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Cervical Cat Scratch Disease Lymphadenitis in a Patient with Immunoglobulin M Antibodies to *Toxoplasma gondii*

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We report on a young patient with chronic cervical lymphadenopathy and serological and histological evidence for infection with *Bartonella henselae* and *Toxoplasma gondii*. Serological follow-up studies, including testing for avidity of *Toxoplasma*-specific immunoglobulin G antibodies, assisted in the determination of the cause of the acute lymphadenitis. Our results suggest that the clinical symptoms were most likely due to cat scratch disease rather than to acute toxoplasmosis.

Cervical lymphadenitis is a common syndrome in children and young adults that might be caused by infectious or noninfectious agents (6, 8). Among the infectious agents, *Toxoplasma gondii* and *Bartonella henselae* share the unique property that they are usually transmitted to humans by the domestic cat. Cat scratch disease (CSD) is the most common cause of regional, unilateral adenitis in children and adolescents (4). Prior to the identification of *B. henselae* as the main etiologic agent of CSD, the diagnosis was based upon typical clinical and histological findings in the absence of other agents of infectious lymphadenitis, including *T. gondii* (4, 11).

In this paper, we report on a cat owner with chronic cervical lymphadenopathy and histological and serological evidence for infection with both *B. henselae* and *T. gondii*. We performed a battery of additional tests and serological follow-up studies in order to determine the actual cause of lymphadenitis in this patient.

A 27-year-old, previously healthy man was admitted to the laryngorhinootological department of university hospital by a laryngorhinootology specialist for evaluation of chronic cervical lymphadenopathy of approximately 5 weeks' duration. He had been treated with cefpodoxime-proxetil (400 mg/day, taken orally) for 1 week prior to admission without success. Subsequently, magnetic resonance imaging of his neck revealed one enlarged (28- by 40-mm) lymph node in the left submandibular region and several enlarged nodes (<30 mm in diameter) in the left submandibular and supraclavicular regions. It was suggested that mediastinal lymph nodes may also be involved, and the patient was referred to the hospital in order to exclude the possibility of a malignancy.

On admission, the patient was afebrile. Physical evaluation revealed a painless and tender lymph node with a size of approximately 2 by 4 cm in the left submandibular region and two to three smaller nodes in the left supraclavicular region, but otherwise the findings were normal. He had no history of fever or sweating. He owned a 5-year-old pet cat, which he had acquired a couple of years earlier from an animal asylum, and had frequently been scratched and bitten by it. Routine laboratory tests, including complete blood count, blood chemistry exam, and liver enzyme check, were normal. On day 1 after admission, panendoscopy of the aerodigestive tract was performed and revealed no pathological findings. On surgical extirpation, the submandibular lymph node was very tender and erupted spontaneously, revealing pus. The node was subjected to histological examination.

Histological evaluation of the lymph node revealed stellate granulomas with partial central necrosis (Fig. 1a), reactive follicular hyperplasia, aggregates of monocytoid B cells, clusters of epithelioid histiocytes, and microabscesses. While granuloma and microabscess formation were suggestive of CSD, the other histological findings were also consistent with toxoplasmic lymphadenitis. Warthin-Starry staining was subsequently performed, and revealed small pleomorphic bacilli, some of which were in the areas of necrosis and in histiocytes (Fig. 1b).

On day 1 after admission, serological evaluations for toxoplasmosis, syphilis, and human immunodeficiency virus were initiated; on day 3 serological tests for cytomegalovirus, Epstein-Barr virus, *Chlamydia trachomatis*, *Mycoplasma pneumoniae*, and toxoplasmosis (repeat test) were performed. Immunoglobulin M (IgM) and IgG antibodies to *T. gondii* were detected on day 1 and confirmed 2 days later by enzyme-linked immunosorbent assay (ELISA) (Biomerieux, Marcy l'Etoile, France) and indirect immunofluorescence assay (IFA) (Biomerieux). The results of *T. gondii*-specific tests (day 1) are presented in Table 1. All other serological tests were negative or unremarkable. The tuberculin skin test was negative. The patient recovered rapidly after surgery, was discharged after 5 days of hospitalization, and did well thereafter.

After the patient was discharged, serological tests for *B. henselae* were performed in light of the histological findings indicative of CSD. *Bartonella*-specific IFA (MRL Diagnostics, Cypress, Calif.) was performed and revealed an elevated IgG titer of 256 (Table 1). In addition, *B. henselae* (*B. henselae* Berlin-2, as confirmed by partial sequencing of the 16S rRNA gene [2]) was isolated from a blood culture performed at the time of discharge on the patient's pet cat. Serological follow-up

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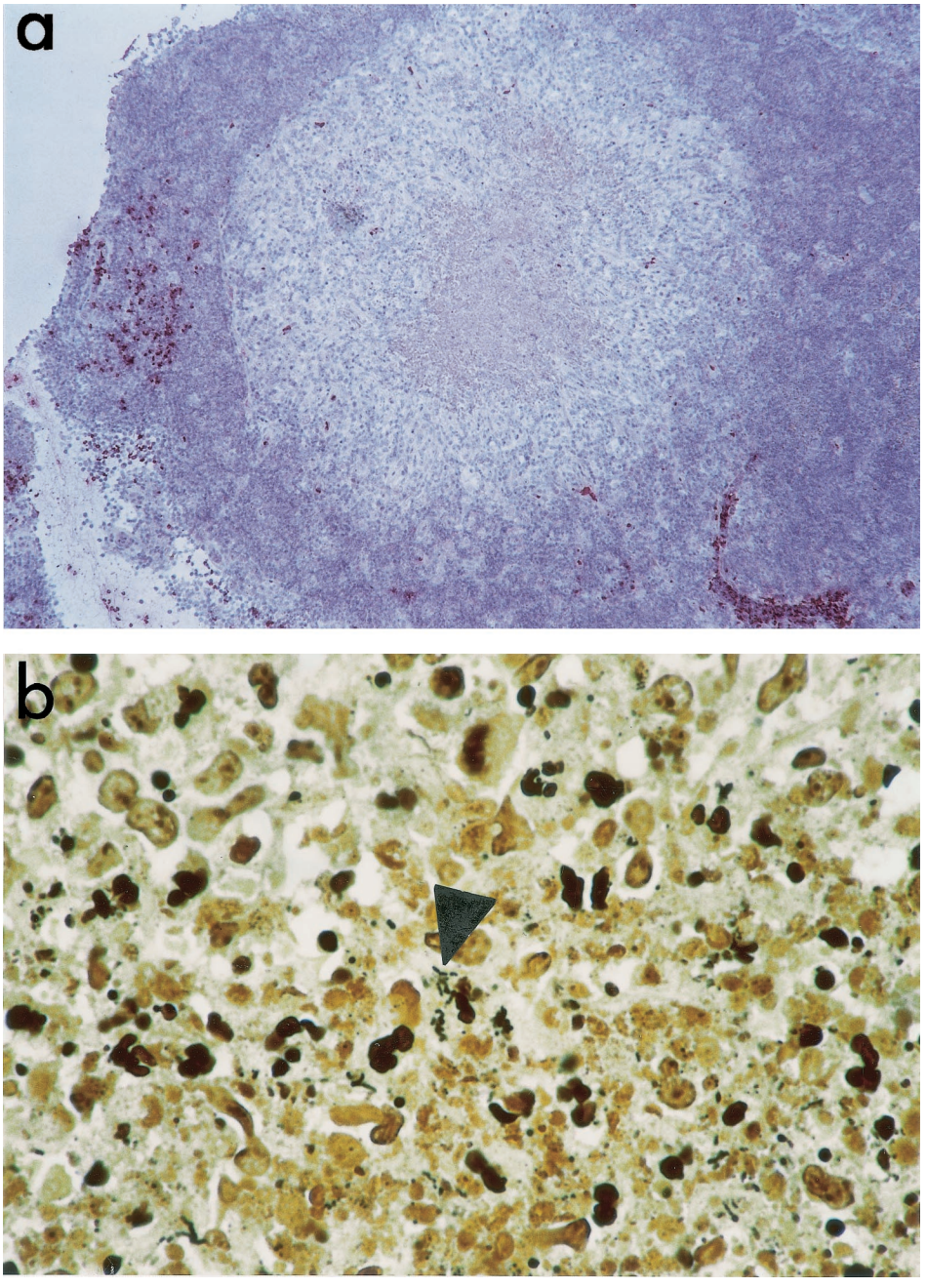

FIG. 1. Histopathological findings in the submandibular lymph node. (a) Round granuloma with central caseation (hematoxylin and eosin stain). Magnification, ×250. (b) Small aggregate of pleomorphic bacilli (arrowhead) (Warthin-Starry stain). Magnification, ×400.

tests were performed at 4 and 13 months after discharge but did not reveal significant changes in anti-*T. gondii*-specific IgM and IgG antibody titers (sera were run in parallel). In contrast, a significant decrease in *Bartonella*-specific antibody titers was found after 13 months (Table 1). Furthermore, a test for avidity of *Toxoplasma*-specific IgG antibodies (VIDAS Toxo IgG avidity test; Biomerieux) performed retrospectively on a serum sample obtained on day 1 after admission revealed the presence of high-avidity antibodies. The avidity index was 54%, indicating that toxoplasmosis had been acquired in the past (≥4 months prior to admission).

The case described here raises two important issues with regard to the diagnostic management of patients with cervical lymphadenitis. First, despite the fact that the patient presented with clinical signs and a history compatible with CSD, *B. henselae* was not included in the initial diagnostic evaluation. Thus, it appears that the awareness of clinicians about CSD has to be increased further. This is especially important since specific serological tests to confirm the diagnosis have recently become available. In our patient, the diagnosis of CSD was first suggested by the typical histological findings, including the presence of pleomorphic bacilli in the lymph node specimen.

TABLE 1. Results of serological tests for *B. henselae*- and *T. gondii*-specific antibodies

Time after admission	Result of:			
	Anti-*T. gondii* IgG ELISA (IU/ml)	Anti-*T. gondii* IgM ELISA (index)	*T. gondii*-specific IFA (titer[a])	*B. henselae*-specific IFA (titer[a])
1 day	600	0.90	256	ND[b]
1 wk	480	0.96	256	256
4 mo	448	0.95	256	128
13 mo	368	0.83	256	32

[a] Cutoff, 64.
[b] ND, not done.

The diagnosis was then confirmed by serological tests. The *Bartonella*-specific IgG antibody titer was elevated at the time of admission and decreased significantly (eightfold) within 13 months. Furthermore, *B. henselae* could be isolated from the blood of the patient's pet cat. In a recent study, we determined the prevalence of *B. henselae* bacteremia in pet cats from Berlin and found a very low prevalence (1%) in this population (1). Therefore, we suggest that *B. henselae* strain Berlin-2, which was isolated from the blood culture of our patient's pet cat, is most likely the causative agent of CSD in this patient.

Second, *T. gondii*-specific IgM and IgG antibodies were detectable at the time of admission. However, testing for *T. gondii*-specific IgG antibody avidity, performed retrospectively on a serum sample obtained at day 1 after admission, revealed the presence of high-avidity antibodies, consistent with an infection acquired at least 4 months prior to admission (7). In addition, serological follow-up tests did not reveal significant changes in *T. gondii*-specific antibody titers, and positive titers in IgM ELISA have been reported as late as 8 months after the onset of clinical manifestations (3, 10). We cannot completely exclude the possibility that infection with *T. gondii* (which may have been acquired as much as 4 to 6 months prior to admission) may have contributed to the clinical presentation of this patient. In this regard, symptoms of toxoplasmic lymphadenitis have been reported to wax and wane and even persist for 1 year or longer (3). However, the serological results indicate that the infection had most likely been acquired more than 4 months prior to admission. Since the onset of lymphadenitis occurred approximately 5 weeks prior to admission, acute toxoplasmosis is unlikely to be the cause of the need to hospitalize our patient.

To our knowledge, this is the second case report on a patient with chronic regional lymphadenitis with serologic and anamnestic evidence of toxoplasmosis and CSD. However, in the first case, which was reported in 1974, serological evaluation of CSD was performed by using a complement fixation test to detect *Chlamydia*-specific antibodies (5). Those authors suggested that the elevated levels of *Chlamydia*-specific antibodies in their patient were linked to CSD (5). Interestingly, serological cross-reactions between *Chlamydia*- and *Bartonella*-specific antibodies have also been reported more recently (9). A detailed study of the cross-reactivity of *B. henselae*- and *T. gondii*-specific antibodies has not yet been performed; however, since *B. henselae*-specific antibody titers decreased and *T. gondii*-specific antibody titers remained constant, cross-reactivity of these antibodies most likely did not play a major role in our patient samples.

In conclusion, this report represents a case of serologically confirmed CSD lymphadenitis in a patient with IgM antibodies to *T. gondii*. Follow-up studies and avidity testing for *Toxoplasma*-specific IgG antibodies were most helpful to (i) establish the diagnosis of acute infection with *B. henselae* and (ii) exclude recent infection with *T. gondii*. Evaluation of patients with regional lymphadenitis should include thorough serological testing for *B. henselae* and *T. gondii*.

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