

# First Case Report of Human Granulocytic Anaplasmosis In Mexico With Serological and Molecular Evidence



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## Abstract

Human Granulocytic Anaplasmosis in a tick-borne rickettsial disease caused by *Anaplasma phagocytophilum*, and transmitted by Ixodes scapularis tick. Since the first recognition in 1990 in United States, there is no evidence of human cases in Mexico despite the vector and reservoirs are reported already. We report the first case of Human Granulocytic Anaplasmosis in Mexico with serological and molecular evidence.

**Keywords:** *Anaplasma phagocytophilum*; human; Ticks

## Introduction

Human Granulocytic Anaplasmosis (HGA) is an emerging tick-borne rickettsial disease, caused by *Anaplasma phagocytophilum*; a Gram-negative intracellular bacteria. The first recognition of *A. phagocytophilum* was 1990 in United States [1]. Seroepidemiological rates in endemic areas are as high as 15-36% [2]. *A. phagocytophilum* is transmitted by Ixodes scapularis ticks, as the principal competent vector, and *Peromyscus leucopus* mice as a major host reservoir in the wild cycle. Until now there is no evidence of Mexican cases have been previously reported despite the vector and reservoirs are reported in Mexico [3,4]. We present the first case of HGA acquired in a rural area from Estado de Mexico, Mexico.

## Cases Report

A 5-year-old female, presented in September, 2017 to the emergency department of a tertiary care hospital in Mexico City, with a 2-day history of fever (38.0°C), frontal headache, productive cough, nausea and vomiting, followed by upper limb weakness that began one day prior to the admission. She lived in Estado de Mexico, in a suburban area, with her parents and one sibling. The parents denied recent travel and sick contacts. They didn't own pets, but she had contact with a dog with ticks. Vital signs in the emergency department were notable for a heart rate of 150 beats/min and respiratory rate of 30 breaths/min, with normal temperature. The patient was alert and oriented. The physical exam revealed intercostal retractions and bibasilar crackles, and

the neurologic examination was notable for bilateral upper limb weakness (proximal 2/5 MRC, distal 1/5 MRC) and diminished stretch reflexes in the left arm. The speech was intact and fundi normal. There was no nuchal rigidity and Kernig's sign was absent.

Initial laboratory study results were notable for a white blood cell count of  $16.2 \times 10^3$  cells/mm<sup>3</sup> with 66% neutrophils and 21% lymphocytes, hemoglobin of 14.6 g/dL, platelets of 354 000 cells/mm<sup>3</sup>, creatine kinase of 102 U/L. Liver and renal function tests were within normal limits. Chest radiography revealed interstitial infiltrates predominantly in the right hemithorax. Head CT was normal. Lumbar puncture was performed and cerebrospinal fluid analysis revealed a white blood cell count of 20 cells/mm<sup>3</sup> with predominantly mononuclear cells (81%), red blood cell count of 286 cells/mm<sup>3</sup>, protein 71 mg/dL, glucose 78 mg/dL. Gram stain and CSF culture were negative. The patient was hospitalized and antibiotic treatment with cefotaxime was initiated. A few hours following admission, her respiratory condition deteriorated and orotracheal intubation was performed for invasive mechanical ventilation. A presumptive diagnosis of acute polyradiculoneuropathy was rendered and five sessions of plasmapheresis were performed without clinical improvement.

PCR testing of CSF was negative for enterovirus and VSH infection. Oligoclonal band testing in CSF revealed multiple restriction bands that were also present in serum, and myelin

basic protein was negative. Electroencephalography was normal. T-2 weighted Magnetic Resonance Imaging (MRI) showed a diffuse hyper intense signal within spinal cord from C4 to T4, without contrast enhancement. A nerve conduction velocity test revealed axonal changes and conduction block in the tibial and peroneal nerves. Electromyography showed changes compatible with bilateral L2-L4 radiculopathy. One week after admission, general muscular weakness had progressed to the point that she was unable to move her upper limbs (0/5 MRC, bilateral) and her legs were also affected (proximal 3/5 MRC, distal 2/5 MRC). A course of intravenous immunoglobulin at 2 gr/kg dose was administered. An elective tracheostomy was performed because mechanical ventilation was still required due to respiratory muscle weakness.

Given the unfavorable clinical course despite therapy for acute polyradiculoneuropathy. A written informed consent was obtained to their parents. Were performed in serum and CSF to Western Blott and ELISA for *Borrelia burgdorferi*, and IFA test (IgM and IgG) for *Rickettsia rickettsii*, *Anaplasma phagocytophilum*, *Ehrlichia chaffeensis* and *Borrelia burgdorferi*; and also Polymerase Chain Reaction to DNA extracted by white cells blood was tested by *Rickettsia rickettsii*, *Anaplasma phagocytophilum*, *Ehrlichia chaffeensis* and *Borrelia burgdorferi* for *GroEL* gene as describe [5]. The titer was positive to *A. phagocytophilum* (1:160), and negative for the rest. We run PCR products, finding a positive product for *A. phagocytophilum* (No. Accession KR872895), following the WHO (2008) recommendation by confirmed case. Treatment with doxycycline was started, and gradual improvement of lower limb strength was observed over one week, allowing for ambulation, although upper limb plegia persisted. Improvement in respiratory muscle weakness has allowed for progressive weaning of mechanical ventilation, although she still needs intermittent respiratory support with positive pressure through tracheostomy. A repeat lumbar puncture was performed after 5 weeks of treatment with doxycycline and PCR assay of CSF and blood was negative for *Anaplasma phagocytophilum*. Doxycycline was stopped after 37 days of treatment.

## Discussion

HGA is a tick-borne rickettsial disease caused by *A. phagocytophilum*, and has previously been described in many parts of the United States [2], Canada [6], Europe [7] and Asia [8], but curiously it has not been described in Mexico, even with the reported of their competent vector [3] and reservoirs [4] involving in wild and domestic cycle. Patients presenting clinical manifestation like fever, leukopenia/lymphopenia, thrombocytopenia and increased serum transaminases during the month of March to October, when the pick of tick activities should included in the differential diagnosis such as HGA and other rickettsial diseases [2].

Approximately one-half of symptomatic patients require hospitalization, and 5-7% require intensive care [2]. If the clinical

signs and manifestation are presents, but hasn't historical or epidemiological exposure for tick, should not exclude the diagnosis [7,9]. Few patients report tick exposure one or two weeks before the onset of infection. Diagnostic by PCR could be a sensitive tool and are recommended until 14 days post infection [2,10]. In this case, therefore documentation of infection in a dog, which often is in contact with ticks than humans, should promptly veterinary to warn owners of an increased risk of tick-borne disease. Expansion of tick population can introduced rickettsial agents to new geographical areas, and novel rickettsiae and relationships between vector-host-human will increase [9]. Locally reproducing populations of *I. scapularis* are reported in Estado de Mexico, and it is apparent the first case of locally transmitted of HGA [11]. The present case document the risk for a diseases not previously report to occur in Mexico. From now, we need more epidemiological data, diagnostics tools, and training in health personnel to identified these new cases.

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