
CASE REPORT

Mucocutaneous Lymph Node Syndrome

by

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Abstract

A case of Mucocutaneous Lymph Node Syndrome in a 12-year-old girl of Chinese parentage has been reported.

Principal features of our case were similar to those described in the Japanese Diagnostic Guidelines of mucocutaneous lymph node syndrome.

The differential diagnosis, causes, pathogenesis, treatment and prognosis of the syndrome were reviewed.

As far as we know, this was the first case of MLNS reported from Indonesia.

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Introduction

In 1967, Kawasaki for the first time reported 50 Japanese children with an acute febrile illness, mucocutaneous involvement and associated with swelling of the cervical lymph node, which he called Mucocutaneous Lymph Node Syndrome (MLNS).

In 1970, the Japanese Research Committee for MLNS established the following diagnostic guidelines of MLNS (Kato et al., 1975).

Principal symptoms and signs :

1. Fever lasting from one to two weeks, not responding to antibiotics.
2. Congestion of ocular conjunctivae.
3. Changes of lips and oral cavity;
 - a. dryness, redness and fissuring of lips
 - b. prominence of tongue papillae (strawberry-like)
 - c. diffuse reddening of oral and pharyngeal mucosa.
4. Changes in hands and feet;
 - a. reddening of palms and soles
 - b. indurative edema
 - c. membranous desquamation starting from fingertips (convalescent stage).
5. Polymorphous exanthem of trunk without vesicles or crusts.
6. Acute nonsuppurative swelling of cervical lymph nodes.

Other symptoms or findings :

1. Cardiovascular signs: electrocardiogram changes, gallop rhythm, distant heart sounds, heart murmur.
2. Diarrhoea.
3. Proteinuria and increased numbers of leukocytes in urine sediment.
4. Additional laboratory findings;
 - a. Leucocytosis with shift to the left
 - b. Slight anemia
 - c. Increased ESR
 - d. Positive C-reactive protein
 - e. Increased serum alpha-2-globulin concentration
 - f. Negative ASO titer.

Changes occasionally observed :

1. Arthralgia or arthritis.
2. Aseptic meningitis.
3. Mild jaundice or slight increase of serum transaminase.

Since the establishment of the above-mentioned diagnostic guidelines the disease has been recognized with increasing frequency, to date more than 10,000 cases have been reported in Japan alone (Sonobe et al., 1976). Recently, cases have been reported in the United States (Mellish et al., 1976; Lauer et al., 1976; John and Bebenedetti, 1976) in Britain (Fossard and Thompson, 1977) and in Canada (Radford et al., 1976).

This report is about the case of Mucocutaneous Lymph Node Syndrome, which as far as we know is the first case reported from Indonesia.

Case Report

N, a 12-year-old girl of Chinese parentage, was admitted to the AK Gani hospital on January 8, 1978, with the following history: Five days before admission she suffered from fever. On the next day she became seriously ill with high continuous fever. An erythematous rash was seen on her chest, spreading over the trunk, arms, neck, abdomen, buttock and face, then developed puffiness of face, dry, red cracked lips (fig. 1), swelling of the cervical lymph node (fig. 2), redness and swelling of hands and feet (fig. 3), vomiting and diarrhoea. She had been treated before, with no improvement. She was admitted to AK Gani hospital on the sixth day of illness. Four days before the illness, she was discharged from the Charitas hospital in good condition, where she had been admitted for hepatitis. At home she only took vitamins. The past history did not reveal any drug reaction. She suffered from this disease for the first time. All family members were healthy and did not suffer from the same illness.

Physical examination on admission revealed a body weight of 28 kg and body temperature of 38.8°C. She looked ill and lethargic. Her pulse rate was 120/minute and respiration rate 32/minute. Her blood pressure was 128/80. Her face was puffy and red. The mucous membrane of the oral cavity and pharynx was hyperaemic without exudate.

She had a strawberry-like tongue, red cracked lips.

A diffused erythematous non-vesicular rash was seen on her neck, chest, arms, trunk, abdomen and buttock. The rash was pruritic. Indurative edema was found on her hands and feet. Her palms and soles were red.

A tender non-fluctuant 2cm × 3cm lymphnode was palpable below the right and left mandibular angle. No abnormality was found on auscultation of the heart and lungs. The liver was palpable 2cm × 2cm below the right costal margin. The spleen was not palpable. No abnormality was found on neurological examination.

Laboratory studies during her stay in the hospital revealed: Hemoglobin content 11 gm % which rose to 12.4 gm % after convalescent stage. Leucocyte count was initially 13,200/cu.mm with eosinophils 2%, basophils 0%, bands 3%, segments 69%, lymphocytes 24%, monocytes 2% and later fell to 8000/cu. mm with eosinophils 2%, basophils 0%, bands 1%, segments 51%, lymphocytes 43%, monocytes 2%; ESR was 22 mm/hr on admission and later fell to 10 mm/hr. Platelet count was 205020/cu. mm; CT 3'45"; BT 5'25".

Tourniquet test was negative. The total bilirubin serum was 0.3 mg% with a direct bilirubin 0.05 mg% and indirect bilirubin 0.25 mg%. Alkaline phosphatase 2.7 U. Blood cholesterol 180 mg%. Total protein serum 6.09 gm% with



FIG. 1. *Puffiness of face and cracked lips.*



FIG. 2. *Swelling of the Cervical lymphnodes*

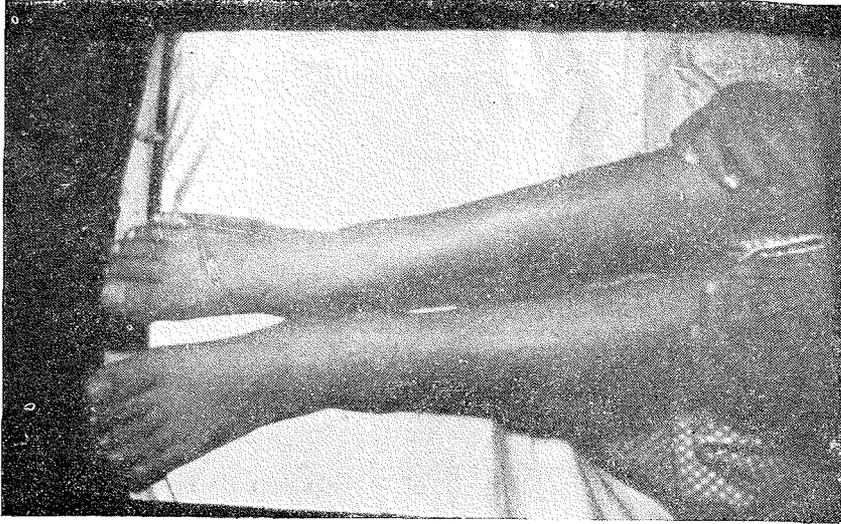


FIG. 3. *Redness and Swelling of hands and feet*

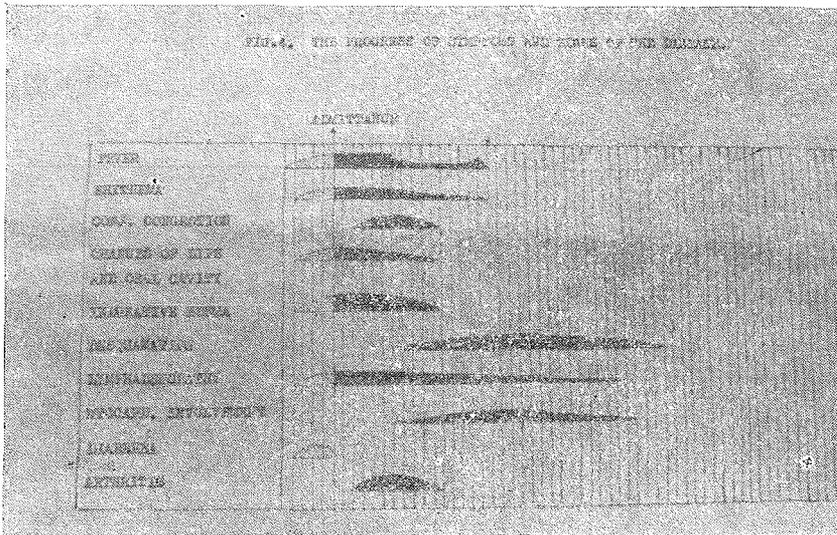


FIG. 4. *The progress of symptoms and signs of the disease*

albumin 3.69 gm% and globulin 2.4 gm%. Blood creatinine 0.6 mg%. SGO-T 96 IU and SGPT 75 IU. Rheumatoid factor was negative. C reactive protein was positive. Anti-streptolysine-0 titer was initially 200 IU, later it became negative. Blood urea 20 mg%.

Salmonella O-antigen was negative. No abnormality was found on stool examination. Urine examination showed slight albuminuria with leucocytes of 2-4/high power field and some cellular cast. Blood, urine, stool and throat cultures were performed prior to antibiotic therapy. The culture failed to demonstrate pathogenic bacteria or fungi, except the throat culture which showed pneumococcus growth. Tuberculin test was negative. Chest roentgenograph showed chronic bronchitis.

Our differential diagnosis on admission was :

1. MLNS
2. Drug eruption
3. Steven-Johnson syndrome
4. Scarlet fever.

Though our working diagnosis was MLNS due to lack of experience, we could not decisively exclude the possibility of drug eruption or Steven-Johnson syndrome. Beside supportive fluid therapy, we also gave the patient corticosteroid (betamethasone) and antihistamine (homochlorcyclisine) and vitamins.

Follow-up : Figure 4 revealed the progress of symptoms and signs of the disease. On the sixth day of admission her temperature dropped to 37.5°C. During the 7th day to the 11th day of admission she was sub-febrile with a temperature of 37.5 to 37.8°C. On the 12th day of admission her temperature increased to 39.2°C.

As we suspected a secondary infection and radiological finding of the chest revealed chronic bronchitis, the patient was treated with ampicillin/cloxacillin 3×500 mg/day for ten days. The fever subsided after 14 days of hospitalization. Conjunctival congestion was noted on the third day of admission and disappeared on the 9th day. Changes of lips and mucous membrane of the oral cavity gradually subsided on the 7th day. On the 6th day of admission indurative edema on her hand gradually decreased. Her finger tips began to peel. At that time desquamation was noted on her neck, chest, trunk, abdomen and buttock. After 14 days of admission peeling of the skin from the tips developed at which time indurative edema also disappeared.

Swelling of the cervical lymph nodes gradually decreased on the 7th day of admission and disappeared on the 24th day. Serial electrocardiograms during the first week to the second week of admission revealed a semiver-tical heart, sinus tachycardia, slurring of R wave in lead III and lead

AVF, QTc of 0,42 s to 0,47 s. On the third week to the fourth week of admission the electrocardiograms showed sinus arrhythmia with an average frequency of 60/minute.

Slurring of R wave was also seen in lead AVL and lead V2. On the 5th week of admission the ECG was within normal limits. Slurring of R wave and arrhythmia disappeared. Edema and pain on her left knee were noted on the third day of admission and disappeared on the 9th day.

The dosage of corticosteroid was tapered off on the 7th day admission and stopped on 12 days after admission. On the 30th day of admission she was discharged in good condition.

Discussion

The clinical findings of our case are similar to those described in the Japanese Diagnostic Guidelines of mucocutaneous lymph node syndrome, in which the dominant signs are fever, ocular conjunctival congestion, reddening of the lips and mucous membrane of the oral cavity, strawberry tongue, diffuse erythematous non-vesicular rash over the trunk, reddening indurative edema of the hands and feet followed by desquamation and cervical lymphadenopathy.

Fever lasting from one to two weeks not responding to antibiotics is one of the characteristic of the disease, sometimes up to 3 weeks (Mellish et al., 1976). In our case the fever subsided on

the 16th day of illness, but on the 17th day it appeared again. We concluded that it was caused by secondary infection.

The fever was accompanied by ocular conjunctival congestion, reddening of lips and mucous membrane of the oral cavity, strawberry tongue and often non-suppurative swelling of cervical lymph-nodes (Kato et al., 1975). The lips may be eroded, dry and fissured. In our case, symptoms and signs appeared one day after the onset of fever.

Swelling of the cervical lymphnode is an important sign of the illness. Characteristically, that a single enlarged node was found in the cervical region measuring more than 1.5 cm in diameter. The enlarged node was minimally tender, firm non-erythematous and non-suppurative (Mellish et al., 1976). Most of the enlarged nodes were unilateral. Mellish et al., (1976) observed just one case with bilateral enlargement among 9 cases; in our case enlargement of lymphnodes was bilateral.

The rash typically appeared within one to five days of the onset of fever. The rash was erythematous; polymorph exanthem without vesicles or crusts usually started on the extremities with pronounced reddening of the palms and soles that spread over the trunk within two days (Kato et al., 1975). The face and trunk were more severely involved than the proximal part of the extremities (Mellish et al., 1976).

Hands and feet swelled with an indurative edema. Changes in the hands and feet were most characteristic and appeared to be a distinct aspect of the syndrome (Mellish et al., 1976). The skin manifestations disappeared in less than a week. During the second week of illness, unusual desquamation began in the junction of the nails and skin on the tips of the fingers and toes (Kato et al., 1975).

In our case desquamation of the tips of the fingers was noted on the sixth day to the 14th day of admission, at which time the clinical symptoms and signs gradually subsided.

Electrocardiographic changes were important and seen in almost all patients (Kato et al., 1975) and in our case it was not an exception. Serial electrocardiograms might detect minimal changes such as decreased voltage of R wave, flat T wave and prolonged PR and QTc intervals (Kato et al., 1975).

In our case the ECG revealed sinus tachycardia followed by sinus arrhythmia, slurring of R wave and prolonged QTc interval. Electrocardiographic changes might suggest the presence of not only coronary lesions but also perivascular myocarditis, which was often seen at autopsies (Mellish et al., 1976).

Lesions of the coronary arteries consisting of aneurysm or stenosis and tortuosity have been seen in angiography in living children with clinical signs of the syndrome (Kato et al., 1975; Red-

ford et al., 1976). The cardiac signs which suggested involvement of the coronary arteries might appear in the first week of illness (Kato et al., 1975). Approximately 1-2% of the reported patients with MLNS died suddenly of myocardial infarction secondary to coronary artery thromboarteritis (Sonobe et al., 1976).

Other important associated findings of the illness were diarrhoea, arthritis, urethritis or sediment abnormalities and aseptic meningitis, with very mild cerebrospinal fluid pleiocytosis (Mellish et al., 1976). In our case lumbar puncture was not performed.

The most consistent laboratory abnormalities were seen in the peripheral blood. There was PMN leukocytosis, slight anemia and increased ESR (Mellish et al., 1976).

Kawasaki (1967) regarded the clinical syndrome of the disease as a disease entity based on its clinical picture. The same features of the syndrome may be seen in a drug eruption, in streptococcal scarlet fever and in Steven-Johnson syndrome.

The presence of high spiking fever, diffuse erythematous maculopapular non-vesicular rash spread to involve the entire body, oral cavity erythema, strawberry tongue, cervical lymphadenopathy and elevated total WBC count with PMN predominance and shift to the left led irresistibly to the clinical diagnosis of streptococcal scarlet fever. Failure to isolate the streptococcus or to show an

elevation in the ASO titer, failure to respond to antibiotic therapy and the appearance of manifestations not reported in the scarlet fever make this diagnosis untenable.

The nonvesicular rash, nonexudative conjunctivitis and the absence of mucosal (mouth and genital) ulceration distinguished this patient from Steven-Johnson syndrome. The changes of the hands and feet so striking in MLNS, have not been described in Steven-Johnson syndrome (Mellish et al., 1976).

The cause and pathogenesis of MLNS are not yet defined (Mortimer, 1976). Many features of the disease suggested an acute infective etiology, but no consistent pathogen has been isolated (Fossard et al., 1977). Recently, rickettsia like bodies were found by electron microscopy in biopsy specimens from the skin and lymphnodes of the patient (Hamashima et al., 1973), but the significance of these structures was uncertain.

Some similarities between this disease and Steven-Johnson syndrome and infantile polyarteritis nodosa have suggested that hypersensitivity might be responsible (Mellish et al., 1976). Circulating immune complexes and increa-

sed concentrations of IgE possibly played a part in the pathogenesis of MLNS and might be responsible for the major complications (Fossard et al., 1977).

Corticosteroid therapy has been used for the treatment of MLNS. Clear evidence of efficacy of corticosteroid in modifying the acute course of MLNS or in preventing its fatal termination has not yet been presented (Mellish et al., 1976). Aspirin therapy may have a place in the therapy of MLNS because of its antipyretic, antiinflammatory effects and its potential in reducing hypercoagulability (Mellish et al., 1976). A hypercoagulable state at a period of vessel injury may produce coronary artery thrombosis. Other more potent anticoagulant therapy may be warranted in patients with both thrombocytosis and evidence of coronary artery disease in the ECG or angiogram (Mellish et al., 1976). Although it is usually a self-limited illness, MLNS is regarded as one of the most important causes of myocardial infarction in childhood in Japan (Kato et al., 1975). Such observations suggest that there may be cardiovascular sequelae of MLNS, especially in late death due to myocardial infarction and mitral regurgitation caused by papillary muscle dysfunction (Kato et al., 1975).

TABLE 1: Revealed the clinical symptoms and signs in our case compared to the Japanese Diagnostic Guidelines of Mucocutaneous Lymph Node Syndrome

Symptoms and Signs	Japanese Diagnostic Guidelines of MLNS	Case
Fever	+	+
Rash	+	+
Ocular conjunctival congestion	+	+
Changes of lips & mucous membrane of the oral cavity	+	+
Changes in hands and feet	+	+
Cervical lymphadenopathy	+	+
Cardiovascular sign — ECG changes	+	+
Diarrhoea	+	+
Arthritis	+	+
Laboratory changes :		
— Leukocytosis	+	+
— Slight anemia	+	+
— Increased ESR	+	+
— (+) C reactive protein	+	+
— (—) ASO titer	+	+
— Increased serum transaminases	+	+

All of the symptoms and signs which appeared in the Japanese Diagnostic Guidelines of MLNS were found in our case. All of the symptoms and signs in our case were also detected in the Japanese Diagnostic Guidelines of MLNS. Thus we can conclude that our case was MLNS.

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