KAWASAKI DISEASE

Mats Hanson

Exit acrdynia in the 1950ies. Enter Kawasaki disease or mucocutaneous lymph node syndrome (MLNS) in 1966. The disease was characterized by (Kawasaki et al. 1974)

Principal symptoms:
- Fever, lasting 1-2 weeks, not responding to antibiotics
- Bilateral congestion of ocular conjunctivae
- Changes of lips and oral cavity
- Dryness, redness and fissuring of lips
- Strawberry tongue
- Diffuse reddening of oral and pharyngeal mucosa
- Changes of peripheral extremities
- Reddening of palms and soles
- Indurative edema
- Membranous desquamation from fingertips
- Polymorphous exanthema of body trunc
- Acute nonpurulent swelling of cervical lymph nodes

Other:
- Carditis, esp. myocarditis and pericarditis
- Diarrhea
- Arthralgia or arthritis
- Proteinuria and increase of leukocytes in urine
- Changes in blood tests
  - Leukocytosis
  - Slight decrease of erythrocyte and hemoglobin levels
  - Increased ESR, positive CRP, Increased alpha2-globulin
  - Negative ASLO

Occasional changes:
- Aseptic meningitis
- Mild jaundice or slight increase of serum transaminase

Individual cases do not show all symptoms. The frequency ranged from 75% for lymph node swelling to fever 95% One to two percent of the patients died suddenly of cardiac failure. Autopsies showed infantile periarteritis nodosa-like arteritis accompanied by coronary thrombosis and aneurysm.

Melish (1982) lists associated features and adds more detail: Arthritis is present in 35-40% of patients, usually knees, hips and elbows are involved. Central nervous system effects are seen in nearly all patients. Pronounced irritability and lability of mood are characteristic of the syndrome. Severe lethargy in one third, aseptic meningitis in one quarter of patients. Gastrointestinal manifestations (diarrhea and abdominal pain) also in one quarter. 10% have hepatitis with some elevation of SGOT and SGPT. Peripheral gangrene of fingers and toes occur rarely.

Cardiac disease is discovered in at least 20% of cases. During the acute febrile period, severe tachycardia and gallop rhytm are the most common manifestations. Cardiac aneurysms is present in 17-20 %. More than half of the patients will show resolution of aneurysms within one year. The coronary vessels are likely to remain abnormal even if repaired and recanalized and may result in premature atherosclerosis and/or premature myocardial infarction in later life. The features of fatal Kawasaki's
disease are indistinguishable from what has been known as infantile periarteritis nodosa (Melish, 1982).

After Kawasaki's description of the new disease, Donald Cheek, one of the researchers on acrodynia in the 1950ies and especially interested in the elevated epinephrine (adrenalin) levels, wrote a letter to Pediatrics: Comment on mucocutaneous lymph node syndrome: could it be a heavy metal poisoning? (Cheek, 1975). Kawasaki replied that he thought MLNS could be differentiated from acrodynia clinically and that the mercury concentration measured in the hair of seven patients with MLNS was not significantly different from the hair levels of healthy adult Japanese citizens (Kawasaki, 1975).

The urine mercury levels in six of seven patients with Kawasaki disease was measured by Orlowski & Mercer (1980) and found to be significantly elevated compared to controls (of the same age). A critically ill patient improved after penicillamine treatment. The authors consider both the infant and adult Japanese hair levels to exceed what might be considered normal levels. Comparing the symptoms of MLNS with those of acrodynia, they find fever and coronary artery aneurysm lacking in acrodynia and loss of teeth lacking in MLNS, otherwise the diseases are identical. Orlowski and Mercer did not find coronary arteritis and aneurysms reported from mercury poisonings and suggest that further research in this area seems justified. They also state that historically we know that there is a marked individual susceptibility to mercury which leads to a considerable variation in clinical presentation and course. They also point out that the temporal and geographic relationships between the appearance of MLNS or Kawasaki disease and the Minamata Bay contamination with mercury in Japan is impressive. Also the appearance of MLNS in the United States has paralleled the increasing concern with environmental pollution of natural bodies of water with mercury.

No infectious agent, except possibly Epstein-Barr virus (Barbour et al, 1979), has been implicated in MLNS. Only one substance has been found which is able to produce the syndrome - mercury! Adler et al. (1982) reported a case, diagnosed as MLNS because of the symptoms, which turned out to be caused by mercury brought home by a sibling and scattered throughout the house. It is also an interesting connection that Swedish researchers now find an association between chronic fatigue syndrome, Epstein-Barr virus reactivation and mercury levels in blood cells, originating from amalgam fillings (Lindwall et al., 1988).

A recent 400-page conference report on MLNS did not mention mercury anywhere! (Kawasaki Disease, Progr. in Clin. & Biol. Res. vol. 250 1988).

Consider the hypothetical situation that the Kawasaki disease patients had appeared 30-40 years earlier. What would the diagnosis have been? Undoubtedly acrodynia for everyone. Conversely, a substantial proportion of earlier acrodynia children would have qualified for a MLNS diagnosis.

Fever was usually not reported in acrodynia-cases in England, USA or Australia but did occur. However, in Germany, fever was very common and the poisoning was usually misdiagnosed as scarlet
fever. Since acrodynia manifestations were delayed from days to weeks and even months after the mercury exposure and fever often belonged to the acute reaction after exposure (calomel disease), it should certainly be easy to overlook the connection between the fever period and the acrodynia complication.

The cause of death of acrodynia children, before antibiotics, was usually pneumonia, other infections or unknown. Autopsy cases of MLNS demonstrate heart damage and the apparent cause of death is myocardial infarction due to acute thrombosis of aneurysmally dilated coronary arteries. Surviving children, studied by coronary angiography and echocardiogram, show reversible coronary aneurysms. These tests were not, or not generally available during the acrodynia period.

A short search in the literature reveals at least 50 papers on the damaging effects of mercury to the heart and circulation. The effects on the nervous system are usually dominating the picture but irregular heart and cold hands and feet are often present and noticed by the mercury-exposed person. Note also the high adrenaline levels measured by Cheek (1951) in acrodynia cases and the often very high blood pressure noted in other studies (Peer, 1935). Peer also mentions that some studies found a dilation of the heart. Notably, the heart in experimental mercury poisonings, is almost a mercury sponge (Trachtenberg, 1974; Cuthbert, et al., 1973).

A few mercury-heart papers are included in the reference list (Rieselmann, 1930; Fellinger & Schweitzer, 1938; Barni & Querci, 1961; Granati & Scafo, 1961; Wojciechowski et al., 1974; Tosi et al., 1976; Wrnosi & Hartmann, 1977). Wronski & Harmann describe panarteritis nodosa in a mercury-poisoned dental assistant. Rieselman describes cardiomyopathy in 33% and cardioneuropathy in another 27% of workers exposed to high mercury levels in mines.

Diagnostic criteria might be useful to delineate a disease in order to work out specific treatments. However, they can also block the mind and directly prevent the proper treatment. A suitable approach to MLNS should be to treat the cases with Dimaval (Unithiol, DMPS, 2,3-dimercapto-1-propanesulfonic acid) and measure urinary excretion. If positive, every effort should be directed towards finding the mercury sources. Bell et al (1981), in an extensive epidemiological study, measured heavy metal levels in the domestic water supply, the least likely source. There are many other: broken thermometers, broken fluorescent lights, amalgam fillings in adolescents and adults, hygiene and household products, non-prescription medications with insufficient declaration of contents, paints etc.

References:


Wronski, R. & Hartmann, F. Ueber eine besondere Verlaufsform der Panarteritis nodosa bei chronisch-schleichenmder