Suid-Afrikaanse Tydskrif vir Geneeskunde : South African Medical Journal

Kaapstad, 11 Junie 1960 Deel 34 No. 24 Volume 34 Cape Town, 11 June 1960

CAT-SCRATCH DISEASE

JAMES MARSHALL, M.D., *Department of Dermatology, University of Stellenbosch*

Cat-scratch disease (*maladie des griffes de chat*, benign lymphoreticulosis) was first described as a clinical entity by Debré *et al.*[1,2] in 1950 and is characterized chiefly by lymphadenitis. The original cases were encountered in France and in the USA (by Foshay), but the disease is now known to occur in most parts of the world.

The majority of cases occur in children or young people, most of whom give a history of having been scratched or bitten by a cat. In the common variety of cat-scratch disease the incubation period between contact and the appearance of skin lesions (not always present) is from 3 to 14 days. The primary lesion is not characteristic and may be an inflamed scratch, an erythematous or even necrotic papule, or an impetigo-like patch. After 1 - 3 weeks the regional lymph glands enlarge to as much as 3 or 4 cm. in diameter and may soften and discharge sterile pus through the skin. Fever, malaise, generalized lymphadenitis and enlargement of the spleen may occur. In the early stages there may be fleeting generalized erythematous macular or papular eruptions, and erythema nodosum has often been noted. The course of the disease is towards spontaneous healing after from 4 days to as long as 6 months. Although cat-scratch disease usually occurs sporadically it is sometimes encountered in little epidemics within a family.

The pathological changes in the skin and lymph glands are suggestive without being diagnostic. The skin lesion is a granuloma with central necrosis. The earliest change in the lymph glands is a proliferation of reticulum cells and lymphocytes in the interfollicular medullary tissue.[3] This is followed by the establishment of a vascularized area of reticulum-cell proliferation surrounded by a limiting zone of lymphoid cells. Next appear micro-abscesses consisting of an aggregate of polymorphonuclear leukocytes in the centre of reticulum cells. Finally there appear foci of fibrinoid necrosis in which are nuclear debris and pyknotic cells. The necrotic areas are bounded by a mantle of proliferating reticulum cells around which is a zone of lymphoid cells. The structure of the gland is preserved, but there is a generalized infiltrate of plasma cells and histiocytes. The germinal follicles show evidence of inflammatory stimulation and there is slight sinus catarrh. Blank *et al.*[4] note that giant cells may be found in the region of the focal lesions and that there may be an appearance suggesting tubercle formation.

Confirmation of the diagnosis of cat-scratch disease is obtained by a skin test using Tyndallized pus or other lymph-gland material. Intradermal inoculation of 0·1 ml. of the antigen evokes, usually within 48 hours, a papule 5 - 15 mm. in diameter, sometimes with central necrosis and a halo of erythema; skin sensitivity persists for months or years after an attack.

Although several hundred cases have been discovered since 1950 only 1 has been reported in South Africa.[3] Prof. James Murray kindly searched the records of the South African Institute for Medical Research, in Johannesburg, and informs me that a tentative diagnosis of cat-scratch disease has been made in 13 cases since 1956; in only 2 or 3 cases had a skin test been carried out.

Case Report

A White man, aged 25 years, presented with an eruption on the left side of the forehead which had been present for 3 days. There were 3 little elevated, erythematous, succulent-looking plaques about 10 mm. in diameter, one studded with tiny vesicles, in a horizontal line above the left eyebrow. The left pre-auricular lymph gland was visibly enlarged and slightly tender. Five days later the skin lesions, treated with aureomycin ointment, were unchanged, but there was a discrete, tender enlargement of the lymph glands, to as large as 2 cm., in the anterior and posterior triangles of the left side of the neck and in both axillae. There were no general symptoms and the spleen was not enlarged.

The glands in the axillae subsided after 1 week, those in the neck after 2 weeks, without any systemic treatment. The skin lesions healed in 2 weeks leaving obvious pock marks.

Cat-scratch disease was suspected when the regional and axillary glands became enlarged, and the patient recalled that he had allowed a cat to clamber about his shoulders a week before the skin lesions appeared; he had not been clawed or bitten. Gland biopsy was not permitted. A supply of cat-scratch antigen was obtained from the Virus Reference Laboratory, London, and an intradermal injection of 0·1 ml. was given 6 weeks after all signs had disappeared. No reaction was apparent after 2 days. The patient departed on holiday, but reported that on the 6th day there had appeared a red swelling about 10 mm. in diameter, and when he was seen on the 16th day there was an infiltrated, pink papule 6 mm. in diameter. The papule finally disappeared after a month.

DISCUSSION

The Clinical Syndromes

In the typical case there is regional enlargement of lymph glands, sometimes accompanied by generalized lymphadenopathy. A primary lesion or the remains of cat scratches or bites may be found. Any gland group may be affected, but those draining the arms suffer oftenest. Suppuration occurs in about 30% of cases; persistent draining sinuses are rare. Hodgkin's disease, tuberculous adenitis, sarcoidosis, lymphogranuloma venereum, infectious mononucleosis, and tularæmia must be considered in the differential diagnosis.

When the inguinal glands are involved (pseudo-venereal type) the picture may be clinically indistinguishable from that of lymphogranuloma venereum.

Cat-scratch disease is one of the causes of Parinaud's oculoglandular syndrome of conjunctivitis and enlargement of the homolateral pre-auricular lymph gland.[5] The common causes for this syndrome are leptotrichosis, tularæmia, and tuberculosis; rarer causes are syphilis, lymphogranuloma

venereum, sarcoidosis, glanders, Newcastle virus infection, sporotrichosis, and rhinosporidiosis.

In the pharyngeal, or anginal, syndrome it appears that the infection occurs through the nasopharynx.

The mesenteric glands may be involved and give symptoms suggestive of appendicitis, and in a thoracic syndrome enlargement of the mediastinal glands and atypical pneumonia have been described.

Involvement of the nervous system may accompany a glandular syndrome, with symptoms indicative of encephalitis, myelitis, meningitis, or neuritis, e.g., convulsive crises, coma, pains of the causalgia type, and diminution of the reflexes and of muscular power.[6]

The disease is preceded in over 80% of cases in most reported series by cat scratches or bites or by simple contact with the animal. The animal concerned is usually perfectly healthy and intradermal tests with human antigens are invariably negative. It seems likely that the cat is simply a mechanical carrier of the cause of the disease from some other source in nature, and that it is infectious for only a few days or weeks. In cases where the cat cannot be incriminated there may be a history of excoriation by thorns, bones, wood or metal objects, or of insect bites, and it is probable that the causative agent is widespread in nature.

Attempts have been made to transmit cat-scratch disease to a variety of animals, but only some monkeys are susceptible. The disease in monkeys is similar to that in man. Mollaret *et al.*[7-12] discovered granulocorpuscles in the cytoplasm of reticulum and plasma cells in early lesions in monkey lymph glands and state that similar inclusions can be found, with difficulty, in human lymph glands. Winship,[13] however, points out that such inclusions can be found in lymph glands in a variety of diseases.

The cause of cat-scratch disease has not been isolated, but Mollaret *et al.*[7-12] believe it to belong to the lymphogranuloma venereum and psittacosis group of micro-organisms. The basis for this theory is the pathological picture, the finding of intracellular inclusions in lesions in man and experimental animals, and the occurrence in some cases of positive complement-fixation tests with lygranum (lymphogranuloma-venereum antigen). The cross-reaction with lygranum has not always been confirmed by other observers, and Armstrong *et al.*[14] believe that the positive reactions which occur in a minority of cases are related to the age of the patient, are of no diagnostic value, and cannot be interpreted as evidence that cat-scratch disease belongs to the lymphogranuloma venereum and psittacosis group. Manning and Reid[15] found that the incidence of positive complement-fixation tests to psittacosis antigen was 23% in 35 patients with positive cat-scratch skin tests and 60% in 10 cases with a histological diagnosis of cat-scratch disease; in a control series of normal blood donors the incidence of positives was 2%.

The skin test with cat-scratch antigen appears to be the most reliable method of confirming a clinical diagnosis. It is almost always positive during and for long after an attack. Performance of the test may reactivate healing or apparently healed lesions even when there is no local reaction to the injection. In a few typical cases the test has been negative, suggesting that more than one agent or type of agent may be involved. The incidence of positive skin tests in normal controls has been investigated. Bettley and Fairburn,[16] in a series of 40 cases, found that 3, who had contact with cats, gave positive reactions. Hunziker[17] found 2 positive reactors in a series of 50; both gave a history of adenopathy which might have been cat-scratch disease. Gifford[18] performed skin tests on 28 veterinary surgeons and found 7 who gave a positive reaction; only 1 had had the disease. It seems likely that positive reactions in normal controls may often indicate past inapparent infection. The Frei skin test for lymphogranuloma venereum is invariably negative in cases of cat-scratch disease. It is probable that cat-scratch antigen, like lymphogranuloma-venereum antigen, causes a reaction in subjects immunized by infection by virtue of its containing a specific component, in contradistinction to the non-specific reactions caused by lepromin[19] or Kveim[20] antigen, which are perhaps only foreign-body reactions that can be evoked in certain individuals or disease states.

Cat-scratch disease, particularly in its minor forms, must occur much more frequently than the records suggest, and it should be remembered when any case of inexplicable lymph-adenopathy is under investigation. A history of contact with cats and the histological picture in the lymph glands may suggest the diagnosis, but confirmation should be obtained by performance of the skin test.

Claims are often made that aureomycin or some other antibiotic has hastened cure, but the assessment of the value of therapy is obviously difficult in a disease which often subsides spontaneously in a few weeks.

SUMMARY

A case of cat-scratch disease in its typical form is reported. The literature is reviewed, and the various clinical syndromes that may occur and the conditions they may simulate are described.

Dr. Patricia Bradstreet, Director of the Standards Laboratory, Central Public Health Laboratory, London, kindly supplied the cat-scratch antigen.

REFERENCES

1. Debré, R., Lamy, M., Jammet, M. L., Costil, L. and Mozziconacci, P. (1950): Bull. Soc. Méd. Hôp. Paris, **66**, 76.
2. *Idem* (1950): Sem. Hôp. Paris, **26**, 1895.
3. Dreosti, A. E. and Murray, J. F. (1953): S. Afr. Med. J., **27**, 81.
4. Blank, H. and Rake, G. (1955): *Viral and Rickettsial Diseases of the Skin Eye and Mucous Membranes of Man*. London: Churchill.
5. Levitt, J. M. (1957): J. Amer. Med. Assoc., **165**, 1955.
6. Debré, R. and Job, J. C. (1954): Acta paediat. (Uppsala), **43**, suppl. 96.
7. Mollaret, P., Reilly, J., Bastin, R. and Tournier, P. (1950): Bull. Soc. Méd. Hôp. Paris, **66**, 423.
8. *Idem* (1950): *Ibid.*, **66**, 687.
9. *Idem* (1950): Presse méd., **58**, 282.
10. *Idem* (1950): *Ibid.*, **58**, 1353.
11. *Idem* (1951): *Ibid.*, **59**, 681.
12. *Idem* (1951): *Ibid.*, **59**, 701.
13. Winship, T. (1953): Amer. J. Clin. Path., **23**, 1012.
14. Armstrong, C., Daniels, W. B. MacMurray, F. G. and Turner, H. C. (1956): J. Amer. Med. Assoc., **161**, 149.
15. Manning, J. D. and Reid, J. D. (1958): Amer. J. Clin. Path., **29**, 430.
16. Bettley, F. R. and Fairburn, E. (1953): Lancet, **1**, 520.
17. Hunziker, N. (1958): Acta allerg. (Kbh.), **12**, 311.
18. Gifford, H. (1955): Ann. Intern. Med., **95**, 828.
19. Kooij, R. and Gerritsen, T. (1956): Int. J. Leprosy, **24**, 171.
20. Kooij, R. (1958): Dermatologica (Basel), **117**, 336.