's history and physical examination is the key in establishing the diagnosis of KDSS. No laboratory values are included in the classical diagnostic criteria of KD, but nonetheless may support a diagnosis. Echocardiography should be performed in all patients with KD as soon as diagnosis is suspected to establish a reference point for longitudinal follow-up and treatment efficacy. It is the imaging modality of choice for detection of coronary artery abnormalities and assessment of myocardial function [17]. In addition, initial coronary artery diameter noted on echocardiography is a factor in identifying patients at high risk of developing a coronary artery aneurysm and therefore warranting augmentation of initial intravenous immune globulin therapy. KDSS patients need early aggressive management to reduce systemic and vascular inflammation. The recommended treatment for KDSS includes the use of intravenous immune globulin combined with aspirin and vasoactive drugs. Also, other patients can maintain normal blood pressure by intravenous normal saline. In cases of resistant KD, other therapeutic options would include additional IVIG, corticosteroids, plasmapheresis, methotrexate, tumor necrosis factor inhibitors, cyclosporin and interleukin-1 blockers [19].

The prognosis for most patients with KDSS is excellent. Long term morbidity is primary related to the degree of coronary artery involvement. The rare fatal outcomes from severe cardiac involvement are generally the result of either myocardial infarction or arrhythmias, although aneurysm rupture can also occur. Mistaken or late diagnosis, or complete lack of IVIG treatment, is associated with potentially fatal outcomes [18]. Recurrence rate is low with a reported rate of 6.9 per 10000 person-years with highest incidence in children less than three years of age who had cardiac sequelae during the first episode [20]. Follow up after discharge includes monitoring for recurrence of fever and repeat echocardiograms to assess for cardiac involvement. After the baseline echocardiogram is obtained at diagnosis, echocardiography is usually repeated at approximately two and six weeks of illness to evaluate for coronary involvement [21]. Our patient was seen at the out-patient department after one week from discharge with a repeat 2D Echocardiography showing residual bilateral coronary artery aneurysm.

SUMMARY

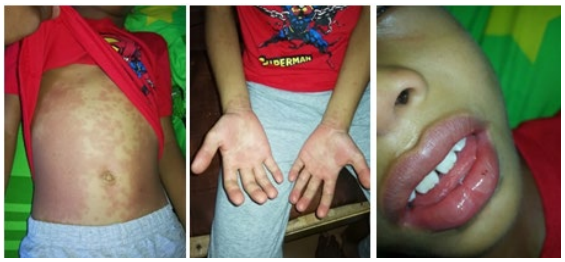
This report presented a seven-year-old male with fever, rash, conjunctival suffusion, edema and erythema of the hands, and right lateral neck swelling. He also presented with signs of respiratory distress and shock. Initially, he was managed as a case of toxic shock syndrome, however this was ruled out due to bacterial growth on blood culture, Pantoea spp. 2D-Echocardiogram showed bilateral coronary artery aneurysm, confirming the diagnosis of Kawasaki disease shock syndrome. Management included appropriate

antibiotics, intravenous fluids, intravenous immune globulin, and aspirin, which all provided notable improvement for this patient. Kawasaki disease shock syndrome is a rare disease recognized worldwide and is commonly misdiagnosed as toxic shock syndrome. The exact cause of KD is still unknown however, it may be triggered by an infection or an inappropriate immune response to an infection. In this case, septicemia caused by Pantoea spp could have provoked a cascade of immune responses ultimately playing a role in the pathogenesis of Kawasaki disease shock syndrome.



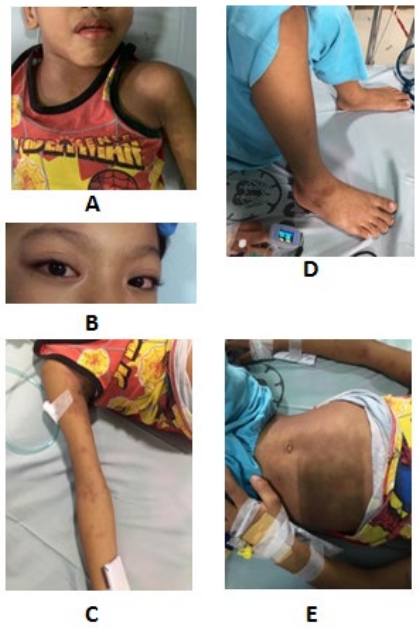
A B C

Figure 1. Image of KAC on Day 3 of Illness with noted appearance of erythematous maculopapular rash on the (a) trunk, (b) back, and (c) neck



A B C

Figure 2. Image of KAC on Day 4 of illness with (a) progression of maculopapular rash on the trunk now coalescing into plaques, (b) erythema and edema of bilateral hands, and (c) dry lips



A D B C E

Figure 3. Image of KAC on D5 of illness with noted (a) dry lips, (b) conjunctival suffusion with limbal sparing; progression of the rash involving the (c) upper extremities, (d) lower extremities, and the (e) trunk

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