Encephalitis in cat scratch disease with persistent dementia

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Abstract

Encephalitis in cat scratch disease is uncommon and usually reversible. The patient with cognitive impairment and severe memory disorder did not improve after a 30 month follow up. MRI revealed disseminated lesions in the white matter of the cerebral hemispheres.

Cat scratch disease (CSD) or benign inoculation lymphoreticulosis was first recognised in 1932¹ and described in France in 1950.^{2,3} The disease is uncommon and is characterised by subacute and often suppurating lymphadenitis, occurring a few days after a cat scratch or bite. Incidence of neurological complications is low, ranging from 1-3%.^{4,5} About 60 such cases have been documented, mainly presenting as acute encephalitis.^{5,6} The benign course of encephalitis has been emphasised, but we present an MRI documented case characterised by severe neurobehavioural results.

Case report

A 47 year old engine driver was admitted to hospital in January 1988 for mental confusion and headache of recent onset. On admission, he presented a grand mal seizure with post-ictal coma. Examination noted pyramidal syndrome with bilateral Babinski's sign and intermittent decerebrate posturing but no meningism. His temperature was 39° C. An inflamed right epitrochlear lymph node and small ipsilateral axillary and cervical nodes were found. These nodes had appeared one month earlier with weakness, three weeks after the patient had had his right hand bitten by a kitten. His white cell count was $15 \times 10^9/l$ with $14 \times 10^9/l$ polymorphonuclear leucocytes and 450 lymphocytes. His cerebrospinal fluid (CSF) was clear, with a normal pressure; protein content was 0.53 g/l, without cells, and normal glucose concentration. Initial treatment consisted of penicillin, tetracyclin, sulfamethoxazol-trimethoprim, and acyclovir.

He regained consciousness four days later and remained confused and agitated for a few more days. Since then, neurological examination has been normal, apart from a severe intellectual deterioration with apathy, lack of initiative, and memory defect which lasted over the 30 months of follow up. He never recognised hospital and medical staff despite frequent outpatient visits. Eventually he could not live unassisted by his wife and did not resume his work nor his hobbies as a dog trainer. His oro-alimentary and sexual drives, however, remained normal.

Initial EEG demonstrated non-specific bilateral slowing, a subsequent one being normal. CT scan and arteriography were normal. MRI study performed eight months after the onset detected bilateral small foci of increased signal in the periventricular white matter (figure) on T2 weighted sequences. Skin test with tuberculin was positive. Intradermal reaction with cat scratch disease antigen (Hanger-Rose test) performed 18 months after onset was positive with a 10 mm² area of induration and a surrounding 25 mm² erythematous area.

INITIAL PSYCHOMETRIC EVALUATION AND EVOLUTION

The patient was disoriented for time and place. He remembered with difficulty his job and his children's names and could not recall his address or old and recent political events. He was dysphoric and had no confabulation; his verbal span was 5. On the Wechsler Bellevue test in February 1988 his global IQ was 85 (verbal IQ 85, performance IQ 89), and the deterioration quotient was 28%. A subsequent evaluation in June 1989 found similar low values. Mini Mental State score remained between 15 and 20 (out of 30) without significant improvement over the 30 months of follow up. Spatial organisation was deficient, as shown in the Hooper visual organisation test (14/30) and in the Trail-making B memory tests, with Signoret. Whiteley's battery⁷ with a modified scale (unpublished), confirmed global deficit. Verbal and visual memory were tested

Figure Transverse MRI slice with T2 sequence (TR = 1800 msec; TE = 60 msec) showing bilateral hyperintense foci.

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Table CSF cytochemical results and antibodies titres in serum

	Date of investigation			
	25 January 1988	27 January 1988	9 February 1988	21 April 1989
<i>CSF results</i>				
White cells ($\times 10^6/l$)	<2	40	<2	<2
Polymorphonuclears (%)	—	93	67	2
Lymphocytes (%)	—	5	28	84
Monocytes (%)	—	2	5	14
Red cells (mm^3)	<10	5040	1500	22
Protein (g/l)	0.50	0.71	1.20	0.38
<i>Antibodies in serum</i>				
<i>Chlamydia psittaci</i> (IgG/IgM)*	256/0	128/0	64/0	64/0
<i>Chlamydia trachomatis</i> (IgG/IgM)*	128/0	64/0	64/0	64/0
<i>Toxoplasmosis</i>				
IgG (U/ml)*	80	8	8	8
Elisa (U/ml)	—	>20	0	0
IgM	—	0	0	0

*Immunofluorescence test.
—Not tested.

independently with immediate recall of stories or drawings, serial learning, paired associated learning, and delayed recall. Memory was poor whatever the test condition, the performances ranging from 5 to 6 SD below the normal values for age and education matched controls. Deficit was more distinct, however, for verbal than for visual memory. Performances had improved two months later but remained below the 2 SD range except for paired associated learning which was in the normal range. Similar deficit was found in a third evaluation 14 months later.

HISTOPATHOLOGY

A biopsy specimen of the epitrochlear lymph node was taken one week after antibiotic treatment. Examination with haemalum-phloxine-saffron staining showed numerous granulomas, many of them being surrounded by a fibrohyalinised capsule containing lymphocytes. Granulomas were formed of epithelioid cells, some of them with central necrosis. They were surrounded by palisade-forming, predominantly epithelioid histiocytes with some lymphocytes. Some giant cells were present. No altered polymorphonuclear cells were found. A Warthin Starry silver impregnation did not show any gram-negative pleomorphic bacillus.

LABORATORY INVESTIGATIONS

CSF composition was initially normal, but later analyses showed pleocytosis and finally albumino-cytological dissociation (table). Serological studies were repeatedly negative for Epstein Barr virus, influenza, cytomegalovirus, brucella, rickettsia, tularemia, legionella, herpes, Lyme disease, poliomyelitis, HIV type 1, and syphilis. Levels of IgG antibodies against chlamydia as detected by immunofluorescence were elevated initially, before decreasing to a residual level three months later. Anti-toxoplasmosis IgG was also detected. IgM antibodies were present. CSF analysis for antibodies was negative. Blood and CSF cultures were normal.

Discussion

Our case satisfies the four diagnostic criteria of CSD: history of a close exposure to a cat with

primary skin lesion; regional, mostly epitrochlear, adenopathy; positive cat scratch disease antigen intradermal reaction; and negative tests for other infections. Lymph node biopsy specimens showed non-caseating granuloma. The lack of polymorphonuclear cells in our case may have been related to the antibiotic treatment in the days preceding the biopsy. Many causal agents have been proposed such as herpes virus, chlamydia, or atypical mycobacteria. Recently a small gram negative pleomorphic bacillus has been isolated in the lymph node⁸ and in inoculation site⁹ with silver impregnation stain and has been cultured¹⁰; this agent has been assigned to *Rothia dentocariosa* but the assignment of the bacillus to the disease remains debatable.¹¹ As in many cases, we did not observe this bacillus. Positive serological tests for chlamydia and toxoplasma could be due to crossed antigenicity or non-specific IgG synthesis associated with a concurrent infection. The presence of antibodies against *Chlamydia psittaci* could be explained by exposure to canaries a few months before encephalitis.

We are aware of only 59 cases of neurological manifestations in CSD, mostly presenting as encephalitis.^{5 12 13} The course of encephalitis is usually stereotyped. Onset occurs two days to two months after the initial skin lesion, with headaches, malaise, anorexia, and slight fever. Neurological expression is usually limited to a generalised convulsion, followed by agitated coma for one to four days. As most patients recover without further illness, this encephalitis is considered benign. The course may be more severe, however, with a death rate as high as 8%.⁵ CSF examination, EEG, and CT scans are uninformative. The pathogenesis of neurological complications remains obscure. Direct bacterial invasion, vasculitis,¹⁴ and immunoallergic mechanisms¹² have all been incriminated. The later theory is supported in our case both by the delayed high CSF protein content and by MRI pictures which show disseminated punctiform areas of increased signal in the white matter of the hemispheres. No other case of CSD encephalitis studied with MRI has been reported.

Our observation is unique because of the

severe and lasting neurobehavioural changes after the acute episode of encephalitis. The reason for such a course is unknown as our patient did not differ from those with benign encephalopathy either on clinical, biological, or therapeutical grounds. Psychometric testing showed low IQ with altered spatial and constructive abilities. Memory deficit was initially global and then persisted as an anterograde deficit. The pattern of memory impairment might suggest an amygdalo-hippocampal involvement. Severity of cognitive impairment, however, makes it difficult to assess anatomo-clinical correlations of the amnesic syndrome.

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