Cat Scratch Disease

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MIURA, T., TORINUKI, W. and TANAHASHI, Y. Cat scratch disease. Tohoku J. exp. Med., 1975, 117 (4), 373-380 — Cat scratch disease developed on a 40-year-old wife was reported. Umbilicated papules closely resembling those in herpetic skin infection developed on the areas which had been scratched by a cat a week ago. Obtained findings in the present case led us to a speculation that this disease was caused by herpes virus. 72 cases of this disease have been reported in Japan, and they were reviewed in the present paper. ——— cat scratch disease: primary skin lesion

Cat scratch disease is a recognized clinical entity characterized by non-bacterial lymphadenopathy with or without primary skin lesions developed after being scratched by a cat. Since the first presentation of this disease in 1950 by Debré, over 1000 cases have been reported in the literature during recent 25 years. Warwick summarized over 550 items including scientific articles, case reports and editorials in 1967, Margileth collected 145 patients from the literature in 1968, and Carithers et al. summarized 152 patients seen in a pediatric practice between October 1965 and May 1968. In Japan, 72 cases have been reported so far since the first description by Hamaguchi and Nagano in 1953.

Discussions have been made by many investigators not only on clinical characteristics but also on the causative agent of this disease. In general, pathogenesis of the disease is considered that an unknown agent, possibly a kind of virus, invades the body through scratched area and causes regional lymphadenitis with general symptoms as fever, fatigue, and so on, although the agent has not been identified yet.

The majority of patients recognize lymphadenopathy at first without noticing previous contact with cat and then consult with a surgeon or internist complaining of enlarged lymph nodes, during which inoculated sites may become obscure. Little has been known about primary skin lesions in this disease.

The present patient consulted our out-patient-clinic complaining of skin lesions consisted of umbilicated papules with fever which developed a week after she had been scratched by a cat. Details of the patient are presented and cases reported in Japan are reviewed.

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A 40-year-old house-wife consulted with the Department of Dermatology, Tohoku University School of Medicine, Sendai, on 19th November, 1974, complaining of several umbilicated papules on the left shoulder, left forearm, and both legs. According to her, she and other 7 members of her family had sometimes been scratched by her pet, a Siamese cat, in the past, but the wounds used to be healed up within a few days. However, several new eruptions have developed this time on the areas that had been scratched by the cat a week ago. Moreover, she got accidentally a scratched wound by a zipper of a mat on the left forearm about a week ago, and similar eruptions have developed on that area. She has been healthy, and no contact with other animals was revealed. There was no one suffering from herpetic infection in the family. She did not notice any swelling of lymph node at the time of visit except for a slight fever and skin lesions.

Physical examinations revealed her body temperature was 37.1°C. On the left shoulder, three finger-tip-sized reddish papules were arranged in a linear fashion, and each center of them was depressed and covered with crust (Fig. 1). On the left forearm, several umbilicated papules were grouped and coalesced each other to form a key-shaped plaque covered with blood crust (Fig. 2). Several other umbilicated pustules or vesicles of rice-grain-size were scattered with erythematous halos on the left hand, trunk, right forearm, back of right hand, and both legs. Two lymph nodes of little-finger-tip size were palpable; one in the left retroauricular and the other in the left axillary region.

Laboratory examinations revealed no abnormality in urine, blood, and serum protein. ASLO titer, CRP and RA reactions were normal, Wasserman's reaction was negative. Paul-Bunnel's reaction was negative. No bacteria nor fungus was cultured from pus obtained from pustules. Materials obtained from pustules and
nails of the cat were separately inoculated to monkey kidney cells, and subcultures were repeated. No virus was obtained from any of them. Complement fixation tests were carried out between patient's sera and herpes- and chlamydia-antigens at various different periods of time according to Kolmer's method at the Tokyo Special Reference Laboratory, Tokyo (Table 1). The results showed that antibody titers to herpes zoster antigen were higher than those to herpes simplex antigen, and that no antibody was revealed to psittacosis antigen. Histopathology of the pustule showed a ballooning degeneration of epidermal cells which resulted in reticular degeneration of the epidermis and an abscess formation in the dermis consisting mainly of lymphocytes and histiocytes (Fig. 3). Electron microscopic examination of the pustule revealed that there was a dense distribution of fine granules about 25 nm in diameter in the cytoplasm of infiltrated neutrophils in the abscess (Figs. 4 and 5). PAS staining was negative. Minomycin, a derivative of tetracycline, of 200 mg of daily dose was given for successive 10 days, and the swelling of lymph node has disappeared within a week after administration. The

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**TABLE 1. Serum antibody titers**

<table>
<thead>
<tr>
<th>Antigens</th>
<th>Date of examination</th>
<th>Normal Japanese*</th>
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<tbody>
<tr>
<td></td>
<td>20 Nov. 26 Nov. 4 Dec. 25 Dec.</td>
<td></td>
</tr>
<tr>
<td>Herpes simplex</td>
<td>× 8 × 8 × 8 × 8</td>
<td>× 8 (20–320)</td>
</tr>
<tr>
<td>Herpes zoster</td>
<td>× 32 × 32 × 32 × 32</td>
<td>× 8 (20–320)</td>
</tr>
<tr>
<td>Psittacosis</td>
<td>&lt;× 5 &lt;× 5 &lt;× 5 &lt;× 5</td>
<td>&lt;× 5</td>
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* Mean value and range observed in normal Japanese subjects of 30 to 50 years of age.
umbilicated papules and pustules showed a slow disappearance during the course, but several new pustules developed scattering on the chest a few days after administration without any complaints. All lesions healed up 2 weeks after the first examination.
Seventy-two cases, including the present one, have been reported in the literature. 69 cases were Japanese and 3 were foreigners. 35 cases were male (49%) and 28 female (39%). Sexes of remaining 9 cases were not described in the reports. The disease most frequently occurred in younger ages of under 30, particularly in those from 11 to 20 years (Fig. 6), and in summer and autumn (Fig. 7). Contact with cat was observed in 48 cases of all (67%), and the syndrome developed 1 to 4 weeks after scratched by cat in the majority of them (Fig. 8). In 7 cases it developed after they had been bitten by a cat. The scratched areas were revealed in 40 cases (56%), and they located on hands and fingers (57%), face (18%), arms (13%), legs (8%), and chest (5%). Primary skin lesions were observed in 36 cases (50%); scar in 14, papule in 6, erythema with pustule and swelling in 6, induration in 4, bitten wound in 2, linearly demarcated lesion in 2, and granulomatous induration in 1 case. No characteristic umbilicated papules have been observed except for the present one. Regional lymphadenopathy was common in axillary (54%), cubital (22%), neck and mandibular (14%), and inguinal (10%) regions. Histopathology of the enlarged lymph node was examined in 40 cases of
patients (56%), and a typical granulomatous reaction with necrosis was observed in 33 cases of them (83%). A purulent inflammatory reaction was observed in 7 cases. The specific skin test was examined in 25 cases of patients (35%), and positive reaction was obtained in 21 cases of them (84%). Serum antibody titers to turalemia, psittacosis, and lymphogranuloma antigens were examined in 4 cases; results being within normal ranges. Paul-Bunnel’s reaction was negative in 2 cases. General symptoms such as fever, malasia and so on, were noted in the majority of patients, and high fever was observed in 23 cases of all (32%). A severe headache and vomiting developed in 1 case combined with hepatosplenomegaly. Antibiotics of various kinds were given in 31 cases of patients, but their effectiveness was uncertain. Incision and discharge of pus from the enlarged lymph node or total extirpation of the node gave a good result in 9 cases. Spontaneous remission was confirmed in 3 cases. Steroid hormone was given by mouth in 3 cases.

**DISCUSSION**

For criteria for diagnosing the cat scratch disease Warwick (1967) described that the diagnosis could be made when 3 of the following 4 criteria were found in a patient; 1) a positive skin test to specific Hanger-Rose antigen, 2) negative laboratory studies for other causes of lymphadenopathy, 3) history of cat scratch, and 4) characteristic histopathology of a biopsied lymph node. Carithers et al. (1969) mentioned the following 5 points; 1) lymphadenitis, 2) positive skin test reaction with an antigen specific for this disease, 3) presence of an identifiable inoculation site, 4) history of contact with a cat, and 5) absence of other disease. They particularly emphasized that the skin test would be one of the most important criteria for diagnosing the disease. For example, Warwick (1967) reported that about 90% of clinically diagnosed cases could be confirmed with the skin test, and Margileth (1968) also emphasized that 94% of patients gave positive skin tests; the rate being so high. In the present review of cases in Japan, however, the skin test was examined only in 35% of reported cases, and positive reaction was obtained in 84% of them. Histopathology of the enlarged lymph node, on the other hand,
was examined in 56% of cases and a typical finding was obtained in 83% of them. So it seems likely that the diagnosis of cases in Japan was mainly based upon either histopathology of enlarged lymph nodes or previous history of the contact with cat; the latter was revealed in 67% of cases. In the present case, difficulty of getting the specific antigen made us impossible to examine the skin test; enlarged lymph nodes were too small in their sizes to get the specific antigen, and they so rapidly disappeared within a week that histologic examination was not carried out. The present case, however, can be considered to belong to the category of this disease because of the followings; 1) primary skin lesions developed 1 week after scratched by a cat. 2) regional lymphadenopathy with general fever, and 3) negative laboratory data for other causes of lymphadenopathy. And also the following facts observed in the present case may lead us to speculate that this disease might be caused by herpes virus: 1) Primary skin lesions had an umbilicated appearance which is typical to that in herpetic skin lesions. 2) Lesions developed not only on the areas where scratched by the cat but also where injured by a zipper of a mat with a similar incubation time. 3) Histology of the eruption showed balloononing and reticular degenerations of the epidermis. 4) Serum antibody titer was higher to herpes virus antigen than to psittacosis antigen. Repeated subcultivations of materials obtained from the lesion and of nails of the cat yielded no virus. This speculation therefore could not be confirmed. Electron microscopic observation failed to demonstrate herpes-like particles in the cytoplasm of an infiltrated neutrophil in the dermis. Kalter et al. (1969) reported that round particles, about 100 nm in diameter, were densely distributed in the lymph node tissue of this disease. In the present case, small round particles, about 25 nm in diameter, were revealed scattering in the cytoplasm as shown in Fig. 5. These could not be considered as glycogen granules because PAS staining was negative. Since the negative staining examination for these particles was not carried out, their nature still remains uncertain.

In the present review, primary skin lesions were observed in 50% of the cases. The rate was roughly equal to that reported by Margileth (1968) but was lower than that by Carithers et al. (1969); the latter being 96%. In the literature, scars, papules, and indurations were commonly described, but there were no cases of umbilicated papules as shown in the present one. Biopsies of skin lesions also have received little attention. Johnson and Helwig (1969) reported that histopathologic changes in the skin lesions in this disease were equivalent to those in the lymph nodes which consisted of a central acellular zone of necrosis surrounded by histiocytes, giant cells, and a mantle of lymphocytes. In the present review, there was one report in addition to the present one concerned with histology of the skin lesions. Urabe and Yasumoto (1964) described that typical granulomatous changes were observed in biopsied skin lesions. In the present case, as described above, observed findings were not similar to the afore-said ones but to those in herpetic skin infection.

The sex distribution in the present review was roughly equal to both sexes,
this was also mentioned in the report by Margileth (1968). The disease was most common in younger ages of 11 to 20 years and in summer and autumn in Japan. Warwick (1967) and Margileth (1968) also stated that the disease was more common in children, 80% of the patients being under 20 years of age, and that it was common in late fall and in early winter. In the present review, the disease developed in 7 cases after they had been bitten by a cat. In the report by Margileth (1968), there were found 2 cases caused by dog bite, but no cases by cat bite in the literature. Atypical clinical features were observed in 3 cases in Japan, which consisted of encephalitis-like symptoms with abnormal findings in the spinal fluid, leucemoid reaction with hepatosplenomegalgy, and purpura. Carithers et al. (1969) summarized atypical cases in which encephalitis or purpuric lesions developed. It may be correct to say that there was no effective management for this disease. Antibiotics seemed to be uneffective, and incision of enlarged lymph nodes and discharge of pus looked like the best for the management.

Acknowledgment

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References