CASE RECORDS of the MASSACHUSETTS GENERAL HOSPITAL

Case 5-2025: A 30-Year-Old Woman with Headache and Dysesthesia

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PRESENTATION OF CASE

Dr. Carlos A. Portales Castillo (Medicine): A 30-year-old woman was admitted to this hospital because of headache and dysesthesia.

The patient had been in her usual state of good health until 8 days before the current presentation, when a burning sensation developed in the feet. During the next 2 days, the burning sensation progressed to involve the legs and worsened with light touch. Treatment with ibuprofen did not alleviate her symptoms. She had concurrent fatigue, which she attributed to jet lag after returning from a 3-week trip that had included travel in Thailand, Japan, and Hawaii.

Five days before the current presentation, the patient was evaluated in the emergency department of another hospital because of dysesthesia in the legs. The temporal temperature was 37.2°C, the blood pressure 120/60 mm Hg, the pulse 106 beats per minute, the respiratory rate 18 breaths per minute, and the oxygen saturation 100% while she was breathing ambient air. The examination was reportedly normal. The results of blood tests of renal function were normal, as were the blood levels of electrolytes and glucose. The blood level of creatine kinase was normal, as was a screening test for Lyme disease. The white-cell count was 8680 per microliter (reference range, 3900 to 11,000), and the eosinophil count was 870 per microliter (reference range, 0 to 450); laboratory test results are shown in Table 1. The patient was discharged from the emergency department with a plan for follow-up with her primary care physician.

Three days before the current presentation, dysesthesia progressed to involve the trunk and arms, and headache developed. The patient began taking acetaminophen frequently, but headache worsened. The temporal temperature measured by the patient at home was 38.3°C on one occasion, 2 days before the current presentation.

One day before the current presentation, the patient was evaluated in the emergency department of a second hospital because of worsening dysesthesia and headache. The temporal temperature was 36.4°C, the blood pressure 123/78 mm Hg, the pulse 90 beats per minute, the respiratory rate 18 breaths per minute, and the

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N Engl J Med 2025;392:699-709.
DOI: 10.1056/NEJMcpc2412514

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Table 1. Laboratory Data.

Variable	Reference Range, Adults, First Hospital	5 Days before Current Presentation, First Hospital	Reference Range, Adults, Second Hospital	1 Day before Current Presentation, Second Hospital	Reference Range, Adults, This Hospital*	On Current Presentation, This Hospital
Hematocrit (%)	34.0–46.0	40.6	35.0–47.0	39.4	34.0–46.0	38.8
Hemoglobin (g/dl)	11.0–15.0	13.8	11.8–15.8	13.3	11.0–15.0	13.5
White-cell count (per μl)	3900–11,000	8680	4200–10,200	13,300	3900–11,000	15,500
Differential count (per μl)						
Neutrophils	1800–7000	5280	2400–7600	8480	1800–7700	13,480
Lymphocytes	1000–4000	1880	1000–3300	2750	1000–4800	1100
Monocytes	0–800	530	300–900	930	200–1200	750
Eosinophils	0–450	870	0–400	1050	0–900	10
Basophils	0–200	70	0–120	70	0–300	70
Bands	0–90	50	0–50	50	0–100	80
Platelet count (per μl)	130,000–400,000	348,000	140,000–440,000	430,000	130,000–400,000	471,000

* Reference values are affected by many variables, including the patient population and the laboratory methods used. The ranges used at Massachusetts General Hospital are for adults who are not pregnant and do not have medical conditions that could affect the results. They may therefore not be appropriate for all patients.

oxygen saturation 100% while she was breathing ambient air. The examination was reportedly normal. The results of blood tests of renal function were normal. The blood level of carbon dioxide was 19 mmol per liter (reference range, 21 to 30), and the anion gap was 17 mmol per liter (reference range, 7 to 16). The white-cell count was 13,300 per microliter (reference range, 4200 to 10,200), and the eosinophil count was 1050 per microliter (reference range, 0 to 400). Other laboratory test results are shown in Table 1. After treatment with intravenous ketorolac and lorazepam, headache abated. The patient was discharged from the emergency department with a plan for follow-up with her primary care physician.

After the patient arrived home from the emergency department, she took zolpidem (which had been prescribed for a family member) to help with sleep. On the day of the current presentation, confusion developed; in the morning when she awoke, she thought she needed to pack for vacation and was not redirectable when her roommate attempted to help her lie back down in bed. When confusion did not resolve after several hours, the patient's partner brought her to this hospital for further evaluation.

Medical history included irritable bowel syndrome. Medications included dicyclomine and linaclotide. The patient lived in a coastal region of New England with a roommate. She worked in an office. She did not smoke tobacco, drink alcohol, or use illicit drugs. The patient had returned from a 3-week trip 12 days before the current presentation. During the first week of the trip, she visited Bangkok, Thailand. She toured the city and ate various street foods but no raw food. During the next 5 days, she was in Tokyo, Japan, where she spent most of her time in the hotel and ate several meals of sushi. During the last 10 days of the trip, she was on vacation in Hawaii, where she swam in the ocean several times and frequently ate both salad and sushi.

On examination, the temporal temperature was 37.3°C, the blood pressure 131/96 mm Hg, the pulse 62 beats per minute, the respiratory rate 24 breaths per minute, and the oxygen saturation 93% while the patient was breathing ambient air. The body-mass index (the weight in kilograms divided by the square of the height in meters) was 26.3. She was alert but not oriented. She appeared restless and did not answer questions consistently or follow commands. The neck was supple with normal motion. No rash was present. Intramuscular lorazepam was administered. A peripheral intravenous catheter was placed, and intravenous fluids were administered. Laboratory and imaging studies were obtained.

Microscopic examination of thick and thin blood smears showed no parasites. Blood samples were obtained for culture. Computed tomography of the head showed no acute intracranial abnormalities.

Lumbar puncture was performed for evaluation of cerebrospinal fluid (CSF); the opening pressure was 25 cm of water (reference range, 10 to 25). Analysis of the CSF showed 694 white cells per microliter (reference range, 0 to 5), of which 81% were lymphocytes, 9% were monocytes, 8% were eosinophils, and 2% were neutrophils. The CSF glucose level was 36 mg per deciliter (2.0 mmol per liter; reference range, 40 to 70 mg per deciliter [2.2 to 3.9 mmol per liter]), and the total protein level was 101 mg per deciliter (reference range, 15 to 45). Gram's staining of the CSF revealed many white cells and no bacteria. Treatment with intravenous ceftriaxone, vancomycin, acyclovir, and dexamethasone was started.

A diagnostic test was performed.

DIFFERENTIAL DIAGNOSIS

Dr. Joseph Zunt: This previously healthy young woman initially had dysesthesia, or burning sensory symptoms, involving the feet. The symptoms were exacerbated by light touch, a condition known as allodynia. The sensory symptoms progressed to involve the legs. On initial evaluation of these sensory changes, the complete blood count showed mild eosinophilia.

SENSORY CHANGES AND EOSINOPHILIA

If we frame the problem representation in this case as a previously healthy woman with a subacute onset of sensory symptoms and peripheral eosinophilia, a reasonable first step in the diagnostic process would be to consider disease processes that could account for both her sensory symptoms and eosinophilia. The patient's rapidly progressive sensory symptoms could be consistent with the Guillain–Barré syndrome, which in rare cases can be associated with eosinophilia. However, the examination at the time of the initial presentation at the first hospital was reportedly normal, which suggests intact reflexes and strength. Persons with the Guillain–Barré syndrome usually have a combination of sensory and motor symptoms, and hyporeflexia is a characteristic finding in patients with this disease. Purely sensory Guillain–Barré syndrome has been reported, but it is quite rare.[1]

The use of ibuprofen can produce eosinophilia, and this patient took ibuprofen at the onset of her illness; however, sensory symptoms associated with the use of ibuprofen would be very atypical.[2] Eosinophilic granulomatosis with polyangiitis (EGPA) is associated with eosinophilia and can produce sensory abnormalities that mimic those associated with the Guillain–Barré syndrome. However, the absence of both purpuric lesions on the legs and pansinusitis makes a diagnosis of EGPA unlikely.[3]

HEADACHE AND FEVER

The patient's clinical course progressed to include headache, fever (as measured by the patient at home), and extension of sensory symptoms to involve the trunk and arms. She presented to a second hospital, where she did not have fever, but laboratory studies showed persistent eosinophilia, as well as mild anion-gap metabolic acidosis. The progression of sensory symptoms, in addition to the onset of headache and fever (albeit measured at home), suggest an illness that could involve her peripheral nervous system or central nervous system (CNS). In these circumstances, I would recommend neuroimaging and lumbar puncture for evaluation of CSF.

In my experience, there is often a hesitancy to perform lumbar puncture — perhaps owing to a lack of experience in performing the procedure, concern that it is too invasive, or the associated risks. The risk of headache after lumbar puncture is approximately 5 to 10%, but more serious complications, such as meningitis or epidural hematoma, are very rare.[4] When I am asked about the circumstances under which I would recommend lumbar puncture, I frequently refer to the old adage that states that if you think about something, do it. Lumbar puncture to rule out CNS infection should be strongly considered in any patient presenting with new headache in the presence of fever.

CONFUSION

Confusion developed after this patient took one dose of zolpidem. Although confusion can be an adverse reaction to zolpidem, the development of confusion in this patient with sensory symptoms, headache, and possible intermittent fever

suggests the possibility of encephalitis and further increases concern about a CNS infection. At this point in the patient's illness, lumbar puncture was performed. CSF studies were notable for pleocytosis (694 white cells per microliter, of which 8% were eosinophils), a slightly decreased glucose level, and an elevated protein level; the opening pressure was elevated.

EOSINOPHILIC MENINGITIS

The patient's CSF studies showed approximately 56 eosinophils per microliter. This finding is consistent with eosinophilic meningitis, which is defined by the presence of at least 10 eosinophils per microliter of CSF or eosinophils accounting for more than 10% of CSF leukocytes.[5]

Several noninfectious causes of eosinophilic meningitis can be quickly ruled out in this patient's case, since she did not have a CSF shunt or signs or symptoms of cancer.[6,7] Medications can cause eosinophilic meningitis, and ibuprofen (which this patient took shortly after the onset of her illness) is one of the most commonly implicated medications associated with aseptic meningitis. In a review of 71 episodes of aseptic meningitis in 36 patients, the latency between the use of ibuprofen and the onset of headache was less than 24 hours in more than three quarters of the patients. A majority of the patients had headache, fever, and altered mental status. The median CSF white-cell count was 280 per microliter (reference range, 9 to 5000), with neutrophilic predominance in 72% of the patients; eosinophils were detected in only 1 patient. In addition, 61% of these patients had an underlying autoimmune connective-tissue disorder.[8] In a separate review, the most frequent underlying condition associated with drug-induced aseptic meningitis was found to be systemic lupus erythematosus.[9]

REFINING THE PROBLEM REPRESENTATION

Infections are the most common cause of eosinophilic meningitis and are an important consideration in this patient. A key aspect of this patient's presentation is her recent travel. Twelve days before the current presentation, she returned from a 3-week trip that had included time spent in Bangkok, Tokyo, and Hawaii. With this information in mind, the problem representation could be refined to a previously healthy young woman who recently traveled to regions where parasites are endemic, presents with a subacute onset of progressive sensory changes, and is found to have peripheral eosinophilia and eosinophilic meningitis.

EOSINOPHILIC MENINGITIS IN THE RETURNING TRAVELER

As a neurologist specializing in infectious diseases, I am most interested in the activities, exposures, and diet a patient has had in countries that were visited before the onset of neurologic symptoms. This patient provided a history of eating various street foods (but no raw food) in Bangkok, several meals of sushi in Tokyo, and frequent meals including sushi and salad in Hawaii. Her travel and diet history can be used to further refine the list of infectious pathogens that can produce eosinophilic meningitis.

Given the wide variety of infectious pathogens that are present across the globe, as well as the temporal variation and potential for outbreaks of specific pathogens, I rely on several sources to help determine which possible infections I should consider in returning travelers. I consult sources such as the Centers for Disease Control and Prevention, which has a Web page (https://wwwnc.cdc.gov/travel) that includes a variety of useful maps that show the geographic distribution of pathogens, as well as information regarding the life cycles of such pathogens and the recommended diagnostic approaches and treatment for many infectious diseases. The Emerging Infections Network of the Infectious Diseases Society of America (https://ein.idsociety.org/) has a listserv that serves as a sentinel network to gather epidemiologic information and alerts members of infectious outbreaks. The World Health Organization has a Web page (https://who.int/emergencies/disease-outbreak-news) that provides a search tool for infectious disease outbreaks in any area of the world. In addition, given the relatively small network of neuroinfectious disease clinicians worldwide, it is often possible to contact colleagues by email or WhatsApp (a smartphone app for video-teleconferencing) to find out what a patient may have been exposed to while visiting a specific region or country.

Organisms associated with eosinophilic meningitis that this patient could have been exposed to during her travels are summarized in Table 2. Many of the infectious causes of eosinophilic meningitis in the tropical and subtropical coun-

tries that this patient visited are associated with ingestion of undercooked fish or food that either contains infected snails or slugs or has been contaminated by them. Gnathostomiasis is caused by infection with an organism that is endemic to both Southeast Asia and East Asia, and this patient could have been exposed while eating sushi in Tokyo. However, she did not have excruciating migratory radicular pain or migratory cutaneous swelling, both of which are characteristic of gnathostomiasis. Paragonimiasis is caused by infection with an organism that is endemic to Asia and Africa, and this patient could have been exposed if she ate crab sushi in Tokyo. However, she did not have gastrointestinal symptoms, cough, or migratory cutaneous swelling, findings that are characteristic of paragonimiasis.

Sparganosis is caused by infection with the larvae of spirometra species, an organism that is endemic to Japan. Patients with sparganosis may present with fever, fatigue, headache, seizure, and paresthesia. Although this patient had several of these symptoms, she did not report any ingestion of raw snakes, frogs, pork, or freshwater fish, animals known to host the organism.

Contact with contaminated water during the patient's visits to Bangkok and Tokyo could have exposed her to *Strongyloides stercoralis*, the causative organism of strongyloidiasis. However, the absence of the cutaneous manifestations of this disease in this patient makes strongyloidiasis unlikely. Schistosomiasis, caused by infection with schistosoma species, would also be unlikely, given the absence of cutaneous symptoms associated with schistosomiasis in this patient and the fact that this disease has been nearly eradicated in Thailand and Japan.

Baylisascariasis is caused by infection with *Baylisascaris procyonis*, an organism that is endemic to Japan and other countries where raccoons live. However, this disease is most common in children who have ingested soil contaminated with raccoon feces.

Coccidioidomycosis and cryptococcosis can cause eosinophilic meningitis. However, the patient had not traveled to areas in which *Coccidioides immitis* is endemic (such as the western United States and Central and South America), and she was not known to have human immunodeficiency virus infection, which would confer an increased risk of cryptococcosis.

ANGIOSTRONGYLUS CANTONENSIS INFECTION

The most common cause of eosinophilic meningitis is angiostrongyliasis, which is caused by the nematode (roundworm) *Angiostrongylus cantonensis*. Human infection, which was initially described in Taiwan, is now distributed across many tropical and subtropical regions in Southeast Asia and the Pacific Islands (including Hawaii), with expanding distribution that now includes locally acquired infections in Europe, Australia, the southern United States, and the Caribbean.[14] Only five cases of angiostrongyliasis were confirmed in Hawaii in 2024; however, given that 9 to 10 million tourists visit Hawaii each year, many people may be exposed to infection but may not have symptoms until after they leave Hawaii.[15] Infection can be acquired through multiple sources: ingestion of raw or undercooked infected snails or slugs; ingestion of vegetables or fruits contaminated by infected snails, slugs, or flatworms or by slime from snails or slugs that contains infectious larvae; or ingestion of infected paratenic hosts (e.g., land crabs, freshwater prawns, or frogs) that have consumed an infected snail (Fig. 1).[14] The average incubation period is 1 to 2 weeks after ingestion.[16]

In an animal model of eosinophilic meningitis after experimental infection with *A. cantonensis*, ingested larvae migrated to the CNS by hematogenous spread, and some appeared in the brain within 4 hours after ingestion. In less than 2 weeks, larvae appeared in the subarachnoid space of the posterior fossa and then gradually spread to the cerebral hemispheres. After several months, larvae provoked a severe acute inflammatory reaction involving primarily eosinophils. After the parasite died, granulomas formed on the surface of the cerebral or cerebellar hemispheres. Parasites were detected in the subarachnoid space without a surrounding inflammatory reaction — a finding that suggests that the parasites were still alive after 3 months of infection.[17]

In humans, general symptoms of eosinophilic meningitis due to angiostrongyliasis include headache, nausea and vomiting, and fever. If the path of the parasite in humans is similar to that seen in rats and in experimentally infected calves, neurologic symptoms occur after the parasite leaves the bloodstream, enters muscle, migrates to the peripheral nerves, and then enters the CNS. The resulting migratory sensory abnormalities may

Table 2. Causes of Eosinophilic Meningitis Considered in This Patient.*

Disease (Causative Organism)	Neurologic Manifestations	Other Manifestations	Areas of Endemicity	Exposures	Considerations in This Patient
Angiostrongyliasis (*Angiostrongylus cantonensis*)[10,11]	Migratory dysesthesia or paresthesia, headache, eye involvement, or bowel or bladder dysfunction	Fever, gastrointestinal symptoms, or pruritus	Tropical and subtropical regions of Southeast Asia and the Pacific Islands (including Hawaii), with reports of locally acquired infections in Europe, Australia, the southern United States, and the Caribbean	Consumption of raw or undercooked infected snails or slugs; consumption of vegetables or fruits contaminated by infected snails, slugs, or flatworms or by slime from snails or slugs that contains infectious larvae; consumption of infected paratenic hosts (land crabs, freshwater prawns, or frogs) that have consumed an infected snail	Consumption of salad and sushi in Hawaii
Gnathostomiasis (*Gnathostoma spinigerum*)[11]	Excruciating migratory pain in a radicular distribution (radiculomyelitis), weakness, cranial neuropathy, or subarachnoid hemorrhage	Migratory cutaneous swelling, fever, or mild gastrointestinal symptoms	Southeast Asia, East Asia, and South America	Consumption of contaminated raw fish, crayfish, or freshwater eel	Consumption of sushi in Japan but no dermatologic manifestations or radicular pain
Strongyloidiasis (*Strongyloides stercoralis*)[11]	Mental status changes, meningismus, focal neurologic symptoms dependent on location of abscess	Abdominal pain, fever, migratory rash (larva currens), or pulmonary symptoms (wheezing)	Tropical and subtropical regions but also present in the United States and Europe	Contact with parasite in contaminated water or direct penetration of skin by filariform larvae	No migratory rash
Sparganosis (*Spirometra mansoni*, *S. mansonoides*, and *S. proliferum*)[12]	Seizure, hemiparesis, CNS symptoms dependent on location of CNS lesion, or eye abnormalities (pain, blindness, or proptosis)	Migratory subcutaneous nodules	Asia (*S. mansoni*), the Americas (*S. mansonoides*), and Korea and Japan (*S. proliferum*)	Consumption of raw snakes, frogs, pork, or freshwater fish or consumption of water contaminated by an infected intermediate host	No reported consumption of raw snake or pork
Toxocariasis (*Toxocara canis*)[11]	Subtle cognitive impairment or hyperactivity (in children), dementia (in adults), ocular neuritis, or blindness (may appear similar to retinoblastoma)	Lethargy or fever; visceral larva migrans can produce granuloma in various organs, including the brain (most common in children)	Global distribution (areas in which dogs are present)	Ingestion of soil (geophagia, pica); children are at highest risk	Symptoms and CT imaging findings not suggestive of this infection

Schistosomiasis (*Schistosoma mansoni*, *S. japonicum*, and *S. haematobium*)[11]	Symptoms that are most often due to granuloma formation around parasite eggs and may affect the brain or spinal cord; *S. japonicum* is most likely to affect the brain, *S. mansoni* affects the spinal cord, and *S. haematobium* may affect either the brain or spinal cord	Urticarial swelling, eosinophilia, or Katayama fever (bloody diarrhea, fever, cough, headache, myalgia, and abdominal pain)	Tropical and subtropical areas (85% of infections in Africa)	Penetration of skin by parasite in contaminated water during bathing or washing clothes or by walking barefoot	No dermatologic manifestations, and schistosomiasis nearly eradicated in areas where patient traveled
Baylisascariasis (*Baylisascaris procyonis*)[11]	Cognitive impairment, retinitis, or ocular larva migrans	Cardiac pseudotumor	North America, Europe, China, and Japan	Ingestion of soil contaminated with *B. procyonis* larvae from raccoon feces; children are at highest risk	Symptoms and CT imaging findings not suggestive of this infection
Paragonimiasis (*Paragonimus westermani*)[11]	CNS involvement in rare cases: seizure, headache, fatigue, weakness, or transverse myelitis	Migratory subcutaneous swelling, pulmonary symptoms (cough or hemoptysis), or gastrointestinal symptoms	Asia and Africa	Consumption of infected freshwater crab or crayfish	No cutaneous manifestations or gastrointestinal symptoms, and neuroimaging findings not suggestive of this infection
Coccidioidomycosis (*Coccidioides immitis*)[13]	Headache, altered mental status, focal neurologic deficits, or meningismus	Pulmonary symptoms, dyspnea, fever, night sweats, or dermatologic manifestations	Southwestern United States, Mexico, and South America	Inhalation of aerosolized arthroconidia	No travel to area of endemicity
Cryptococcosis (*Cryptococcus neoformans* and *C. gattii*)	Headache, meningismus, evidence of increased intracranial pressure, or myelopathy	Fever, pulmonary symptoms, or rare cutaneous manifestations	Global distribution (*C. neoformans*) and Australia and the Pacific Northwest of the United States, with expanding geographic distribution (*C. gattii*)	Inhalation of spores from pigeon droppings (*C. neoformans*) or the environment (*C. gattii*)	No evidence of HIV infection (*C. neoformans*) and no characteristic neuroimaging findings

* CNS denotes central nervous system, and HIV human immunodeficiency virus.

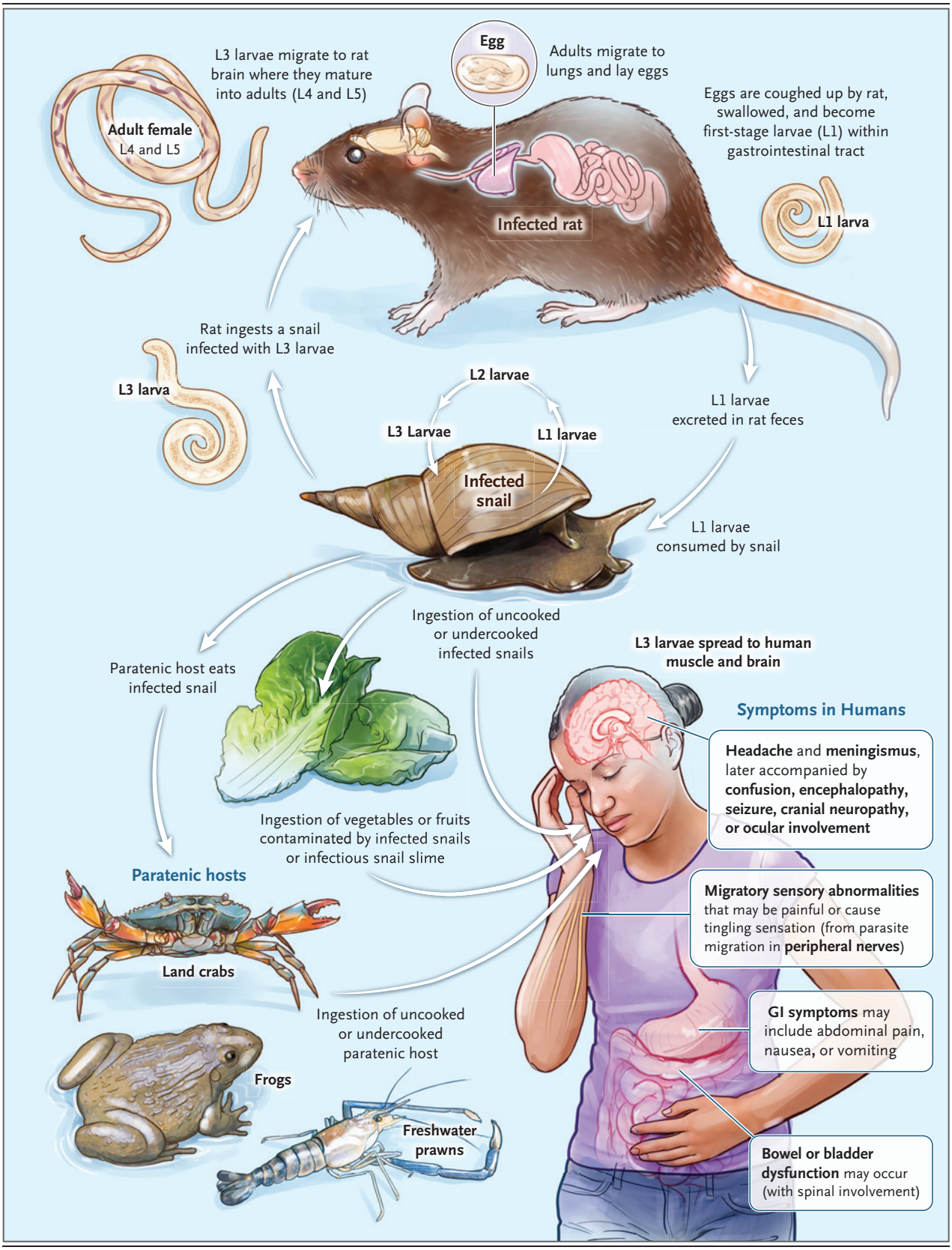

Figure 1 (facing page). Life Cycle of *Angiostrongylus cantonensis* and Symptoms of Infection.

A rat ingests a snail infected with the third larval stage (L3) of *Angiostrongylus cantonensis*; the L3 larvae migrate to the rat brain, where they mature into adults (L4 and L5), and then migrate to the lungs, where they lays eggs that are coughed up by the rat, swallowed, and become first-stage (L1) larvae within the gastrointestinal tract. The L1 larvae are excreted in rat feces and then consumed by the snail. A snail ingests rat feces containing the L1 larvae. Within the snail, the larvae develop into second-stage (L2) and then L3 larvae. Some of the L3 larvae are present in slime produced by the snail and are infectious, although the infectious dose of slime is not defined. A human becomes infected in one of three ways: by ingestion of vegetables or fruits contaminated by infected snails, slugs, or flatworms or by infectious slime from snails or slugs; by ingestion of uncooked or undercooked infected snails or slugs; or by ingestion of an uncooked or undercooked paratenic host (e.g., land crab, freshwater prawn, or frog) that has eaten an infected snail. After an incubation period of 1 to 2 weeks, a human infected with *A. cantonensis* may have gastrointestinal (GI) symptoms, such as abdominal pain, nausea, or vomiting. L3 larvae spread hematogenously to muscle and the brain, where they can develop into L4 and L5 larvae but do not migrate to the lungs or produce eggs. Once in muscle, the parasite enters a peripheral nerve and can migrate through the nerve to the spinal cord, often resulting in migratory sensory abnormalities that may be painful or evoke a tingling sensation; these abnormalities do not typically occur in a dermatomal pattern. When the spinal cord is involved, bowel or bladder dysfunction may occur. Once the parasite enters the central nervous system, initial symptoms typically include headache and meningismus, which are later accompanied by confusion, encephalopathy, seizure, cranial neuropathy, or ocular involvement.

be painful (dysesthesia or allodynia) or evoke a tingling sensation (paresthesia) and may include bowel or bladder dysfunction.[18] The parasite can enter the CNS either through migration along the peripheral nerve or by direct hematogenous spread; both paths can result in headache, confusion, encephalopathy, seizure, or ocular involvement.[18]

A presumptive diagnosis of CNS angiostrongyliasis can be made in a patient with eosinophilic meningitis who has traveled or lived in an area in which *A. cantonensis* is endemic and who has characteristic symptoms and signs.[19] In this patient's case, given her travel through an area where the parasite is endemic (Hawaii), the presence of characteristic symptoms and signs, and a diagnosis of eosinophilic meningitis made on the basis of CSF analysis, she meets the criteria for a presumptive diagnosis of angiostrongyliasis. A definitive diagnosis could be made by identification of *A. cantonensis* larvae in CSF or by confirmatory testing with an enzyme-linked immunosorbent assay, nucleic acid amplification testing (NAAT), or next-generation sequencing.[20-22]

DR. JOSEPH ZUNT'S DIAGNOSIS

Eosinophilic meningitis due to *Angiostrongylus cantonensis* infection.

DIAGNOSTIC TESTING

Dr. Daniel Y. Chang: Early and accurate diagnosis of angiostrongyliasis is crucial for guiding treatment. Although this patient's clinical history, evaluation, and eosinophilia in the CSF provided clues, the parasite was not detected on microscopic examination of the peripheral blood or CSF. The lack of detection on smears was not unexpected, given the low sensitivity and specificity of this conventional diagnostic approach.[23,24]

In contrast, NAAT has emerged as a promising diagnostic tool for the identification of *A. cantonensis* infection owing to its high sensitivity and specificity.[21,25-27] The use of NAAT in targeting specific *A. cantonensis* gene sequences allows for the direct detection of parasite DNA in CSF. This molecular diagnostic technique offers the advantage of detecting low parasite burdens, which is particularly valuable in patients with early-stage infections or atypical presentations. Studies have shown that the diagnostic sensitivity of NAAT can exceed 90%, which substantially facilitates early diagnosis and reduces reliance on invasive procedures such as brain biopsy. Moreover, these assays can differentiate between *A. cantonensis* and other parasitic causes of eosinophilic meningitis, thereby enhancing diagnostic accuracy. Thus, this patient's CSF sample was sent to the National Institutes of Health for NAAT, which revealed the presence of *A. cantonensis* DNA in the CSF.

However, the implementation of NAAT in routine clinical practice faces challenges, including the need for specialized laboratory equipment and technical expertise. As such, only a few specialized laboratories (including the State Laboratories Division of the State of Hawaii

Department of Health) have the ability to perform this assay, which leads to increased turnaround times. Nevertheless, NAAT for *A. cantonensis* in CSF is a clinically significant advancement in the diagnostic landscape of angiostrongyliasis; such testing provides clinicians with a highly sensitive and specific tool to confirm infection and guide timely therapeutic interventions.

MICROBIOLOGIC DIAGNOSIS

Eosinophilic meningitis due to *Angiostrongylus cantonensis* infection.

DISCUSSION OF MANAGEMENT

Dr. Amy K. Barczak: On the basis of the patient's travel history, CSF cell count, and CSF levels of glucose and total protein, a presumptive diagnosis of eosinophilic meningitis due to *A. cantonensis* infection was made. Antibacterial therapy was discontinued, and after CSF NAAT for herpes simplex viruses and varicella–zoster virus showed negative results, treatment with acyclovir was also stopped.

Limited data are available to help guide the management of meningitis due to *A. cantonensis* infection. Most studies have excluded persons with severe presentations, including cognitive changes. Results of existing studies are thus extrapolated to treatment of such persons. Glucocorticoids have been shown to be effective in rapidly resolving symptoms of meningitis due to *A. cantonensis* infection[28,29]; therefore, a 14-day course of high-dose prednisone was started in this patient. Data are less clear regarding the benefit of anthelmintic agents, although many experts recommend using them in conjunction with glucocorticoids. Among anthelmintic medications, albendazole is considered to be the agent of choice because it crosses the blood–brain barrier and achieves reasonable therapeutic levels in CSF.[30] The results of a study of albendazole alone for the treatment of angiostrongyliasis showed slightly fewer patients with symptoms at 14 days in the albendazole group than in the placebo group.[31] The results of another study showed no substantial difference in the number of patients with symptoms at 14 days between the group that was treated with glucocorticoids and the group that was treated with albendazole plus glucocorticoids.[16] Anthelmintic therapy should not be used without concurrent treatment with glucocorticoids.

After uncertainties, potential benefits, and potential drawbacks of anthelmintic treatment were discussed with the patient, the decision was made to add albendazole therapy to the treatment plan. A 14-day course of albendazole was started, together with prednisone. Serial lumbar puncture can be helpful in patients with persistently elevated intracranial pressure or ongoing headaches. However, in this patient, the use of serial lumbar puncture was determined not to be needed for symptom management.

Dr. Portales Castillo: Headache and dysesthesia abated with a combination of directed therapy (albendazole and prednisone) and gabapentin and amitriptyline (indicated for dysesthesia). On the sixth hospital day, the patient was discharged home.

FINAL DIAGNOSIS

Eosinophilic meningitis due to *Angiostrongylus cantonensis* infection.

This case was presented at Neurology Grand Rounds.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

We thank Dr. Shibani S. Mukerji for review of the case presentation and Dr. Edward T. Ryan for comprehensive review of the manuscript.

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