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Welcome to *Infectious Disease Reports*: a message from the Editor

David M. Aronoff

Division of Infectious Diseases, Department of Internal Medicine, The University of Michigan Health System, Ann Arbor, MI, USA

Welcome to the new online-only, international, Open Access, peer-reviewed journal, *Infectious Disease Reports (IDR*). It is a profound honor to lead this new journal, and I would like to share with you my vision for *IDR* and take this opportunity to encourage you to submit your work for peer review. It is a great challenge to define the scope of a new infectious disease journal given the wide breadth of our rapidly-evolving field. Infectious diseases present both ongoing and emerging threats to human health. In addition to the "usual offenders" that reap havoc on global human populations (e.g., malaria, tuberculosis, pneumonia, HIV/AIDS), we regularly find ourselves challenged by unexpected and emerging infectious disease threats. Recent examples include epidemics/pandemics (e.g., H1N1 influenza, Ebola virus, severe acute respiratory syndrome [SARS]); large-scale outbreaks (e.g., *Vibrio cholerae, Escherichia coli,* Norovirus, other food-borne infections); antimicrobial and antiviral resistance (e.g., extremely drug-resistant tuberculosis [XDR-TB], extended-spectrum beta lactamases, antiviral-resistant HIV); and the transcontinental migration/importation of infectious agents (e.g., monkeypox, West Nile virus, tuberculosis). In this light, the scope of *IDR* must be broad, to capture and address the rapidly-shifting global challenges faced by the ID community.

The editorial staff at *IDR* are committed to insuring that manuscripts published here are novel and meet the needs of a diverse audience. Because our field of infectious diseases includes longstanding problems and emerging threats, *IDR* seeks to publish manuscripts including:

- expert reviews (both invited and unsolicited) that identify current gaps in our knowledge
- original investigations (including basic science, translational and clinical research)
- case series and case reports, which are often the heralds of emerging ID threats.

In addition, *IDR* encourages the submission of manuscripts that include the use of novel research tools or address our field from a multidisciplinary perspective. Examples of innovative areas that could be targeted for reviews or original manuscripts include studies of human microbial ecology or the use of systems biology, nanotechnology, and metagenomics to address problems in infectious diseases. I envision manuscripts in *IDR* addressing the following areas (in no particular order):

- international health/pandemics
- microbial pathogenesis and host immunology
- virology
- bacteriology
- mycology
- parasitology
- vaccinology
- epidemiology
- diagnostics (including novel, rapid, and field-based methods)
- treatment.

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The Open Access, online-only era is upon us. An exciting consequence of online access is the ease with which we can reach out across geographical, cultural, and political barriers to communicate about the latest infectious disease problems and solutions. In many international regions, Open Access is seen as a natural, financially sustainable alternative to standard publishing. PAGEPress, the publisher of *IDR*, is committed to offering a publication platform to developing and developed countries alike.

We have populated the Editorial Board of *IDR* with a balance of young (emerging) and established infectious disease experts to ensure that our manuscripts are current, of wide interest, address controversies and unanswered questions, and help stimulate further advances in the field. I strongly encourage you to submit your work to *IDR*. I look forward to seeing *IDR* grow into a major infectious disease journal that makes robust contributions to controlling the global threat of human infection.

Carpal tunnel syndrome and HIV infection. A case report and literature review

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Abstract

The first clinical case of carpal tunnel syndrome (CTS) in Cuban HIV-infected patient was described, and the scientific literature indexed in: PUBMED/MEDLINE, LILACS and BIREME were revised. The case presented was a male with HIV infection without preceding opportunistic illnesses, $CD4^+$ T cell count over 200 cells/mm^3 and clinical symptoms of pain, tingling and numbness in the right hand and wrist for three months. The electrophysiological study was compatible with CTS. The pharmacological treatment did not modify the symptoms and the patient received specific surgical treatment with absolute resolution of symptoms. CTS is a compressive neuropathy that can occur in HIV-positive individuals with as similar frequency as in the general population. The association between HIV infection and CTS is scarcely described in the medical scientific literature and probably does not represent a different phenomenon from what happens in the HIV-negative population. Nevertheless, its clinical recognition among other neurological and muscle-skeletal manifestations in HIV-infected patients is important.

Introduction

Carpal tunnel syndrome (CTS) is a compartment compressive neuropathy of the median nerve in the wrist. The disease has a prolonged course of pain, paresthesia and functional limitation of the upper extremities in the median nerve distribution. Although CTS has been described as one of the most common peripheral neuropathy, the prevalence in the general population differs from the published studies.[1] A recent study in Holland reported a crude annual incidence of 1.8 cases per 1000 people.[2] The most extensive research conducted in Switzerland identified a prevalence of 3.8% by clinical diagnosis and 2.7% after considering clinical and electrophysiological findings.[1] Although the syndrome is often an occupational disease predominantly in women,[3] several factors such as obesity, hypothyroidism, and connective tissue diseases have been related in the genesis of this medical condition.[4,5]

Peripheral neuropathic manifestations often occur in HIV-positive individuals. The cytopathic effect of HIV, certain opportunistic infections involving the peripheral nervous system, and in recent years, the neurotoxicity of some antiretroviral drugs, have been raised among the possible etiologies.[5] However, the association between CTS and HIV infection has only been reported anecdotally related with *Mycobacterium avium* complex co-infection.[6] After the advent of highly active antiretroviral therapy (HAART), few case reports have been published and postulated a possible association of the CTS with the prolonged use of viral protease inhibitors (PIs).[5] This communication describes the first case of CTS in a Cuban HIV-infected patient.

Case Report

The patient was a 35-year-old male with sexual acquired HIV infection since December 2004, so far without suffering from AIDS-related opportunistic diseases or other co-morbidities. He was admitted in the Department of Infectious Diseases at Gustavo Aldereguía Lima Teaching Hospital, concerning pain, numbness and tingling in the right upper limb, primarily in the hand and wrist for three months. Few weeks before the admission symptoms progressively worsened, were more frequent at night, and were not alleviated with analgesics and non-steroidal anti-inflammatory drugs (NSAIDs). The patient had no treatment for HIV infection.

There was no history of trauma, skin lesions suggestive of herpes zoster, fever or headache. There were no clinical stigmata of hypothyroidism or rheumatic disease. The patient had no occupational risk for CTS. Physical examination identified painful hyperesthesia in the rights wrist and forearm at the distribution of the median nerve, and positives Tinel (paresthesia painful strike to the distal wrist crease) and Phalen (paresthesia in the distribution of the median nerve to the dorsal flexion of the wrist at 90º to 60 seconds) signs. There were no signs of muscle atrophy or loss of tactile discrimination at the thenar eminence of the right hand. The Body Mass Index (BMI) was 23.8.

The blood analysis showed no abnormalities, the sedimentation rate (ESR) was 15 mm/h; C-reactive protein and rheumatoid factor were negative. There were no alterations in blood chemistry, including normal values of total CPK, LDH, TSH and FT4. His absolute $CD4^+$ T cell count was 234 cells/mm^3 and the Plasma Viral Load for HIV was 320 copies/mL. The radiographs of the cervical spine and cranium-spinal joint showed no bone abnormalities. The electrophysiological study of upper limb was considered diagnostic of CTS according to the criteria of Kimura *et al.* and Portillo *et al.* (Table 1).[7,8]

Discussion

The prevalence of CTS in HIV positive individuals does not appear to be higher than in the general population. A Spanish study con-

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Contribution: AR-C, clinical diagnosis, patients' follow-up, assessment of HIV infection evolution, review of the manuscript; DB-R, surgical treatment, preparation of the manuscript; YB-J, review of the manuscript; BCJ-M, preparation of the manuscript; YB-J, preparation of the manuscript; YL-P, preparation of the manuscript.

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ducted by Asensio *et al.* identified CTS in the 0.9% of HIV-infected patients.[9] In the United States, Márquez *et al.* described this medical condition in the 2.6% of 75 HIV-positive cases with HAART.[10] The 63% of adults with CTS attended in a rheumatic diseases clinic in Lusaka, Zambia had HIV infection.[11]

Several factors and clinical situations have arisen in the genesis of this syndrome (Table 2). Many of them, as some occupational activities, hypothyroidism, rheumatoid arthritis and obesity, are also mentioned in HIV-infected individuals.[5,9,12] Clinical observations published by Sclar and Manfredi related CTS with the HAART-associated metabolic syndrome particularly to PIs.[5,13] One explanation for this observation has been the myxedematous accumulation in the carpal tunnel and secondary compression of the median nerve.[12] Asensio *et al.* found no relation between the lipodystrophy secondary to PIs and CTS.[9] The patient did not have the above diseases and has not been receiving HAART when the CTS was diagnosed, therefore, as happened with other published cases, it would be hasty to establish association with HIV infection or HAART. There is a communication of CTS in HIV-positive individual treated with recombinant growth hormone.[14]

The patient had the typical clinical characteristics of the disease limited to the right hand and wrist, the characteristic pain with nocturnal worsening and paresthesias, which were partially relieved with the flapping of the hands (Flick sign). The electrophysiological study identified prolongation of motor and sensory distal latencies of the right median nerve and increase of the sensory conduction velocity exceeding 41.9 m/s, confirming the diagnosis. It was also found prolongation of the distal motor latency of left median nerve. The electrophysiological involvement of both median nerves in the absence of bilateral clinical manifestations has been described in several communications.[1,7,8]

The revised series highlights the high sensitivity of symptoms and clinical signs, over 90%.[12] Some authors have raised the lack of a gold test for the diagnosis of CTS, while others argue that the combination of clinical findings with electrophysiological abnormalities is sufficient for the diagnosis.[15] Although the clinical symptoms are not necessarily related with the severity of neurological impairment, the presence of atrophy is correlated with the most severe and significant alterations in the electro-physiological studies, indicating axonomyelinic damage.[7] Other clinical aspects such as Tinel and Phalen signs appear earlier and in the presence of suggestive electrophysiological findings help to the early diagnosis of the syndrome.[7,15]

Several studies included CTS among HIV-associated rheumatopathies and described alterations of the ESR and C-reactive protein.[10,12] However, these findings were not identified in our patient, and it could depend on the few inflammatory components of the disease in the presented case. CTS associated to rheumatoid arthritis, amyloidosis, chronic renal failure, and infectious diseases like tuberculosis, might be related with acceleration of the ESR and increasing of inflammation markers.

The patient received many treatments with NSAIDs, which only slightly modified the symptoms. It was coordinated with the Neurosurgery Staff and surgery was performed. Surgical treatment is indicated for moderate and severe stages of the disease. It can be performed by conventional or endoscopic techniques, in both cases it consist in decompressing the median nerve through the opening of the flexor retinaculum.[12] There is

Table 1. Electrophysiological study findings.

Measurements	Right median nerve	Right cubital nerve	Left median nerve	Left cubital nerve
PML (mseg)	8.8	7,4	8,0	7,0
DML (mseg)	5.0	2.4	4.8	2.8
PMA (mseg)	9.9	6.2	9.2	6.3
DMA (mseg)	7.3	6.0	8.9	6.0
DSL (mseg)	4.4	2.0	3.6	2.1
MCV m/s	68.21	69.36	62.50	63.29
SCV m/s	44.62	41.2	41.8	41.4

L: latency, A: amplitude, M: motor, S: sensorial, CV: nerve conduction velocity, P: proximal, D: distal.

Table 2. Diseases, clinical conditions and socio-occupational factors associated with carpal tunnel syndrome.

	Diseases, clinical conditions and socio-occupational factors
I	Endocrine-metabolic
	Diabetes mellitus
	Hypothyroidism
	Acromegaly
	Obesity
	HAART-related metabolic syndrome
II	Rheumatologic and muscle-skeletal disorders
	Rheumatoid arthritis
	Carpal and metacarpal osteoarthritis
	Colles fracture
	Luxation of semilunar bone
	Cumulative trauma of the wrist
	Gout
III	Chronic infection
	Tuberculosis and other mycobacterial infections
	HIV/AIDS
IV	Chronic and inflammatory disorders
	Chronic renal failure and hemodialysis
	Amyloidosis
V	Occupational factors
	Office work
	Manufacturing
	Construction
	Healthcare personnel, nurses, home services and others
VI-	Sports, sport climbing
VII	Other states and conditions
	Pregnancy
	Menopause
	Smoking
	Genetic factors
	Hormone therapy
VIII	CTS idiopathic (15%)

agreement among studies regarding the efficacy of surgery in the remission of clinical manifestations of CTS.[12,16] The patient had successful recovery and when this report was wrote (one year after surgery), he was absolutely asymptomatic and with no functional limitation of the hand.

Conclusions

CTS can be diagnosed in HIV-positive patients with as similar frequency as in the general population. Based on current evidence, there is a controversial association among HIV infection, HAART and CTS, and probably does not represent a different phenomenon from what happens in HIV-negative population. However, the clinical recognition of the syndrome between the numerous neurological and muscle-skeletal disorders related with HIV infection and AIDS is important.

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Dengue hemorrhagic fever in a peripheral blood stem cell transplant recipient: the first case report

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Abstract

Dengue infection, a mosquito-borne infectious disease in tropical and subtropical areas, has recently become an emerging global disease. The clinical course of dengue infection may be unfavorable in immunocompromised patients. In this report, we present a 16-year old female patient with acute myeloid leukemia who received allogeneic peripheral blood stem cell transplant five months prior to presentation. She was hospitalized at King Chulalongkorn Memorial Hospital, Bangkok, Thailand, due to fever, headache, and myalgia for one day. During hospitalization, she developed capillary leakage syndrome and progressive thrombocytopenia. A diagnosis of dengue hemorrhagic fever was made and confirmed by positive dengue serology and polymerase chain reaction testing. She made a full recovery 14 days after hospitalization. Our case possibly acquired dengue virus from infected mosquitoes while visiting her relatives four days before her present illness. In conclusion, this is the first reported case of dengue hemorrhagic fever in a peripheral blood stem cell transplant recipient. In addition, we review all previous reports of dengue infection in organ transplant recipients.

Introduction

Dengue infection is an acute infectious disease caused by four dengue virus serotypes 1, 2, 3, and 4.[1-7] The principal vector is Aedes aegypti, a mosquito with worldwide distribution in many tropical and subtropical areas. The clinical spectrum of dengue infection varies from asymptomatic to severe disease. All serotypes produce a similar clinical illness characterized by acute fever, headache, generalized myalgia, nausea, and vomiting, and induce a life-long immunity that is specific to the infecting serotype.[7,8] A small proportion of infected individuals may develop a severe form of disease, dengue hemorrhagic fever (DHF), characterized by fever, thrombocytopenia, hemorrhagic manifestations, and excessive capillary leakage probably leading to dengue shock syndrome (DSS) and death.[1-7] The clinical course of dengue infection may be unfavorable in immunocompromised patients. Bone marrow transplant recipients have an impaired cell-mediated immunity, placing them at increased risk of infections. We report a case of DHF in a peripheral blood stem cell recipient, and review all previous reports of dengue infection in organ transplant recipients.

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Case Report

A 16-year old female was hospitalized at King Chulalongkorn Memorial Hospital, Bangkok, Thailand, due to a high-grade fever without chills, bitemporal headache, generalized myalgia, and nausea one day prior to admission. She had returned four days before from visiting her relatives at Chon Buri, East Thailand. The patient had been diagnosed with acute myeloid leukemia (type M4) 14 months prior to the present illness when she noted acute fever, petechial rash, and bleeding of her gums and nose. She received induction and a consolidation course of chemotherapy. Allogeneic peripheral blood stem cell transplantation was performed five months before the present illness. She was in complete remission when last seen one month prior to her present illness. Complete blood count (CBC) showed hematocrit of 28%, white blood cell count of 4.89×10^9/L (neutrophil 46%, lymphocytes 40%, and monocytes 6.9%), and platelet count of 186×10^9/L. Her current medications include cyclosporine, acyclovir, and cotrimoxazole. Physical examination revealed an acutely ill patient with body temperature of 39.7°C and bilateral anterior cervical lymphadenopathy. CBC showed hematocrit of 33%, white blood cell count of 6.3×10^9/L (neutrophil 80%, lymphocyte 8%, atypical lymphocyte 5%, and monocyte 7%), and platelet count of 120×10^9/L. Three days after hospitalization, a relapse of acute myeloid leukemia could not be excluded, and hence bone marrow was examined and revealed decreased cellularity, adequate megakaryocytes, increased histiocytes and eosinophils, consistent with reactive marrow to probable certain infection.

Eight days after hospitalization, she noted petechial rash over both her legs, and physical examination revealed moderate hepatomegaly and right pleural effusion. CBC showed hematocrit of 38%, white blood cell count of 8.84×10^9/L (neutrophil 79%, lymphocyte 5%, atypical lymphocyte 13%, and monocyte 3%), and platelet count of 16×10^9/L. DHF was suspected, and later confirmed by enzyme-linked immunoassorbant assay[9] and reverse transcriptase-polymerase chain reaction (PCR) testing.[10] A diagnosis of primary dengue infection was made with dengue IgM of more than 40 U and IgM/IgG ratio of or more than 1.8:1 (dengue IgM rose from 86.65 to 121.03 U, and IgG rose from 49.18 to 134.01 U). Twelve days after hospitalization, she developed convalescent rash over her extremities. She eventually made a full recovery, and was discharged 14 days after hospitalization.

Discussion

This is the first reported case of dengue hemorrhagic fever in a peripheral blood stem cell transplant recipient. Our case had primary dengue infection, and possibly acquired dengue virus from infected mosquitoes while visiting her relatives at Chon Buri. Clinical manifestations of dengue infection in immunocompromised patients are usually similar to those noted in immunocompetent individuals. However, some patients experienced a longer duration (more than seven days) of illness than that in healthy individuals (4-7 days).[1-3] A 23-year old renal transplant recipient developed dengue hemorrhagic fever which lasted for 19 days.[11] Our patient also had a 12-day course of dengue hemorrhagic fever.

In addition, an unusual presentation of dengue infection has been reported.[12,13] A 25-year old patient with aplastic anemia with dengue infection developed polyserositis while he underwent conditioning for allogeneic stem cell transplant from his brother.[12] Another case of unusual dengue infection was described in a renal transplant recipient who developed acute colitis one week after returning from Southeast Asia.[13]

Furthermore, a transmission of dengue infection from an organ transplant donor during transplantation has been reported.[11,14] One case of possible transmission of dengue infection from a living donor to a renal transplant recipient was described.[11] This patient developed acute fever five days after receiving a kidney transplantation from his mother who later had a positive PCR test in the blood for dengue virus serotype 1. Another case of dengue infection transmission was described in a bone marrow transplant recipient during a dengue epidemic in Puerto Rico in 1994.[14] A 6-year old recipient developed an acute febrile episode four days after a transplant, and eventually died. Dengue serotype 4 was isolated from the blood and post-mortem tissues. The donor developed a dengue-like illness two days after a transplant. A diagnosis of dengue infection was confirmed by a positive dengue IgM from ELISA testing.

There are a few studies on the histopathology of bone marrow in dengue infection, and most of them are from post-mortem cases with severe dengue infection.[15-17] Diffuse hypocellularity with and without hemophagocytosis is always described in bone marrow of patients with dengue hemorrhagic fever. In our case, examination of bone marrow revealed diffuse hypocellularity despite being performed early in the course of dengue infection.

This is the first report describing dengue hemorrhagic fever in a peripheral blood stem cell recipient. A high index of suspicion of dengue infection should be given to every transplant patient living or returning from endemic areas who presents with an acute fever in association with viral syndrome.

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Repeated *Dientamoeba fragilis* infections: a case report of two families from Sydney, Australia

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Abstract

We report cases of two unrelated families who both presented with recurrent *Dientamoeba fragilis* infections. Subsequent antimicrobial therapy resulted in the clearance of *D. fragilis* and total resolution of gastrointestinal symptoms in both families. This report highlights the potentially recurrent nature of *D. fragilis* infections and the need for laboratories to routinely test for this organism.

Introduction

Dientamoeba fragilis is a pathogenic amoeboid protozoan parasite that is closely related to the Trichomonads. The parasite has been shown to cause gastrointestinal disease in a wide range of patient groups, has a world-wide distribution and is often more prevalent than *Giardia*.[1,2] Chronic symptoms have been reported previously in patients presenting with *D. fragilis* infection.[3] One study found that 32% of *D. fragilis* infected patients had persistent diarrhoea and associated symptoms of greater than 2 weeks duration.[4] We report two separate cases of repeated *D. fragilis* infection in family members sharing the same residence who by genotyping were determined to be infected by different strains of *D. fragilis.*

Case Report

Case #1

A 41-year-old male (patient #1) presented with a history of chronic diarrhoea and weight loss over a period of several months. A faecal sample was collected and routine bacteriological cultures were performed along with investigation for parasites. Due to the chronic nature of the condition no virology was performed on the samples given the acute, self-limiting nature of viral gastroenteritis. No bacterial pathogens were detected by culture. Parasitology testing was performed on faecal samples fixed in sodium acetate acetic acid formalin and permanently stained using a modified iron-haematoxylin stain as previously described.[4] Diagnosis of *D. fragilis* infection was made based on the finding of binucleate, pleomorphic, granular, amoeboid cells, typical of *D. fragilis* in the initial stained smear.[4] The patient was treated with metronidazole, symptoms improved, and on follow up examination of stool sample (n=1) no parasites were detected, indicating that the infection was successfully cleared. Several months after the initial presentation and subsequent successful treatment of the *D. fragilis* infection the patient presented again with gastrointestinal complaints including a variation in bowel motions from watery diarrhoea to unformed faecal motions. Stool samples were resubmitted again and underwent routine bacteriological culture, and permanent staining of fixed faecal smears for the identification of protozoan parasites. In addition a portion of stool sample underwent DNA extraction and PCR using specific primers targeting the SSUrDNA of *D. fragilis* as previously described.[5] No bacterial pathogens were identified, while microscopic analysis of the stained smears detected *D. fragilis* trophozoites and the *D. fragilis* PCR was also positive for *D. fragilis* DNA. After the diagnosis of dientamoebiasis was made the patient was treated with doxycycline and iodoquinol. The patients symptoms resolved after treatment and subsequent stool samples submitted post treatment (n=2) were negative for *Dientamoeba* by both microscopy and PCR.

At the same time the patient's mother, a 75-year-old female (patient #2), who cohabited at the same residence as her son also presented with a history of gastrointestinal symptoms including bouts of diarrhoea and unformed stools, faecal urgency, digestive problems and food intolerance. Microbiological analysis was undertaken on stool specimens including microbial cultures, parasitology testing, and *D. fragilis* specific PCR. Bacterial cultures were negative and the permanent stained faecal smears of the mother's stool specimen demonstrated the presence of *Blastocystis hominis*. No *Dientamoeba* trophozoites were detected by microscopy. However a positive *D. fragilis* PCR result was obtained from the mother's stool demonstrating the presence of *Dientamoeba* DNA. Sequencing of the PCR products from mother and son was undertaken as previously described.[5] The *Dientamoeba*-specific PCR product obtained from the stool of the patient's mother was sequenced and found to have identical SSU rDNA sequence as that obtained from her son.[5] Given that the SSU rRNA gene displays insufficient variability to be used as a definitive epidemiological marker the previously described *D. fragilis* typing method of C-profiling was undertaken on both samples.[6]

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Both *D. fragilis* samples yielded different C-profiles indicating the strains were not genotypically identical (Figure 1). Patient #2 was treated with secnidazole, nitazoxanide and doxycycline, which resulted in total parasitological clearance and resolution of the patient's symptoms. Follow-up samples collected after treatment and again some 3 months later failed to detect any *D. fragilis* either by microscopy or by molecular methods. As *Enterobius vermicularis* has been proposed by some as a possible vector for transmission of *D. fragilis*, multiple sticky-tape tests were collected from both *D. fragilis* infected patients. A total of 6 tape tests were collected and examined; no *E. vermicularis* ova were detected.

Case #2

A family comprising of the father (58 years of age), mother (49 years of age), son (13 years of age) and daughter (10 years of age) presented to their local general practitioner with gastrointestinal complaints after a holiday to Tasmania. The gastrointestinal symptoms included diarrhoea, abdominal pain and bloating. One month after the holiday in April 2008, all four patients submitted stool samples for routine bacteriological cultures along with investigation for parasites. No bacterial pathogens were isolated. However *D. fragilis* was detected by microscopy of permanently stained faecal smears as previously described, in three out of the four patients (father and both children). Both children also presented with a peripheral eosinophilia. In May all four patients were treated with metronidazole and

symptoms resolved. No follow-up stool samples were collected to check for clearance of parasite. Four months later in September, three of the family (father, son and daughter), presented with gastrointestinal symptoms, faecal samples were resubmitted and *D. fragilis* was detected by permanent stained microscopy in all three patients with the father also having the non-pathogenic flagellate *Chilomastix mesnili* present. All three patients were subsequently treated with paramomycin for 10 days. Follow-up stool samples were collected one month after cessation of treatment and no *D. fragilis* was detected by microscopy. Five months later the family once again presented with gastrointestinal complaints and microbiological analysis of faecal samples were performed. *Dientamoeba fragilis* was detected in 2/4 family members (father and son) by microscopy of permanent stained smears,. Faecal samples were then collected from all members of the family and an RT-PCR was performed as described.[7] The PCR assay detected *D. fragilis* in all family members, including the two members who were microscopy negative for *D. fragilis* only 5 days earlier. In order to fingerprint the *D. fragilis* strains, C-profiling was used to determine if the infection was from a single source. Only two samples, from the father and son were able to be fingerprinted using this technique and both strains were shown to be genotypically different (Figure 1). Treatment was initiated for all family members (paramomycin for 10 days). All family members reported resolution of symptoms and follow-up molecular analysis of stool samples one month later detected no *D. fragilis* DNA. Follow-up two months later showed that the family was still symptom and parasite free.

Discussion

Dientamoeba fragilis is a protozoan parasite that has recently emerged as an important cause of parasitic gastrointestinal disease.[1,4] Recent studies have shown the organism to be widespread with relatively high prevalence rates ranging from 8.9% to 16.8% in developed regions of the world.[8-10] Gastrointestinal symptoms attributed to *Dientamoeba* infection most commonly include diarrhoea and abdominal pain, with chronic infection often reported.[4,11,12] Numerous studies have shown antimicrobial therapy targeting and eliminating *D. fragilis* will result in marked clinical improvement for patients suffering from dientamoebiasis.[3,12,13]

All patients from both families presented with a repeated *D. fragilis* infection over prolonged periods of time. Bacterial etiological agents were excluded by routine testing. *Dientamoeba* was detected by either microscopy or PCR (or both) in the patients' samples. The PCR detected *D. fragilis* infections that would have been subsequently missed if microscopy only had been used. Molecular testing has been shown to provide excellent sensitivity and specificity when compared to microscopy for the detection of *D. fragilis* and provides an additional diagnostic tool for laboratories with this capability.[7] The symptoms described in all patients included a variation in bowel motions with bouts of diarrhoea, unformed stool samples and faecal urgency along with stomach pain and cramps.

In case #1, patient #1 had a previous *D. fragilis* infection which initially seemed to respond to therapy; however the patient presented again several months later. Whether the latter infection was a new infection from a different source, a reinfection from the same source or even treatment failure is unknown. Samples from the first episode of infection were not collected for molecular analysis. As it was possible that the reinfection was due to selection of resistant *D. fragilis* strains and subsequent treatment failure both patients were treated with combination therapy to eradicate the organism. One patient was treated with doxycline and iodoquinol while the other secnidazole, nitazoxanide and doxycycline. Both patients responded to treatment with eradication of the organism and resolution of symptoms. The patient who was treated with secnidazole, nitazoxanide and doxycycline did complain of side effects from the antimicrobial agents.

The patients from case #2 had gastrointestinal complaints for over a year and even though treatment was given on several occasions to family members, *D. fragilis* and gastrointestinal complaints returned. As some members of the family had resolution of symptoms and clearance of *D. fragilis* from stools after treatment it must be assumed that the patients were getting re-infected. After treatment with metronidazole after the initial *D. fragilis* "outbreak" amongst the family, no follow-up stool samples were examined for clearance of the parasite. Subsequent symptomatic presentations occurred only in the father and children. When all family members were treated at the same time, the symptoms and parasites were cleared, and to-date, several months later, the family remains symptom and parasite free.

Molecular testing, using C-profiling, was performed and both *D. fragilis* isolates from case #1 (patients #1 and #2) were shown to be different, indicating infection from a different source. C-profiling on case #2 samples also showed the strains were not identical. C-profiling is a method that has been used for the molecular epidemiological typing of *D. fragilis* that targets the internal transcribed spacer regions (ITS).[6] The ITS regions have been used extensively for phylogenetic analyses and as a molecular epidemiological marker of other parasites and in particular members of the Trichomonadidae.[6] The method detects intragenomic variation in the *D. fragilis* ITS region which leads from direct amplification of samples to sequencing fluorograms that are too complex to interpret, due to multiple ITS sequence variants in a single isolate. However, since the ITS regions of *D. fragilis* are extremely AT rich and the C-content is low by deleting fluorogram peaks representing the other nucleotides (A, T and G), it is possible to analyse C nucleotide residues producing chromatographs that are reproducible and easy to interpret. Bart *et al.* clearly demonstrated that the intragenomic variation of the ITS regions of *D. fragilis* can be used as a molecular epidemiological marker.[6] In both cases the *D. fragilis* strains were shown to be genotypically different, so it must be assumed that both patients obtained the infection from a different source.

Sticky-tape tests collected from all patients were negative for *E. vermicularis* and so it must be assumed that infection occurred by direct transmission. Recent studies have not shown a role for *E. vermicularis* in transmis-

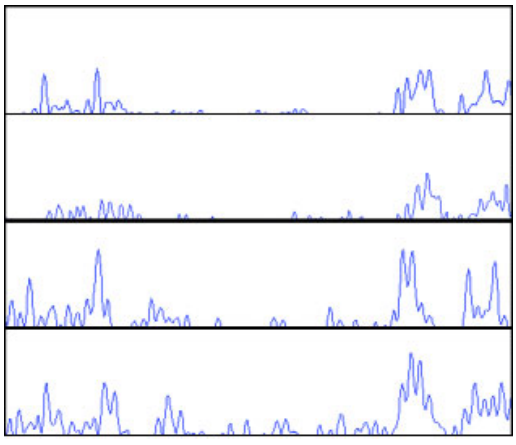

Figure 1. C-profiles from Case 1 and Case 2. From top to bottom Case 1 patient 1, patient 2, Case 2 father, Case 2 son.

sion of *D. fragilis*.[4]

This report highlights the repeated nature of some *D. fragilis* infections. Given that the organism can be treated effectively with a number of antimicrobial agents, all laboratories should provide a parasitological service capable of detecting this organism. All family members or those living in the same residence should be screened for *D. fragilis* as asymptomatic carriers may provide an ongoing source of infection.

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Salmonella typhimurium epidural empyema in an HIV-infected patient

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Abstract

Salmonella focal intracranial infections are reported rarely. They tend to occur in immunocompromised patients. We present here a case of *Salmonella typhimurium* epidural empyema, with osteomyelitis of the adjacent frontal bone, in a 37-year-old human immunodeficiency virus positive man who presented with a three-day history of headache, fever, and sweats. He was treated successfully with antibiotics and surgical drainage.

Introduction

Non-typhoidal salmonella (NTS) infection is a common occurrence among human immunodeficiency virus (HIV) infected patients, and salmonella bacteremia is a frequent finding. The estimated incidence of salmonellosis among patients with acquired immunodeficiency syndrome (AIDS) has been 20- to 100-fold more than that among the general population.[1] Before the era of AIDS, central nervous system (CNS) localization of NTS infection was reported rarely and meningitis was the most common location, described more frequently in children.[2,3] Salmonella focal intracranial infections are unusual in HIV infected patients. We report a case of an HIV patient with a *Salmonella typhimurium* infection presenting as epidural empyema, with adjacent osteomyelitis of the frontal bone.

Case Report

A 37-year-old HIV positive man presented at our department on December 10, 2007 with a three-day history of headache, fever, and sweats. Physical examination revealed a Glasgow coma score of 15/15, a temperature of 38.2°C, a blood pressure of 110/70 mm Hg, a pulse rate of 90 beats/min, and a respiratory rate of 20 breaths/min. No neurological deficit was detected. HIV infection was diagnosed 10 years ago, and antiretroviral therapy (zidovudine-didanosine-lopinavir/ritonavir) had been started in October 2007, when he had esophageal candidiasis with a CD4 cell count of 12/mm^3 (3%) and an HIV viral load of 110,000 RNA copies/mL.

The laboratory results showed low hemoglobin (11.1 g/dL), normal WBC count (6100/mm^3 with 4500 neutrophils), and normal platelets (349,000/mm^3). The prothrombin time was normal (75%), as were the values of glucose, creatinine, and electrolytes. Absolute CD4 cell count was 71/ mm^3 (9%). HIV viral load was not performed. On lumbar puncture the cerebrospinal fluid was normal. The chest X-ray was unremarkable. A contrasted computed tomography scan (CT) (Figure 1) and magnetic resonance imaging (MRI) (Figure 2) of the head revealed epidural empyema in the left frontal region, associated with adjacent osteolytic lesions in the frontal bone. There were no signs of brain herniation.

The patient was treated initially with parenteral cefotaxime (12 g daily) combined with metronidazole (1500 mg daily). Antiretroviral therapy was continued. After 48 hours of antibiotic therapy, fever resolved but the

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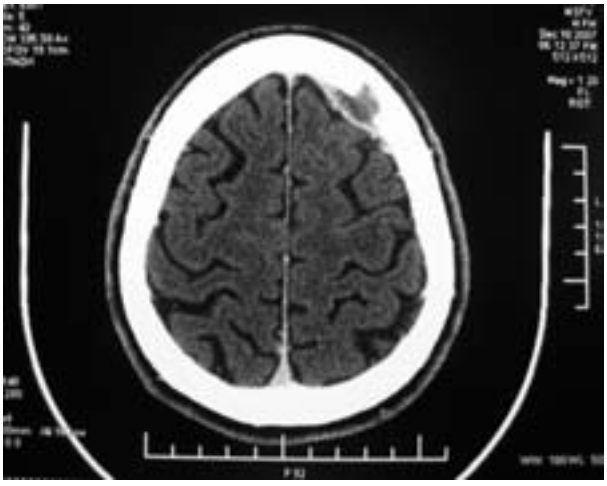

Figure 1. Computed tomography scan of the head showing a 4x1.5-cm left epidural lentiform hypodensity with an adjacent frontal bone defect.

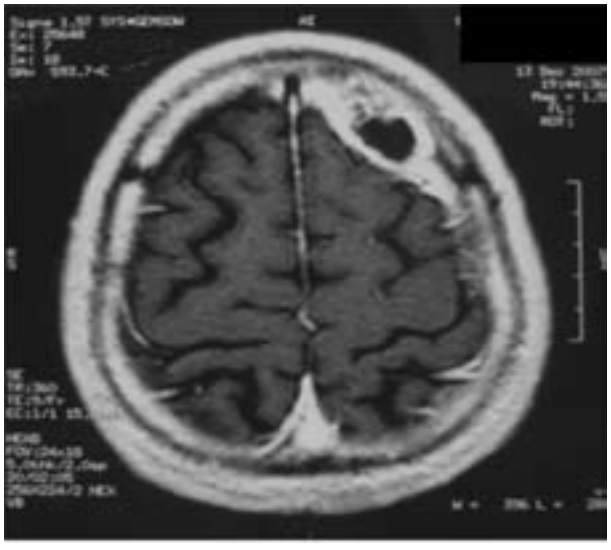

Figure 2. Enhanced T1–weighted magnetic resonance image showing a 5-cm epidural collection with adjacent osteolytic lesions in the left frontal area.

patient complained of persistant headache. A craniotomy was performed on December 14, producing epidural purulent fluid that was drained. Pus culture yielded a pure growth of a gram-negative bacillus, which was identified as *Salmonella typhimurium*. A disk diffusion susceptibility test showed the isolate to be susceptible to cefotaxime, ciprofloxacin, and choramphenicol, but resistant to amoxicillin and cotrimoxazole. The antibiotic therapy was changed to ciprofloxacin per os (1000 mg daily). Within two days following the drainage of the fluid collection, the headache subsided. Blood cultures showed no growth after seven days of incubation. Stool culture was not performed. The patient was discharged without any neurological complications. Ciprofloxacin was continued for a period of 12 weeks. A repeat CT scan of the head performed at the end of antibiotic therapy showed the resolution of the epidural empyema (Figure 3). At nine months of follow-up, the patient remained clinically very well. Viral load was of <25 RNA copies/mL and CD4 cell count was 198/mm^3 (12%).

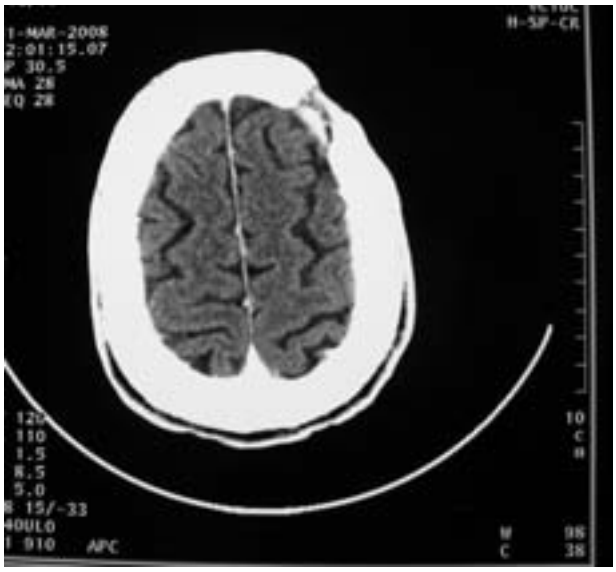

Figure 3. Computed tomography scan of the head performed at the end of antibiotic therapy showing the removal of the epidural empyema.

Discussion

The incidence of NTS infection among patients with AIDS exceeds that among the general population.[1] Frequently salmonellosis in this population is complicated by bacteremia, especially in patients with CD4 counts of <100/mm^3.[4] However, suppurative complications, particularly those affecting the CNS, have been reported rarely.[1] NTS meningitis is the most common location of CNS salmonella infection, but remains rare.[5] Either brain abscess, subdural empyema, or epidural empyema mostly occurs as a complication of salmonella meningitis, but may be an isolated infection.[6,7] Our patient had epidural empyema without meningitis. *S. enteritidis* and *S. typhimurium* are the most frequently encountered serotypes associated with salmonella CNS infections.[8]

NTS are food-borne pathogens that primarily cause gastroenteritis, then can reach the bloodstream via the lymphatics, especially in immunocompromised persons.[8] However, not all individuals with invasive NTS infections have concurrent diarrhea or isolation of the bacteria from the stool.[9] In a Spanish study, only 34% of AIDS patients with NTS bacteremia had diarrhea, and salmonella were isolated from the stools in only 4%.[9] Sarria *et al.*, in their study of 11 cases of *S. enteritidis* brain abscesses, found antecedent gastroenteritis in only four patients.[6] Neither intestinal infection nor salmonella bacteremia had been detected in our patient. However, the possibility of transient hematogenous spread of *S. typhimurium* from a pre-existing asymptomatic intestinal infection could not be eliminated.

Although NTS localized infection has not been reported in the literature as a possible manifestation of immune restitution syndrome, we think this supposition could be advanced for our patient. In fact we observed this infection two months after the beginning of antiretroviral therapy, concomitant with an increase of CD4 count. However, our hypothesis lacked the HIV viral load decrease parameter, which was not available when this NTS infection was diagnosed.

Clinical symptoms associated with epidural empyema are nonspecific: headache, fever, seizures, decreased level of consciousness, focal neurological deficit. In our patient, these symptoms were limited to headache and fever. Consequently the diagnosis often is unsuspected or delayed. Therefore early imaging studies, namely CT scan and MRI of the head, are required to make a prompt diagnosis.[6]

Our patient had skull osteomyelitis complicating the epidural empyema. Salmonella skull osteomylitis is extremely rare. It has been noted in two patients with salmonella brain abscess before the era of AIDS.[10,11] More recently Mastroianni *et al.* reported a case of frontal salmonella osteomyelitis without intracranial complications in an HIV patient,[12] and Aliaga *et al.* reported a case of salmonella subdural and epidural cerebral empyema with concomitant osteomyelitis of the frontal bone in an HIV patient.[13] In addition salmonella osteomyelitis associated with epidural infection was described in patients with sickle cell disease.[14,15]

High mortality rates have been reported for patients with intracranial infections caused by NTS, and a significant number of survivors developed permanent neurological sequelae.[7,16] Treatment failure was observed particularly when antibiotics were used alone without surgery.[15] The use of an adequate antimicrobial regimen combined with early surgical drainage will result in the best probability of cure.[7,17] The most reliable choices appear to be third-generation cephalosporins and fluoroquinolones because of their high activity against most salmonella strains with high brain tissue and CSF concentrations. Either chloramphenicol or cotrimoxazole could be used as an alternative drug if there is a contraindication to cephalosporins and quinolones.[16] The recommended duration of treatment is at least four weeks in meningitis and at least six weeks in brain abscess or empyema.[16,17] Our patient received prompt antimicrobial therapy and surgical drainage, and the duration of antibiotic therapy was prolonged to 12 weeks because he had skull osteomyelitis. He was cured without any sequelae and no relapse was noted at nine months of follow-up.

Conclusions

Salmonella focal intracranial infections are rare but should be considered by clinicians as a cause of acute CNS disorder in patients with advanced HIV disease. Early diagnosis and treatment are important in order to improve the prognosis of this CNS infection.

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