MUCOCUTANEOUS LYMPH NODE SYNDROME IN MALAYSIA

D. SINNIAH, N.NAGAPPAN & M.CHOO

INTRODUCTION

ACUTE febrile mucocutaneous lymph node syndrome (MLNS), a febrile exanthematous illness of young children was first described in Japan by Kawasaki (1967). Since the establishment of diagnostic guidelines by the Japanese Ministry of Health and Welfare (1974), the disease has been recognised with increasing frequency in many different countries including the United States (Melish *et al.*, 1976; Korea (Kim *et al.*, 1975), Hawaii (Melish *et al.*, 1974) and Greece (Valaes, 1975).

We present here a report of three cases of mucocutaneous lymph node syndrome from the University Hospital, Kuala Lumpur, which we believe are the first to be recognised in Malaysia.

REPORT OF CASES

CASE 1: A 5 year old Chinese girl was hospitalised in November 1977 with a 4 day history of cough, anorexia, and fever non-responsive to ampicillin. She had mild jaundice, conjunctival injection, erythema of the mouth, pharynx and tongue and a generalised maculopapular rash with redness of the palms and soles. The cervical nodes were enlarged and the liver was 2 cm palpable below the rib margin; the rest of the clinical examination revealed no abnormalities.

Investigations revealed the following: haemoglobin 10.6 g/dl, white blood cell count 12.4 x 10^9/l, polymorphs 87%, lymphocytes 10%, monocytes 2%, eosinophils 1%, platelet count 230 x 10^9/l, ESR 86 mm/hr, serum total bilirubin 61.6 umol/l, unconjugated bilirubin 27.4 umol/l and conjugated bilirubin 34.2 umol/l, SGOT 23 iu/l; SGPT 56 iu/l, serum alkaline phosphatase 234 iu/l. Serum IgG, IgA, IgM, complement C_3, and C_4 were normal. Other tests with normal or negative results included Monospot test, Widal test, Weil-Felix reaction, antistreptolysin O titre, mantoux test, LE cells, rheumatoid factor, viral cultures of nasopharyngeal washings and stool, urine and blood cultures and chest X-ray.

Four days after admission the child developed acute left heart failure with gallop rhythm and electrocardiogram (ECG) revealed uniformly low voltages, PR interval O.16 sec and depressed ST-T segments in V_3 and V_5. She responded well to digoxin and lasix. The fever settled on the seventh hospital day and on the tenth day she was observed to have desquamation of the finger tips. She was then discharged and has remained well since.

CASE 2: A 4 year old Indian boy was admitted in December 1978 with a 8 day history of fever, conjunctival injection and a mild transient erythematous rash on the trunk. On examination, he was febrile, temperature 38°C and toxic. Ulcers were observed on the lips and buccal mucosa and there was moderate cervical right axillary, and supratrochlear lymphadenopathy. The liver was 1.5 cm palpable below the rib margin. The rest of the clinical examination was normal. Investigations revealed, haemoglobin 12.7 g/dl, total white blood cell count 11.7 x 10^9/l, polymorphs 78%, lymphocytes 17%, monocytes 4%, eosinophils 1%, platelets 250 x 10^9/l, ESR 71 mm/hr, serum total bilirubin 5 umol/l, SGOT 23 iu/l, SGPT 80 iu/l, serum alkaline phosphatase 206 iu/l, serum total proteins 73 g/l, albumin 31g/l and globulin 42 g/l. Chest X-ray was normal. Cultures of throat washings, blood and stools were negative for both bacteria and viruses. Monospot, Widal and Weil-Felix tests were negative. Serology for arboviruses, CMV, herpes, measles rubella and toxoplasma were negative. LE cells and tests for rheumatoid factor were negative. Bone marrow

D. Sinniah AM. MA. MD. FRACP. FRCPI. DCH.
N. Nagappan MBBS. MRCP.
M. Choo MBBS. MMED.

Department of Paediatrics, University of Malaya, Kuala Lumpur, Malaysia.

examination revealed active granulopoeisis and lymphocytosis suggestive of a viral infection.

Patient became afebrile 6 days after admission and developed desquamation of the finger tips and around mouth. He has remained well since.

CASE 3: A 2 year old Indian boy was admitted in January 1979 with a 6 day history of fever followed by swelling of the feet and the appearance of a macular rash over the face and trunk two days before admission. On examination, temperature was 38°C and the child appeared toxic with conjunctival injection and ulcerations of the lips and buccal mucosa. The cervical nodes were enlarged and discrete. The results of the rest of the clinical examination were negative. Investigations revealed, haemoglobin 9.6 g/dl, total white blood cell count 14.8 x 10^9/1, polymorphs 58%, lymphocytes 38%, eosinophils 2%, monocytes 2%, platelet count 262 x 10^9/1, ESR 96 mm/hr, serum total proteins 91 g/1, serum albumin 30 g/1, serum globulin 61 g/1 and serum total bilirubin 6.8 umol/1. Chest X-ray and electrocordiogram were normal. Other investigations with normal or negative results included. Latex ASL test, ASOT, Monospot test, cultures of blood and urine, serological tests for arbovirus, toxoplasma, herpes, CMV and other related viruses. Left cervical node biopsy revealed prominent germinal centres and a picture of reactive hyperplasia (fig 1). The patient's temperature returned to normal on the fourth hospital day and on the seventh day he was observed to have desquamation of the finger tips (fig 2). He was discharged and has been well since.

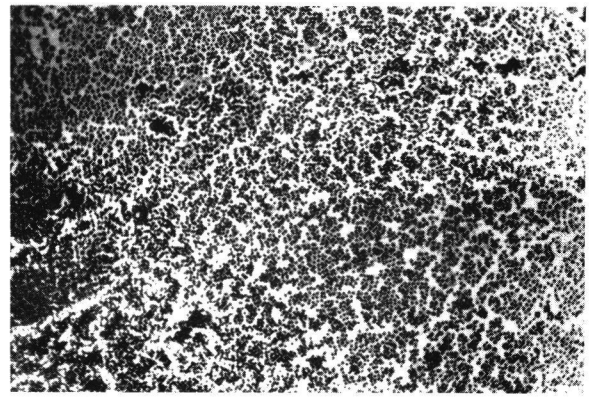

Fig. 1. Left cervical lymph node biopsy revealing reactive hyperplasia

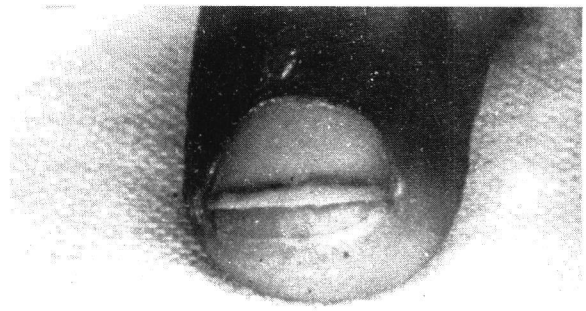

Fig. 2. Desquamation of the finger tip in a case of MLNS

DISCUSSION

The MLNS is an acute febrile mucocutaneous illness which typically begins with high fever lasting one to two weeks unresponsive to antibiotics, conjunctival injection, reddening of the oral cavity, lips, palms and soles, induration and oedema of hands and feet, polymorphous erythematous macular rash involving the trunk, non-suppurative cervical lymphadenitis, desquamation of the finger tips and cardiographic changes (Yamamoto, 1975). Laboratory investigations usually reveal leukocytosis with a shift to the left, mild anaemia, elevated ESR and normal ASOT. Bacterial and viral cultures are unrewarding. The mortality rate is 1.5% (Yanagawa, 1976) and almost all deaths are caused by sudden rupture or thrombosis of aneurysms in the main coronary arteries (Tanaka, 1972). Abnormal electrocardiograms have been recorded in 90% of non-fatal cases (Yanagisawa *et al.*, 1974). There is difficulty in differentiating the underlying thromboarteritis in the MLNS from that seen in infantile periarteritis nodosa making

the distinction between the two disorders unclear (Tanaka *et al.*, 1971). Elevated $\propto 2$ globulin and IgE have been reported in some cases (Kusakawa and Heiner, 1976). The aetiology of MLNS is still unknown. The significance of rickettsia-like bodies which have been visualised by electron microscopy in biopsy specimens of skin and lymph nodes is still uncertain (Hamashima *et al.*, 1973). Aspirin therapy is now considered to have a place in therapy of MLNS for its anti-inflammatory effects and its potential in reducing hypercoagulable states.

Table I summarises the findings in our patients as compared with the diagnostic criteria established by the Research Committee on MLNS of the Japanese Ministry of Health and Welfare (1974). The clinical features of our 3 patients are consistent with the established guidelines.

Table I
Criteria for the diagnosis of MLNS based on the definition proposed by The Research Committee on MLNS of the Japanese Ministry of Health and Welfare

Criteria	Case No.		
	1	2	3
1. Fever lasting 5 or more days unresponsive to antibiotics	+	+	+
2. Bilateral conjunctival injection	+	+	+
3. Redness and fissuring of lips, orosphoryngeal mucosa, strawberry tongue	+	+	+
4. Oedema of extremities, reddening of palms and soles, desquamation of finger tips	+	+	+
5. Polymorphous non vesicular	+	+	+
6. Acute non-suppurative lymph adenopathy	+	+	+
* Absence of other well-known aetiologies	+	+	+

Diagnosis based on meeting at least 5 of the above 6 criteria plus * criteria.

SUMMARY

Mucocutaneous lymph node syndrome (MLNS); a newly recognised disease, widely prevalent in Japan has more recently been recognised in USA, Korea, Hawaii and Greece.

We have recently seen three children, 2 to 5 years of age with MLNS in the University Hospital, Kuala Lumpur which we believe are the first to be recognised in Malaysia. All three cases had the principle features characteristic of MLNS, including myocarditis in one case. The detection of these cases over a 2 year period indicates that MLNS affects children in Malaysia as in Japan and other countries. With increasing awareness more cases undoubtedly will be recognised.

REFERENCES

Hamashima, Y., Kishi, K., Tasaka, K(1973): Rickettsia-like bodies in infantile acute febrile mucocutaneous lymph node syndrome. *Lancet* **ii,** 42.

Japan MCLS Research Committee (1974): Diagnostic guidelines of infantile acute febrile mucocutaneous lymph node syndrome. 2nd ed. Japan Red Cross Central Hospital, Tokyo.

Kawasaki, T. (1967): MCLS: Clinical observation of 50 cases. *Jap. J. Allerg.* **16:** 178-222.

Kawasaki, T., Kosaki, F., Okawa, S. et al (1974): A new infantile acute febrile mucocutaneous lymph node syndrome (MLNS) prevailing in Japan. *Pediatrics* **54:** 271-276.

Kim, J., Yeo, Y., Lee, D.B.; Cited by Kato, H., Koike, S., Yamamoto, M. et al (1975): Coronary aneurysms in infants and young children with acute febrile mucocutaneous lymph node syndrome. *J. Pediatr.* **86:** 892-898.

Kusakawa, S., Heiner, D.C. (1976): Elevated level of immunoglobulin E in the acute febrile mucocutaneous lymph node syndrome. *Pediatr. Res.* **10:** 108-111.

Melish, M., Hicks, R., Larson, E. (1974): Mucocutaneous lymph node syndrome (MCLS) in the US (abstract). *Pediatr. Res.* **8:** 427.

Melish, M.E., Hicks, R.M. and Larson, E.J. (1976): Mucocutaneous lymph node syndrome in the United States. *Am. J. Dis. Child.* **130:** 599-607.

Tanaka, N. (1972): Study for autopsied cases of MCLS (in Japanese) *Acta Paediat. Jap.* **76:** 696-697.

Tanaka, N., Naoe, S., Kawasaki, T. (1971): Pathological study on autopsy cases of mucocutaneous lymph node syndrome in childhood, particularly in relation with periarteritis nodosa-like arteritis. *Med. J. Jap. Red Cross Cent. Hosp.* **1:** 85-91.

Valaes, T. (1975): Mucocutaneous lymph node syndrome (MLNS) in Athens, Greece. *Pediatrics.* **55:** 295.

Yamamoto, K. (1978: The diagnostic guide of MCLS (in Japanese). *Pediatr. Jap.* **16:** 782-783, 1975 cited by Sachiko Hirose and Yoshihiro Hamashima: Morphological observations on the vasculitis in the mucocutaneous lymph node syndrome. *Eur. J. Ped.* **129:** 17-27.

Yanagawa, H. (1976): The epidemiology of MCLS (in Japanese) *Jap. J. Clin. Med.* **34:** 275-283.

Yanagisawa, M., Kobayashi, N., Matsuya, S. (1974): Mycardial infaction due to coronary thromboarteritis, following acute febrile mucocutaneous lymph node syndrome (MLNS) in an infant. *Pediatrics* **54:** 277-281.