



Bartonella henselae of the brain; diagnostic challenge

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Abstract

A 13 and 35-year-old female patients presented because of fatigability, nocturnal febrile illness, generalized body aches and worsening headache. In the course of the illness both patients developed worsening headache and attacks of epileptic seizure. Brain MRI imaging showed intraaxial cerebral heterogeneous irregular masses with focal encephalomalacia, cystic component, glial reaction and dystrophic calcification. Histological results of the resected pathology revealed highly vascular mass with features suggestive of Bartonella henselae. In this report, the initial course of the disease was that of febrile illness, a common problem in a tropical country, furthermore the symptoms were not suggestive of cat scratch disease.

Key words: *Bartonella henselae*; brain; cerebral mass

Introduction

Bartonella henselae, a bacterial pathogen known to cause central nervous system disease

in humans. It was first reported in 1990 and described as a new species in 1992. The pathogen is mainly carried by cats and can cause in humans wide spectrum of clinical syndromes that include cat scratch disease, bacillary angiomatosis, endocarditis and relapsing bacteremia. Central nervous system involvement has included encephalopathy, myelopathy, meningitis, cerebral arteritis, optic neuritis and radiculopathy (Brazis et al. 1986), (Carithers and Margilet 1991), (Lewis and Tucker 1986), (Pickerill and Milder 1986), (Selby and Walker 1979).

Although about 40% of cats carry the bacteria in their saliva but they do not themselves show manifestations of the disease. Cat scratch disease mostly is a self-limiting disease that resolves without treatment; however, in immune compromised patients it can cause serious illness. In this paper, we report 2 cases of young females who had bizarre symptoms that lasted for periods of 8 weeks and one year. Development of neurologic symptoms necessitated imaging of the brain which

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revealed intra-axial brain masses with cystic component mimicking cerebral neoplasms. The post-operative diagnosis of *Bartonella henselae* was made.

Case 1

A previously healthy 35-year-old female developed general fatigability, nocturnal low grade fever, worsening headache, generalized body aches and pains. These symptoms have been going on for one year. One month before presentation to the neurosurgical department, the patient developed neck pain, left ear pain with hyperacusia and one attack of generalized epileptic seizure. The patient reported in the past history of the illness vague abdominal pains and diarrhea and general ill health that necessitated blood transfusion. The patient denied history of any skin scratching or joints pain.

MRI brain showed a left temporal heterogeneous irregular mass lesion with focal encephalomalacia, glial reaction and dystrophic calcification (Fig. 1). The patient was operated upon. Left craniotomy flap was reflected. The dura was then opened, this was found adherent to the underlying pia-arachnoid. A bright-yellowish firm nodular mass with a tuft of numerous tiny vessels was encountered. The tumor mass was gradually resected and the vascular part secured by coagulation and freed from the Sylvian vessels.

The patient had uneventful post-operative recovery.

Case 2

A 19 years old female presented because of febrile illness that lasted few weeks to be

followed by headache, failing vision and convulsions. The patient was initially been investigated for the febrile illness without conclusive diagnosis. Development of neurologic symptoms necessitated brain MRI imaging. The images showed intra-axial thick-walled cystic lesion with perilesional edema (Fig. 1). The patient was subjected to surgery where a thick-walled cystic mass with gliotic white to yellowish content was encountered.

The tumor specimens from both cases 1 and 2 were fixed in neutral formalin saline and stained with Hematoxylin and Eosin, Warthin Starry stain and Masson Fontana and Melan-A for melanin. Aggregates of small black filamentous structures suggested *Bartonella* organisms were confirmed by a mono-clonal antibody specific for *B henselae*. It was Mouse monoclonal antibody: Anti-*Bartonella henselae* (Cat Scratch Fever) antibody [H2A10] (ab704) Abcam Call (888) 77-ABCAM (22226. It was obtained from the USA

The cell phenotypes in the lesions were identified by indirect Immunoperoxidase stains that included CD3, CD20, and CD68. IgG and Complement C3a, C3b and C5a were also stained for. CD34 was used for identification of blood vessels.

Results

The histologic sections showed inflammatory lesions composed of chronic inflammatory cells composed of lymphoid cells and macrophages (Fig. 2). Some of the latter contained hemosiderin positive for iron stain. The lesions were negative for GFAP. Marked vascularity of the lesion was a remarkable finding (Fig. 3). There were foci of necrosis.



Warthin Starry stain showed small linear organisms in small groups and aggregates. The features were characteristic of *Bartonella henselae* (Fig. 4)

Discussion

In this report, both patients had states of ill health for periods that extended from few weeks up to more than one year. Both patients were immune competent. The low grade fever, generalized body aches and pains in a tropical country enlist a number of differential diagnoses. In the two patients neither lymphadenopathy nor skin scratching was reported. Remarkable low hemoglobin in the course of the disease that necessitated blood donation could be attributed to either poor nutritional status of the patient during her illness or could be part of the pathogenesis of the disease.

Emergence of headache, visual deterioration, ear pain, hyperacusis and convulsive attacks were the early neurologic symptoms that lead ultimately to the diagnosis of the disease.

Bartonella is known as the only genus of bacteria that induces pathological angiogenesis in mammalian host. The mechanism of *Bartonella* –induced angiogenesis was not well understood. It was found that these bacteria invade human brain vascular pericytes and induces increase pericyte production of vascular endothelial growth factor (VEGF) (Varanat et al. 2013).

This can explain the pathologic remarkable vascularity in our cases. Cases of encephalitis or neuroretinitis have been reported with *Bartonella henselae* infection.

Cerebral bacillary angiomas has been reported in human immunodeficiency virus-infected patients (Spach et al. 1992). However, the patients in this study were found to be immune-competent.

Of particular clinical importance, in the present report the *Bartonella* infection manifested as cerebral neoplasms as shown in the MRI. Role of infectious agents in tumor genesis has been reported (Hansen et al 2007), (Moss et al 2007).

Vasoproliferative tumors induced by *Bartonella* species were reported as benign and can be cured with antibiotic (Rudikoff et al. 1989).

However, in our cases the state of clinical presentation and the absence of supportive evidence of possibility of *B. henselae* disease gave no chance for therapeutic trial.

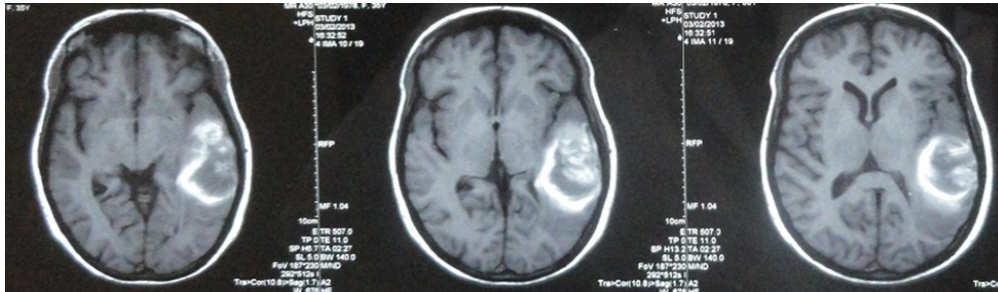
In conclusion *Bartonella henselae* infection of the brain can manifest as cerebral neoplasms and do not necessarily present as classical cat scratch disease. Furthermore the relatively late presentation of patients with this disease and establishment of cerebral neoplasm call for surgical intervention.

References

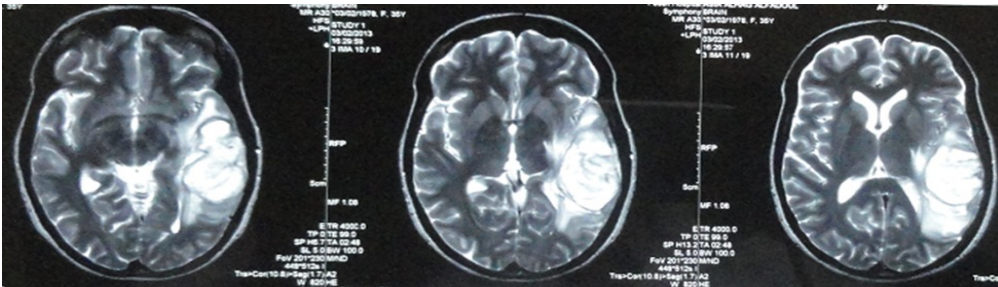
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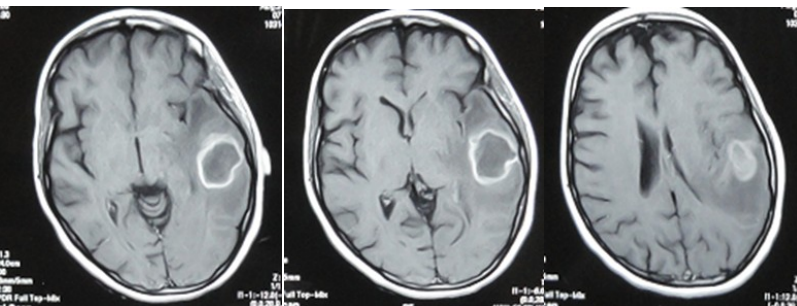
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A



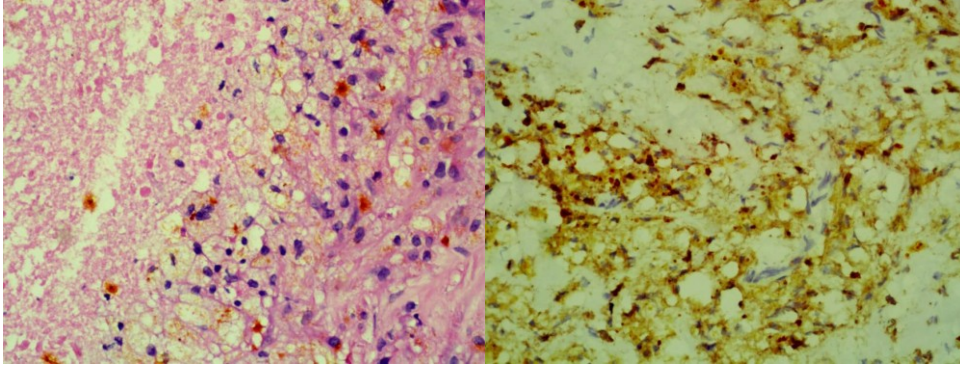
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C

Fig 1.

MRI axial cuts A & B (case 1) and C (case 2) showing intraaxial cerebral heterogeneous irregular masses with focal encephalomalacia, cystic component, glial reaction and dystrophic calcification

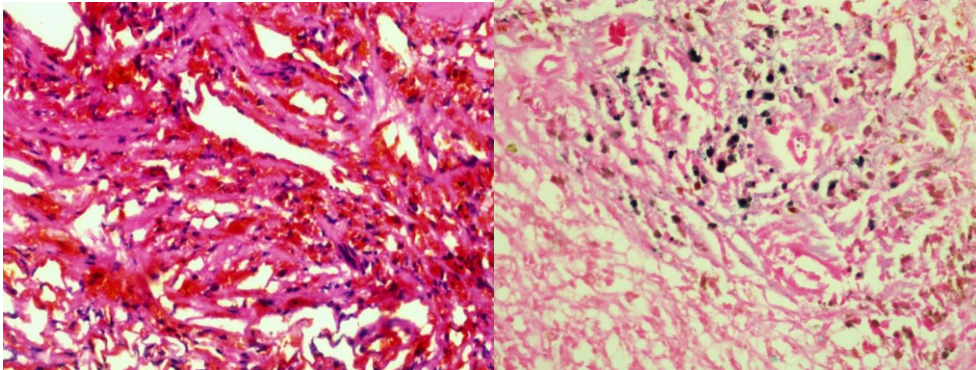


AB

Fig 2.

A shows inflammatory cells consisting of lymphocytes and macrophages. Some of the latter had a clear cytoplasm. In one area there was a focus of necrosis surrounded by chronic inflammatory cells (H&E X40)

B The inflammatory cells are positive for LCA (Immune-peroxidase X40).



A

B

Fig 3.

A lesion shows marked angiomas as seen in the figure on the left (H&E X40)

B Many macrophages contained brown granular material (Upper figure. H&E X40)) that was positive for hemosiderin as shown in the slide at the bottom (Prussian blue stain X40)

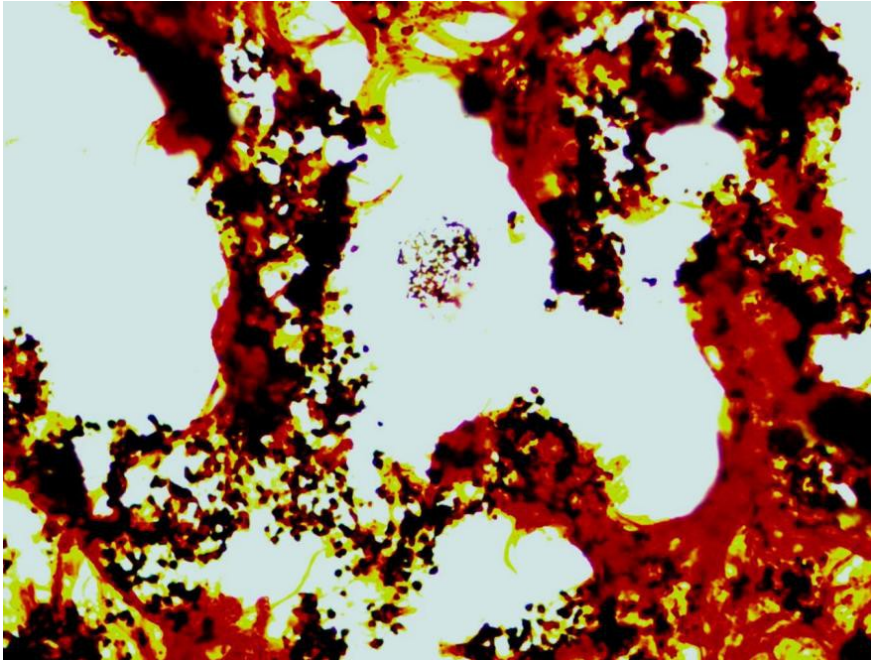


Fig 4. A Warthin-Starry stain showed numerous bacilli. Some are arranged in clumps.