Review articles

Neuroinvasions caused by parasites

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ABSTRACT. Parasitic diseases of the central nervous system are associated with high mortality and morbidity. Many human parasites, such as *Toxoplasma gondii*, *Entamoeba histolytica*, *Trypanosoma cruzi*, *Taenia solium*, *Echinococcus* spp., *Toxocara canis*, *T. cati*, *Angiostrongylus cantonensis*, *Trichinella* spp., during invasion might involve the CNS. Some parasitic infections of the brain are lethal if left untreated (e.g., cerebral malaria – *Plasmodium falciparum*, primary amoebic meningoencephalitis (PAM) – *Naegleria fowleri*, baylisascariosis – *Baylisascaris procyonis*, African sleeping sickness – African trypanosomes). These diseases have diverse vectors or intermediate hosts, modes of transmission and endemic regions or geographic distributions. The neurological, cognitive, and mental health problems caused by above parasites are noted mostly in low-income countries; however, sporadic cases also occur in non-endemic areas because of an increase in international travel and immunosuppression caused by therapy or HIV infection. The presence of parasites in the CNS may cause a variety of nerve symptoms, depending on the location and extent of the injury; the most common subjective symptoms include headache, dizziness, and root pain while objective symptoms are epileptic seizures, increased intracranial pressure, sensory disturbances, meningeal syndrome, cerebellar ataxia, and core syndromes. Many early symptoms of CNS invasion are often nonspecific therefore a diagnosis can be difficult. This article presents the epidemiology, pathophysiology and clinical manifestations of selected parasitic neuroinfections.

Key words: parasite, central nervous system, neuroinvasion, encephalitis, meningoencephalitis

Introduction

Infection of the central nervous system (CNS) by a parasite is considered a serious complication. Generally, while species specific to humans, except *Plasmodium falciparum* and *Taenia solium*, occur mainly accidentally in CNS (ectopic locations), a relatively large number of animal parasites have been found in the human brain or spinal cord (e.g. *Toxoplasma gondii*, *Toxocara canis*, *T. cati, Echinococcus* spp., *Angiostrongylus cantonensis*, *Trichinella* spp.). Some parasitic infections of the brain are lethal if left untreated (e.g., *Plasmodium falciparum*, *Naegleria fowleri*, African trypanosomes), but others can be controlled by the host immune response and can remain for many years as a chronic infection (e.g., *Toxoplasma gondii*, *Trypanosoma cruzi*). Table 1 summarizes a list of parasites from different taxonomic groups that cause neuroinfections in humans. Some examples of endemic neuroparasitic infections are malaria, angiostrongylosis, gnathostomosis, loaosis, baylisascariosis, alveolar echinococcosis, paragonimosis and cysticercosis, while the most common cosmopolitan parasitoses are toxoplasmosis, toxocarosis, cystic echinococcosis and trichinellosis. The signs of CNS invasion depend upon the number and location parasites, and the host immune response. The epidemiology, pathophysiology and clinical presentation for selected parasitic neuroinfections are reviewed in this article. Some issues related to parasites involved in CNS disorders in humans were presented during the 56th Clinical Day of Medical Parasitology – 56. DKPL (Lodz, 2nd June 2017).

Protozoa infections of the CNS

Plasmodium falciparum

The World Health Organization reports that in 2015, 212 million new cases of malaria were reported worldwide, of which around 90% were caused by *Plasmodium falciparum*; there were 429,000 deaths from malaria globally. Cerebral malaria (CM) is the most severe complication, affecting up to 7% of all *P. falciparum* malaria cases, and is one of the most common causes of CNS infection in the world [1]. In the course of CM, mortality is estimated to range from 30% to 50%, with higher values observed in the pediatric population. CM is defined as a febrile and mainly diffuse encephalopathy, with impairment of consciousness being a prominent feature. Unarousable coma may be preceded by severe headache, confusion, drowsiness and in many instances, convulsions. WHO guidelines require the following criteria to be fulfilled for a diagnosis of CM to be confirmed: the coma is not attributable to any other encephalopathy, it is awarded a Glasgow Coma Scale score <11 and that it should persist for at least 30 minutes after a generalized convulsion. Brain swelling, intracranial hypertension and brain stem signs are commonly observed [2].

The typical pathological features of this disease include adhesion and sequestration of *P. falciparum*-infected red blood cells in brain microvessels, ring hemorrhages and Dürck's granulomas. Adult patients with CM demonstrate the presence of axonal injury and blood-brain barrier dysfunction. Extracerebral manifestations aggravating the encephalopathy typically include anemia-hypoxemia-hypoxia, thrombocytopenia, renal and hepatic failure, pulmonary edema, hypotension and bleeding and clotting disturbances [3]. One presentation at the 56th Clinical Day of Medical Parasitology (N. Nowak, Ł. Pielok, J. Stefaniak, UM Poznan) presented a severe case of malaria caused by *P. falciparum* in a 60-year-old patient who returned after a one-week stay in Burkina Faso; in the first days after admission to the clinic, blood parasitemia was 2%, and – the neurological symptoms were accompanied by acute renal failure. Disseminated intravascular coagulation (DIC) is seen in <5% of patients with severe *P. falciparum* malaria and is relatively often observed in cerebral malaria [4]. Infection of red blood cells by *P. falciparum* leads to changes in cell surface proteins and the expression of new proteins, such as PfEMP-1 (*P. falciparum*

erythrocyte membrane protein 1) and MESA (the mature parasite-infected erythrocyte surface antigen). The intracellular adhesion molecule ICAM-1 is the major cellular ligand which conditions the sequestration erythrocytes in cerebral vessels. It has been recently demonstrated that the binding of the parasite to the endothelial protein C receptor (EPCR) is associated with severe malaria [5]. In addition, infected erythrocytes tend to connect with the ABO blood group antigens (particularly group A), receptor 1 (CR1), heparan-sulfate proteoglycans (HSPG) and other membrane antigens of uninfected erythrocytes, forming rosettes that clog the capillaries. Moreover, capillary obstruction is caused by the massive accumulation of immune complexes with the participation of complement components of C3 and C4 [1].

Toxoplasma gondii

It is estimated that antibodies against *Toxoplasma gondii* can be identified in 30% of all humans; this rate varies greatly from 6 to 90% worldwide, depending on the local population. The incidence of primary neurotoxoplasmosis (NT) in immuno-competent individuals is very low, i.e. below 0.02% [6]. NT can often develop or reactivate in immuno-compromised patients, such as those with AIDS, neoplastic diseases and organ transplants. Cerebral toxoplasmosis is an opportunistic parasitic infection, and is a frequent complication of AIDS when the lymphocyte CD4+ cell count drops below 100 cells/mm^3. In Europe, the prevalence of encephalitic toxoplasmosis in HIV-positive patients is reported to be 30–40%, with a mortality rate of 20%. NT is found in 10 to 34% of autopsies on patients with HIV/AIDS. The most common presenting symptom of NT is headache, which is often accompanied by fever, motor weakness, altered mental status, speech and visual disturbances, seizures and cranial nerve abnormalities. The most commonly affected areas in the CNS include the basal ganglia and corticomedullary junction. Tissue cysts (with bradyzoites) in the brain are often spheroidal and usually range in size from 5–50 μm in diameter; however, in rare cases, they can reach over 1 cm [7]. Cerebral toxoplasmosis is characterized by multiple masses of lesions with surrounding vasogenic edema; hemorrhages are occasionally present in the periphery of the lesion. Congenital infection (CT) occurs predominantly after primary infection of a pregnant woman and is usually asymptomatic in the newborn period (75%

of infected newborns). CT has a broad spectrum of nonspecific clinical manifestations; the classic triad of signs (chorioretinitis, intracranial calcifications, hydrocephalus) occurs in 5 to 10% of CT cases. Congenital infection is estimated to be 0.5 of 10,000 live births in the United States, and 2.9 of 10,000 live births in France; however, the incidence of acute infection among *Toxoplasma*-seronegative pregnant women was calculated to be 0.2/1000 in USA and 2.1/1000 in France [8]. Additionally, in 14 to 85% of infected children who did not display symptoms of CT as neonates, chorioretinitis, blindness, hydrocephalus or microcephaly, cerebral calcifications, developmental delay, epilepsy, or deafness may develop after a few months or years [9].

Trypanosoma brucei gambiense/T. brucei rhodesiense

African sleeping sickness is caused more frequently by *Trypanosoma brucei gambiense*, comprising 97% of cases, than *T. brucei rhodesiense*, comprising only 3% [10]. In humans, parasites are found only in the form of trypomastigota, and are transmitted by flies from the genus *Glossina*. *T. brucei gambiense* occurs in West and Central Africa and *T. brucei rhodesiense* in East and Central Africa. The threat of invasion concerns 70 million people. The incidence of infections is falling, with only 3,000 new infections reported in 2015. According to WHO data, worldwide there are about 20,000 infected people [10]. In the course of the disease, CNS involvement occurs via the choroid plexus and circumventricular organs (the postrema, pineal gland, median eminence, dorsal root ganglia), and then crosses the blood-brain barrier without interfering with the endothelium [11]. *T. brucei gambiense* infection is usually of a chronic nature, and the first symptoms show up within a few months to several years after the invasion. In the case of *T. brucei rhodesiense*, the disease is acute and severe, and incubation may last only a few weeks [10,12].

The first stage of the disease is the hemolymphatic stage, in which the forms of trypomastigota multiply in the blood, lymph and peripheral organs. The second stage is meningo-encephalitis, which appears after CNS involvement [10]. Cloudy leptomeninges and a swollen brain are observed in the CNS. The histopathological changes include white matter of the hemispheres, thalamus, hypothalamus, basal ganglia, brainstem and cerebellum. Lymphocytic infiltrates, microglia

hyperplasia, astrocylial proliferation and formation of microglial nodules are visible. Very characteristic of infection are morular (mulberry-like) cells or Mott cells; these bear a small peripherally-located nucleus and eosinophilic inclusions (Russel body) in the cytoplasm, with IgM immunoglobulin on their surface [10,12]. Trypomastigota are rarely observed in the brain.

In the pathogenesis of the disease the B-cells are reactivated by the parasite. The antibodies produced by the B-cells can operate simultaneously as self-antigens by the host, especially against components of the myelin sheath: myelin basic protein, galactocerebrosides, gangliosides and neuro-filament proteins. In addition, due to molecular mimicry, the antigens of *Trypanosoma* sp. resemble host antigens, resulting in the occurrence of cross-reactions [12]. Activated CD8+ T-cells produce numerous proinflammatory cytokines, e.g. INF-γ, TNF-α and IL-2, which can allow parasites to cross the blood-brain barrier. The other host cells produce increased amounts of prostaglandins, especially PGD2, which stimulate cytokine formation. Pro-inflammatory cytokines may affect the sleep regulation center, which is associated with the last stage of the disease: coma [10,12].

One of the drugs used in the treatment is melarsoprol. Unfortunately, 5–10% of treated patients demonstrate an exacerbation of symptoms to encephalopathy, with mortality in such cases reaching 50–70% [12,13].

Trypanosoma cruzi

Chagas disease is caused by the flagellate *Trypanosma cruzi*, transmitted by triatomic bugs, mostly in endemic areas of Latin America [14]. The infection affects eight million people worldwide. The trypomastigota form invades the lymphatic tissue while the amastigota form invades the cardiac muscle cells, esophagus, intestines, and vascular endothelium [15]. CNS involvement occurs in some patients, both during the chronic and acute forms of disease and during reactivation of latent infection. *T. cruzi* enters the epithelium of blood vessels in the CNS, then moving into astrocytes and microglial cells, or by choroid plexus and cerebrospinal fluid [12,14,16]. Such cases present with congestion, edema, scattered petechial hemorrhages and encephalitis. Histopathological examination reveals the presence of amastigota in astrocytes and microglia. Infected patients also have altered mental status, seizures, fever, menigism, focal neurological

deficits and headaches.

Unfortunately, the symptoms of meningo-encephalitis caused by *T. cruzi* are indistinguishable from those caused by other pathogens, e.g. *Toxoplasma gondii*; and in the course is often combined with myocarditis [12,17,18]. From 10 to 35% of patients experience cerebral infarcts, 51.6% display micronecrosis in cerbral cortex, 16.1% display laminal cortical necrosis, and 3.2–15.7% cerebral cortical atrophy. Silent brain microemboli are also reported in many patients. In severe cases, the treatment of encephalitis and myocarditis is ineffective, with mortality reaching 100% [12,17, 18].

Reactivation of the invasion of CNS and heart, and their involvement, is more common in immunosuppressed patients, those with AIDS or with hematologic malignancies, organ transplant recipients and patients treated with corticosteroids [19,20]. In these patients, hemorrhagic and necrotizing lesions with numerous amastigotes and single or multiple necrotic-hemorrhagic nodules may develop, most often within the white matter of the cerebral lobes [12]. The immune response of the organism in the CNS invasion corresponds to the level of CD4+ and CD8+ T lymphocytes and IL-2 and IL-4 proinflammatory cytokines. The most severe disease is seen in patients with level of CD4+ T cells below 200 cells/µl [12,20]. However, experimental studies on mice identified reactivation of invasion in the absence of active INF-γ and IL-12 genes [12].

Neurological changes, among others, menigno-encephalitis, microcephaly, brain calcifications and seizures have also been reported in the congenital Chagas' disease. Fetal infection occurs with a prevalence of 1–10% in infected mothers. In newborns, trypomastigota forms have also been found in the cerebrospinal fluid [20].

Entamoeba histolytica

Entamoeba histolytica is pathogenic amoeba, associated with intestinal and extraintestinal infections (liver, lung, brain). Cerebral amoebosis (CA) has an incubation period starting from a few days to several months and generally develops as a complication of hepatic amoebosis (0.6% of amoebic liver abscess cases). The risk factors encouraging the development of invasive amoebosis are very young age, malnutrition, compromised innate immunity and treatment with high-dose corticosteroids. Brain abscess is often characterized by an abrupt onset of symptoms, which result in rapid progression and early death if untreated. Computed tomography (CT) reveals the presence of irregular lesions without a surrounding capsule, with trophozoites detected in tissue biopsy samples [21]. Amoebic brain abscesses may be single or multiple, their most common sites of involvement being the frontal lobes.

The literature data shows the average age of the patient with CA to be 30 years, and common initial symptoms include headache, vomiting, and altered mental status. Signs of amebic brain abscess include most commonly meningeal signs, facial nerve (VII) palsy, motor paralysis, and seizure. Intestinal symptoms have been found in 50% of cerebral amoebosis cases. A rare case of multilocus brain abscess due to *E. histolytica* infection in an 11-year-old girl was recently described; she presented with progressive drowsiness, diminished movements of the left upper limb and swallowing problems [22]. Most patients have abnormalities in the cerebrospinal fluid but parasites are rarely detected [21]. Goh and Marrone [23] reported the first case of *E. histolytica* meningoencephalitis diagnosed by the presence of motile trophozoites in the cerebrospinal fluid in a 16-month-old Polynesian boy without liver or brain abscesses. It is important to note that computed tomography can be negative in the early stages of encephalitis.

Free-living amoebae

Naegleria fowleri is a free-living amoeba that is commonly found in warm freshwater. Humans most commonly become infected with *N. fowleri* while swimming and diving in natural warm water reservoirs (lakes, rivers), and less frequently in swimming pools with inadequately chlorinated water. The amoebas enter the nasal cavity along with the water and migrate along the olfactory nerve to the brain. The incubation period of primary amoebic meningoencephalitis (PAM) may range from one to a few days. Only trophozoites have been identified within the brain and cerebrospinal fluid (CSF). *In vitro* studies have shown that *N. fowleri* destroys nerve cells through trogocytosis (piecemeal ingestion). Naegleriosis characterized by evere headache, stiff neck, fever (38.5–4°C), altered mental status (mainly confusion), hallucinations, cerebral ataxia (with demonstrable Kernig's and Brudzinski's indications), seizures and coma. The fatality rate associated with PAM has remained over 95% [24]. Increased intracranial

pressure and brain herniation are usually the cause of death. In the advanced stage of PAM, the number of red blood cells increases up to 24,600 per mm^3 CSF, and white blood cells to 26,000 per mm^3 CSF, while the protein and glucose concentration ranges from 100 mg to 1000 mg per 100 mL CSF and 10 mg per 100 mL CSF, respectively [25].

Until 2012, over 310 cases of PAM had been reported worldwide, with most incidents reported in the United States, Australia, and Europe (mainly in France). Recently, one hospital, the Aga Khan University Hospital in Karachi (Pakistan), reported approximately 20 of deaths due to PAM annually [24]. Recent data from the United States note two fatal cases of *N. fowleri* infection in four and 14-year-old boys after swimming in warm fresh water in the summer months [26]. Additionally, a direct association was found between a fatal case of PAM in a four-year-old boy from Mississippi and the presence of *N. fowleri* in tap water at his home and in the water distribution system [27]. Moreover, in 2012, two fatal cases of PAM were reported in a 28-year-old man and 51-year-old woman from Louisiana who used contaminated tap water for nasal irrigations [28].

It should be noted that a course of PAM is acute, fulminant, and leads to necrotizing, and hemorrhagic meningoencephalitis, and that it affects both immunocompromised and immunocompetent hosts [29]. In contrast, infection by other free-living amoebae, *Balamuthia mandrillaris* and *Acanthamoeba* spp., results in other neuroinfection – GAE (granulomatous amoebic encephalitis) which characterized by a chronic protracted slowly progressive development. The incubation period is longer and ranges from weeks to months. These CNS infections are reported to occur mostly in immunocompromised individuals (e.g. posttransplantation, HIV infection), and occasionally in immunocompetent hosts. Numerous trophozoites, and possibly cysts, are observed, which accumulate around the blood vessels. Most patients present with focal neurologic deficits associated with signs of increased intracranial pressure; common symptoms include fever, headache, confusion, visual disturbances, ataxia, and seizures. The mortality rate from CNS amoebic infections remains extremely high and may exceed 90% [30]. Moreover *Acanthamoeba* spp. can cause serious eye infections, especially in contact lens wearers (*Acanthamoeba* keratitis) [31].

Helminth infections of the CNS

Taenia solium

According to the WHO, *Taenia solium* cysticercosis is one of the 17 major Neglected Tropical Diseases (NTDs). It is a zoonotic parasitosis responsible for severe health disorders such as seizures and death in cases of non-treatment. People can be infected by embryonated eggs (oncospheres), which can develop into *cysticercus cellulosae* (cysticerci, encysted larvae) in the muscles, the eyes, the brain and the spinal cord. This helminth invasion occurs in many economically poor countries, especially with warm and mild climates; the highest prevalence of *T. solium* is noted in endemic areas including Latin America, South Asia and South-East Asia, and sub-Saharan Africa [32]. It was estimated that in 2010 approximately 370,710 individuals were infected with *T. solium* cysticercosis globally, resulting in over 28,000 deaths [33]. In endemic areas of *T. solium* invasion, epilepsy is the most common clinical symptom among patients diagnosed with neurocystocercosis (NC); the frequency of NC cases among people with epilepsy has been estimated to be 29% [34]. In turn, the global burden of NC has been estimated be over 2.78 million DALYs per annum. The signs of NC depend upon the number, location and stage of cysticercial degeneration and the host immune response.

The most common type of cyst location is parenchymal (60% to 92% patients with NC) although extra parenchymal areas are also affected: the meninges, ventricles, subarachnoid space of the brain and the spinal cord. On the basis of radiological findings, neurocysticercosis (cysticercus larvae embedding in the parenchyma) is divided into five stages: noncystic, vesicular, colloidal vesicular, granular nodular, and calcified nodular [35]. The racemose variety of NC, caused by *cysticercus racemosus* (cluster of cysts), is characterized by involvement of the ventricular system and subarachnoid spaces. Cysticercus larvae are most commonly associated with symptoms caused by mass effect or by the blockage of cerebrospinal fluid circulation. However, most symptoms in NC are the direct result of the inflammatory process. Clinical manifestations include epilepsy (70-90% of symptomatic patients), intracranial hypertension, hydrocephalus, chronic meningitis, and cranial nerve abnormalities [35].

Echinococcus spp.

In humans, the larval stage of *Echinococcus granulosus* and *Echinococcus multilocularis* cause cystic echinococcosis (CE) or alveolar echinococcosis (AE), respectively. The former is a cosmopolitan tapeworm, while *E. multilocularis* is present in the northern hemisphere. Humans can become infected through the accidental consumption of *Echinococcus* eggs excreted with the feces of definitive hosts: dogs, foxes, and other canids. Cerebral hydatid cysts occur with frequency of 1–2% of all cases of CE [36]; they grow slowly and remain asymptomatic for a long time. Brain CE commonly occurs in pediatric populations. Studies have shown that most patients present with focal neurological deficits or signs of raised intracranial pressure, depending upon the size and location of the hydatid cysts which generally occur in the area of the middle cerebral artery and posterior fossa. Multiple cerebral cysts are very rare. Basarslan et al. [37] reported three multiple intracranial hydatid cysts (total mass 122×110×98 mm) in a 14-year-old child without any neurological deficit.

It should be emphasized that a diagnosis of CE, especially with an abnormal course is difficult (A. Szlauer-Stefańska, B. Szlauer, A. Misiewska-Kaczur, M. Sulima, A. Lass, B. Szostakowska; GUMed, 56.DKPL). False negative blood serum tests for detection *E. granulosus* infection are observed in about 20% of cases. Due to the interpretation difficulties of imaging studies, a biopsy is needed to obtain material for molecular analysis but it is not always possible, especially when hydatid cysts are localized in CNS.

For *E. multilocularis*, the human is an occasional intermediate host in which the oncospheres develop alveolar hydatid cysts without the envelope of the connective tissue of the host. Cerebral occurrence of AE is rare, accounting for only 1% of the patients with hepatic AE, and most frequently leads to death: mortality rates have been found to be as high as 80% [38]. Symptoms of AE appear on average 10 years after invasion. Patients with cerebral cysts typically present with increased intracranial pressure, epilepsy, neurological disturbances such as dysarthria and hemiparesis, and cranial nerve palsies [39].

Toxocara spp.

Neurotoxocarosis (NT) is caused by the invasion of larvae belonging to the species *Toxocara canis* and *Toxocara cati*, which can enter the leptomeninx, gray and white matter of the brain or cerebellum, and spinal cord of infected humans [40]. Before April 2015, over one hundred cases of NT had been described in the literature [41]. It is worth emphasizing that cases were most often reported in male adults (58 % of all cases), with a median age of 42 years. Although human toxocarosis is one of the most common zoonotic helminth infections, NT is rare in pediatric patients. OUN infection often occurs without neurological symptoms, but in symptomatic cases there is no single, clearly defined set of symptoms. Invasion of larvae to the SCS can cause headaches, behavioral changes and occasionally convulsions. The predominant clinical manifestations are myelitis (60%), encephalitis (47%) and/or meningitis (29%), while fever was

Table 1. Selected parasites that cause CNS infection in human

Protozoa	Cestoda	Trematoda	Nematoda
Acanthamoeba spp.	*Echinococcus granulosus*	*Alaria americana*	*Angiostrongylus cantonensis*
Babesia spp.	*E. multilocularis*	*Paragonimus* spp.	*Ascaris suum*
Balamuthia mandrillaris	*Spirometra* spp.	*Schistosoma mansoni*	*Baylisascaris procyonis*
Entamoeba histolytica	*Taenia multiceps*	*S. hematobium*	*Gnathostoma spinigerum*
Naegleria fowleri	*T. solium*	*S. japonicum*	*G. hispidum*
Plasmodium falciparum		*S. mekongi*	*Loa loa*
Toxoplasma gondii		*S. intercalatum*	*Strongyloides stercoralis*
Trypanosama brucei gambiense			*Toxocara canis* *T. cati*
T. brucei rhodesiense			*Trichinella* spp.
T. cruzi			

reported in 23% of cases [41]. NT can result in varying and atypical neurological manifestations. Neurotoxocarosis should be suspected in the event of any neurological syndrome associated with eosinophilia. If the patient has recently travelled abroad, differential diagnosis of eosinophilic meningitis/myelitis is more extensive and includes *Taenia solium*, *Gnathostoma spinigerum*, *Angiostrongylus cantonensis*, and *Baylisascaris procyonis*. The tissue damage caused in the course of these parasitoses can usually be attributed to the result of inflammatory reactions, as the larvae produce glycosylated proteins that induce a CD4-Th2 response with the production of IgE and interleukin-5; this ultimately promotes vascular adhesion and eosinophil differentiation [41].

Baylisascaris procyonis

As the main final host of the nematode *Baylisascaris procyonis* is the raccoon, it is no surprise that it occurs endemically in North America. However, studies conducted in the 1950s indicate a geographic expansion *B. procyonis* into Japan and some European countries, such as Germany and Russia, followed by further expansion into neighboring countries, including Poland. Humans become infected by accidental ingestion of invasive eggs excreted with the feces of raccoon; most cases of baylisascariosis have involved very young children. The growing number of final hosts associated with this nematode is an important fact from an epidemiological point of view; one such definitive host of this roundworm is the domestic dog which constitutes a potential reservoir of the parasite (D. Jańczak, W. Rożej-Bielicka, E. Gołąb; NIPH–NIH, 56.DKPL). In the United States, Canada and Japan, natural and experimental infections with *B. procyonis* have been described in dogs. Human infections with *B. procyonis* are rare, but they can be severe if the parasites invade the brain and the spinal cord. The symptoms of neural larva migrans (NLM) depend on the number of larvae and the inflammatory response of the host. In North America to date, NLM caused by *B. procyonis* has been diagnosed in over 20 humans; patients were mainly young children (<2 years) or individuals with mental disability or developmental impairment [42]. In Germany, a few cases of clinical baylisascariosis have been described in persons who had contact with the raccoons that were kept indoors [42]. It is assumed that the development of NLM occurs after eating a large

number of eggs. The autopsy study of the brain of an 18-month-old child detected 185 larvae in 60 g of tissue [43]. The vast majority number of the cases of human baylisascariosis are fatal or result in severe neurological sequelae. There is only one report in the literature of full recovery; this was observed in a four-year-old boy following very early medical intervention [44].

Trichinella **spp.**

Consumption of raw or undercooked meat may lead to infection with *Trichinella*. Trichinellosis has been reported in 55 countries around the world, and the incidence is dependent on the prevailing culinary habits [45]. There are as many as 12 species/genotypes of *Trichinella* sp. worldwide, with different geographical ranges and specificity for the host. For humans the greatest risk is associated with the consumption of raw pork, horse, boar and dog meat. Most invasions have been caused by *Trichinella spiralis* and *T. britovi*, less often by *T. madurrelli*, *T. pseudospiralis*, *T. nativa* and *T. nelsoni* [45]. Neurological changes in trichinellosis have been reported in 10–20% of patients, with mortality in these cases reaching 50% [46,47]. In acute phase of neuroinvasis, patients exhibit disturbances of consciousness, somnolence, apathy, anisokoria, facial nerve paralysis, disorientation, memory and behavioural disturbances, oculomotor disfunction and Babiński's sign. Meningitis or encephalopathy may also be associated with invasion [45]. Changes in the brain can be visualized in CT or MRI scans, in most cases changes in the brain disappear within four to eight weeks after proper therapy. In some patients, IgG antibodies appear two months after the end of the infection, and resolve within six months in 50% of those infected. All successfully-treated patients are found to be free of antibodies for up to three years following treatment [45].

During *Trichinella spiralis* invasion, Th2 and T regulatory lymphocytes were activated and the level of some proinflammatory cytokines, among others: IL-17, IFN-c, was decreased. These cytokines are important in the course of autoimmune encephalomyelitis. In the animal model, the use of antigens derived from *T. spiralis* has been shown to increase cytokine levels and decrease the severity of autoimmune encephalomyelitis [48].

Strongyloides stercoralis

Strongyloides stercoralis is a small nematode

that causes gastrointestinal parasitosis. It is estimated that between 30–100 million people are infected worldwide, of whom about 50% are show asymptomatic invasion [49,50]. In tropical countries *S. stercoralis* is one of the endemic species, in Africa the incidence of invasion is 0.6%, and 12.6% among HIV-infected patients, and in the USA alone from 0 to 3.8%, [49,51]. Mortality due to strongyloidosis is 80% in patients with HIV [49]. The most important risk factors for immuno-competent persons include travel to endemic countries and contact with soil. However, hyperinvasion may occur in immunosuppressed individuals infected with human T-lymphotropic virus type I (HTLV-1), or those with diabetes, hematological malignancies and alcohol addiction. In patients taking corticosteroids the risk of infection is three to four times higher [51]. Recipients of transplants, particularly the kidneys, and patients with lymphoma are also at increased risk of hyperinvasion. A significant role in the course of invasion is played by the level of T lymphocytes, especially the presence of an elevated Th1 cell count; this is associated with higher IFN-γ levels, reduced Th2 lymphocyte counts, and decreased IL-4 and IL-5 levels [49,51].

The invasive form of the parasite is a filariform larvae occurring in the soil, which actively penetrates undamaged skin. In the human body, the larva enters the bloodstream and travels to the lungs, bronchi and then through the trachea into the throat, where it is swallowed into the gastrointestinal tract and settles in the small intestine [15]. Each stage of the invasion is typified by symptoms associated with the migration of larvae (dermatitis, Loffler's syndrome) and the presence of the mature forms in the intestine, these include chronic diarrhoea, anorexia and vomiting [50]. In cases of auto-invasion, the CNS may also be invaded by filariform larvae, especially in patients with hyperinvasion. The most important symptoms of neuroinvasion include altered mental status, focal seizures, meningitis, cerebral abscesses, granulomatus inflammatory reaction, and obstruction of small vessels with micro-infarcts [12,50]. In hyperinvasion the larvae pass through the intestinal wall and, together with the bloodstream, can enter the other organs. In a few cases, larvae have been found in the cerebrospinal fluid [52]. In addition, on the surface of the epidermis or in the gut, the larvae can carry Gram-negative bacteria including *Escherichia coli*,

Proteus mirabilis, *Klebsiella pneumoniae*, *Enterococcus faecalis*, *Streptococcus bovis*; which promotes bacterial menigitis and bacteremia [12, 50–52].

Angiostrongylus cantonensis

In humans *Angiostrongylus cantonensis* (syn. *Parastrongylus cantonensis*) causes eosinophilic meningitis infections (cerebral angiostrongylosis – CA); this is particularly common in endemic regions of the world such as Southeast Asia, China, the Pacific Basin, Caribbean, and recently South America [53]. To date, more than 100 local CA cases have been documented in Hawaii, which accounts for around 90% of cases in the United States. In Europe, neuropathies due to this nematode have been reported in people traveling to tropical or subtropical climates. *Rattus norvegicus* and other rodents have a predominant role as definitive hosts of *A. cantonensis*, while various species of molluscs, fish, shrimp, amphibians, reptiles can act as paratenic hosts and as sources of human infections.

Humans become infected after ingestion of L3 larvae which migrate to the CNS where they develop into stage L4 or L5 larva and die. The larvae of *A. cantonensis* are neurotropic; they exclusively present in brain and spinal cord, several days to weeks post-infection [54]. The main symptoms are associated with inflammation in the CNS. Interleukin 5 was the first factor identified in the larval killing mechanism. Symptoms develop after an incubation period of up to two weeks. Typical clinical manifestations of neuro-angiostrongylosis include severe and persistent headache, fever, neck stiffness, paraesthesia, and cranial nerve palsy. This parasitosis is fatal in at least 3% of all cases [55].

Gnathostoma spp.

Two species of nematode which infect vertebrate animals may cause human gnathostomosis by migrating larvae: *Gnathostoma spinigerum* and *Gnathostoma hispidum*. This parasitosis occurs mainly in Southeast Asia, South and Central America, and in some areas of Africa. Humans become infected primarily by eating undercooked or raw freshwater fish, frogs, birds, and reptiles containing third-stage larvae [56]. The most severe manifestation of the visceral disease is neurognathostomosis, which includes involvement of the CNS; the parasite can enter the brain,

resulting in paralysis, coma and death. Studies have reported mortality rates of 7% to 12% [57]. The migrating larvae in the CNS cause direct mechanical injury. Subarachnoid hemorrhage can result from larvae passage through a cerebral arteriole. Eosinophilic meningitis caused by *Gnathostoma* spp. is characterized by the presence of erythrocytes in the cerebrospinal fluid (CSF).

Loa loa

Endemic areas for loaosis include West and Central Africa. According to the CDC, about 14.4 million people live in areas with high rates of infection. *Loa loa* encephalitis may occur either spontaneously or following chemotherapy. A few reports have identified direct CNS involvement from *Loa* infections [58,59]; meningoencephalitis and encephalitis have been noted in patients with loaosis. A high density of microfilaria (> 30,000 per ml) is a favorable factor for the development of encephalopathy. However this parasitic neuro-infection is usually a consequence of treatment with dimethyl carbamizine citrate or ivermectin. The symptoms occur gradually, starting two days after treatment and the condition of the patient generally becomes serious after three to five days. Encephalitis in patients with loaosis may involve massive death of microfilariae, leading to vascular embolism and inflammation [58].

References

[1] Hora R., Kapoor P., Thind K.K., Mishra P.C. 2016. Cerebral malaria-clinical manifestations and patho-genesis. *Metabolic Brain Disease* 31: 225-237. doi:10.1007/s11011-015-9787-5

[2] Idro R., Marsh K., John C.C., Charles R.J., Newton C.R.J. 2010. Cerebral malaria: Mechanisms of brain injury and strategies for improved neuro-cognitive outcome. *Pediatric Research* 68: 267-274. doi:10.1203/PDR.0b013e3181eee738

[3] Misra U.K., Kalita J., Prabhakar S., Chakravarty A., Kochar D., Nair P.P. 2011. Cerebral malaria and bacterial meningitis. *Annals of Indian Academy of Neurology* 14 (Suppl. 1): 35-39. doi:10.4103/0972-2327.83101

[4] Sailo L., Pradhan D., Nongthombam R., Bhattacharyya P. 2014. Disseminated intravascular coagulation in malaria: a case report. *Nigerian Medical Journal* 55: 171-172. doi:10.4103/0300-1652.129665

[5] Bernabeu M., Smit J.D. 2017. EPCR and malaria severity: The center of a perfect storm. *Trends in Parasitology* 33: 295-308. http://dx.doi.org/10.1016/j.pt.2016.11.004

[6] Ramachandran R., Radhan P., Anand R., Subrama-nian I., Santosham R., Sai V. 2014. CNS toxo-plasmosis in an immunocompetent individual. *Radiology Case Reports* 9: 908. doi:10.2484/rcr.v9i1.908

[7] Ozaras R., Karaismailoglu B., Vatan A., Hasiloglu Z., Sahin S., Oz B. 2016. Cerebral toxoplasmosis. *International Journal of Medicine* 109: 491-492. https://doi.org/10.1093/qjmed/hcw044

[8] Peyron F., McLeod R., Ajzenberg D., Contopoulos-Ioannidis D., Kieffer F., Mandelbrot L. 2017. Congenital toxoplasmosis in France and the United States: One parasite, two diverging approaches. *PLoS Neglected Tropical Diseases* 11: e0005222. doi:10.1371/journal.pntd.0005222

[9] McAuley J.B. 2014. Congenital toxoplasmosis. *Journal of the Pediatric Infectious Diseases Society* 3: 30-35. doi:10.1093/jpids/piu077

[10] Rodgers J., Bradley B., Kennedy P.G.E. 2017. Delineating neuroinflammation, parasite CNS invasion, and blood-brain barrier dysfunction in an experimental murine model of human African trypanosomiasis. *Methods* 127: 79-87. doi:10.1016/j.ymeth.2017.06.015

[11] Mogk S., Meives A., Boßelmann C.M., Wolburg H., Duszenko M. 2014. The lane to the brain: how African trypanosomes invade the CNS. *Trends in Parasitology* 30: 470-477. doi:10.1016/j.pt.2014.08.002

[12] Pittella J.E.H. Pathology of the CNS parasitic infection. 2013. In: *Handbook of Clinical Neurology*. (Eds. H. Garcia, H. Tanowitz, O. Del Brutto). vol. 114. Elsevier: 65-88.

[13] Checkley A.M., Pepin J., Gibson W.C., Taylor M.N., Äger H.R., Mabey D.C. 2007. Human African trypanosomiasis: diagnosis, relapse and survival after severe melarsoprol-induced encephalopathy. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 101: 523-526. doi:10.1016/j.trstmh.2006.12.001

[14] Simioli F., Sanchez-Cunto M., Velazquez E., Loveras S., Orduna T. 2017. Chagas Disease in the central nervous system in patient infected with HIV: diagnostic and therapeutic difficulties. *Revista Chilena de Infectologia*. 34: 62-66. doi:10.4067/S0716-10182017000100009

[15] Błaszkowska J., Ferenc T., Kurnatowski P. 2017. Zarys parazytologii medycznej. Edra, Urban & Partner, Wrocław (in Polish).

[16] Fernandes H.J., Barbosa L.O., Machado T.S., Campos J.P., Moura A.S. 2017. Meningoencephalitis caused by reactivation of Chagas Disease in patient without known immunosuppression. *American Journal of Tropical Medicine and Hygiene* 96: 292-294. doi:10.4269/ajtmh.16-0225

[17] Cordova E., Boschi A., Ambrosioni J., Cudos C., Corti M. 2008. Reactivation of Chagas Disease with central nervous system involvement in HIV-infected

patients in Argentina, 1992-2007. *International Journal of Infectious Diseases* 12: 587-592. doi:10.1016/j.ijid.2007.12007

[18] Py M.O. 2011. Neurologic manifestation of Chagas Disease. *Current Neurological and Neuroscience Reports* 11: 536-542. doi:10.1007/s11910-011-0225-8

[19] Yasukawa K., Patel S.M., Flash C.A., Stager C.E., Goodman J.C., Woc-Colburn L. 2014. Case report: *Trypanosoma cruzi* meningoencephalitis in a patient with acquired immunodeficiency syndrome. *American Journal of Tropical Medicine and Hygiene* 91: 84-85. doi:10.4296/ajtmh.14-0058

[20] Cordova E., Maiolo E., Corti M., Orduna T. 2010. Neurological manifestations of Chagas' Disease. *Neurological Research* 32: 238-244. doi:10.1179/016164110X12644252260637

[21] Petri W.A., Haque R. 2013. *Entamoeba histolytica* brain abscess. 2013. In: *Handbook of Clinical Neurology*. (Eds. H. Garcia, H. Tanowitz, O. Del Brutto). vol. 114. Elsevier: 147-152.

[22] Tamer G.S., Öncel S., Gökbulut S., Arisoy E.S. 2015. A rare case of multilocus brain abscess due to *Entamoeba histolytica* infection in a child. *Saudi Medical Journal* 36: 356-358. doi:10.15537/smj.2015.3.10178

[23] Goh L.M.L., Marrone J.R. 2013. *Entamoeba histolytica* meningoencephalitis diagnosed by trophozoites in cerebrospinal fluid. *New Microbes and New Infections* 1: 16-17. doi:10.1002/2052-2975.6

[24] Siddiqui R., Khan N.A. 2014. Primary amoebic meningoencephalitis caused by *Naegleria fowleri*: An old enemy presenting new challenges. PLoS *Neglected Tropical Diseases* 8: e3017. doi:10.1371/journal.pntd.0003017

[25] Trabelsi H., Dendana F., Sellami A., Sellami H., Cheikhrouhou F. 2012. Pathogenic free-living amoebae: epidemiology and clinical review. *Pathologie Biologie* (Paris) 60: 399-40. doi:10.1016/j.patbio.2012.03.002

[26] Stowe R.C., Pehlivan D., Friederich K.E., Lopez M.A., Dicarlo S.M. 2017. Primary amebic meningo-encephalitis in children: a report of two fatal cases and review of the literature. *Pediatric Neurology* 70: 75-79. doi:10.1016/j.pediatrneurol.2017.02.004

[27] Cope J.R., Ratard R.C., Hill V.R., Sokol T., Causey J.J. 2015. The first association of a primary amebic meningoencephalitis death with culturable *Naegleria fowleri* in tap water from a US treated public drinking water system. *Clinical Infectious Diseases* 60: e36-42. doi:10.1093/cid/civ017

[28] Yoder J.S., Straif-Bourgeois S., Roy S.L., Moore T.A., Visvesvara G.S. 2012. Primary amebic meningoencephalitis deaths associated with sinus irrigation using contaminated tap water. *Clinical Infectious Diseases* 55: e79-85. doi:10.1093/cid/cis626

[29] Behera H.S., Satpathy G, Tripathi M. 2016. Isolation and genotyping of *Acanthamoeba* spp. from *Acanthamoeba* meningitis/meningoencephalitis (AME) patients in India. *Parasites and Vectors* 9: 442. doi:10.1186/s13071-016-1729-5

[30] Visvesvara G.S. 2013. Infections with free-living amebae. In: *Handbook of Clinical Neurology*. (Eds. H. Garcia, H. Tanowitz, O. Del Brutto). vol. 114. Elsevier: 153-168.

[31] Yoder J.S., Verani J., Heidman N., Hoppe-Bauer J., Alfonso E.C. 2012. *Acanthamoeba* keratitis: the persistence of cases following a multistate outbreak. *Ophthalmic Epidemiology* 19: 221-225. doi:10.3109/09286586.2012.681336

[32] Coral-Almeida M., Gabriël S., Nji Abatih E., Praet N., Benitez W., Dorny P. 2015. *Taenia solium* human cysticercosis: a systematic review of sero-epidemiological data from endemic zones around the World. *PLOS Neglected Tropical Diseases* 9: e0003919. doi:10.1371/journal.pntd.0003919

[33] Torgerson P.R., Devleesschauwer B., Praet N., Speybroeck N., Willingham A.L., Kasuga F, Rokni M.B., Zhou X.N., Fèvre E.M., Sripa B., Gargouri N., Fürst T., Budke C.M., Carabin H., Kirk M.D., Angulo F.J., Havelaar A., de Silva N. 2015. World Health Organization estimates of the global and regional disease burden of 11 foodborne parasitic diseases, 2010: a data synthesis. *PLoS Medicine* 12: e1001920. doi:10.1371/journal.pmed.1001920

[34] Carabin H., Winkler A.S., Dorny P. 2017. *Taenia solium* cysticercosis and taeniosis: Achievements from the past 10 years and the way forward. *PLOS Neglected Tropical Diseases* 11: e0005478. doi:10.1371/journal.pntd.0005478

[35] Singhi P. 2011. Neurocysticercosis. *Therapeutic Advances in Neurological Disorders* 4: 67-81. doi:10.1177/1756285610395654

[36] Ali M., Mahmood K., Khan P. 2009. Hydatid cysts of the brain. *Journal of Ayub Medical College, Abbottabad* 21: 152-154.

[37] Basarslan S.K., Gocmez C., Kamasak K., Ceviz A. 2015. The gigant primary cerebral hydatid cyst with no marked manifestation: a case report and review of literature. *European Review for Medical and Pharmacological Science* 19: 1327-1329.

[38] Batçık O.E., Öğrenci A., Koban O., Ekşi M.Ş., Bilge T. 2016. Cerebral alveolar echinococcosis concomitant with liver and lung lesions in a young adult patient: Case report and literature review. *Turkiye Parazitololoji Dergisi* 40: 169-171. doi:10.5152/tpd.2016.4624

[39] Atalan G., Sivrioglu A.K., Sönmez G., Celik M., Simsek B. 2016. A case of alveolar echinococcosis presenting as cerebral and spinal intradural metastases. *The Eurasian Journal of Medicine Eurasian* 48: 149-152. doi:10.5152/eurasianjmed.2015.15003

[40] Fan C.K., Holland C.V., Loxton K., Barghouth U. 2015. Cerebral toxocariasis: silent progression to neurodegenerative disorders? *Clinical Microbiology Reviews* 28: 663-685. doi:10.1128/CMR.00106-14

[41] Deshayes S., Bonhomme J., de La Blanchardičre A.. 2016. Neurotoxocariasis: a systematic literature review. *Infection* 44: 565-754. doi:10.1007/s15010-016-0889-8

[42] Bauer C. 2013. Baylisascariosis – infections of animals and humans with 'unusual' roundworms. *Veterinary Parasitology* 193: 404-412. doi:10.1016/j.vetpar.2012.12.036

[43] Fox A.S., Kazacos K.R., Gould N.S., Heydemann P.T., Thomas C., Boyer K.M. 1985. Fatal eosinophilic meningoencephalitis and visceral larva migrans caused by the raccoon ascarid *Baylisascaris procyonis*. *New England Journal of Medicine* 312: 1619-1623.

[44] Pai P.J., Blackburn B.R., Kazacos K.R., Warrier R.P., Bégué R.E., 2007. Full recovery from *Baylisascaris procyonis* eosinophilic meningitis. *Emerging Infectious Diseases* 13: 928-930.

[45] Bruschi F., Brunetti E., Pozio E. Neurotrichinellosis. 2013. In: *Handbook of Clinical Neurology*. (Eds. H. Garcia, H. Tanowitz, O. Del Brutto). vol. 114. Elsevier: 243-249.

[46] Nikolić S., Vujosević M., Sasić M., Poluga J., Misić S., Najdanović L., Dulović O., Dragojlović J., Milosević B. 1998. Neurologic manifestations in trichinosis. *Srpski Arhiv Za Celokupno Lekarstv* 126: 209-213 (in Croatian with summary in English).

[47] Knezević K., Turculov V., Canak G., Lalosević V., Tomić S. 2001. Neurotrichinosis. *Medicinski Pregled* 54: 483-485 (in Serbian with summary in English).

[48] Sofronic-Milosavljevic L., Radovic I., Ilic N., Majstorovic I., Cvetkovic J., Gruden-Movsesijan A. 2013. Application of dendritic cells stimulated with *Trichinella spiralis* excretory-secretory antigens alleviates experimental autoimmune encephalomyelitis. *Medical Microbiology and Immunology* 202: 239-249. doi:10.1007/s00430-012-0286-6

[49] Ursini T., Polilli E., Fazii P., Ieraci A., Sindici G., Parruti G. 2013. Late diagnosis of central nervous system involvement associated with lethal dissemination of *Strongyloides stercoralis* in an advanced HIV patient from Nigeria. *International Journal of Infectious Diseases* 17: 280-282. doi:10.1016/j.ijid.2012.11.031

[50] Chandrasekar P.H. 2016. Strongyloidiasis clinical presentation. https://emedicine.medscape.com/article/229312-clinical 29.10.2017

[51] Woll F., Gotuzzo E., Montes M. 2013. *Strongyloides stercoralis* infection complicating the Central Nervous System. In: *Handbook of Clinical Neurology*. (Eds. H. Garcia, H. Tanowitz, O. Dell Brutto). vol. 114. Elsevier: 229-234.

[52] Dokmeci O., Forshay B., Scholand S.J. 2013. Worms on the brain: fatal meningoencephalitis from disseminated strongyloides infection. *Connecticut Medicine* 77: 31-33.

[53] Morassutti A.L., Thiengo S.C., Fernandez M., Sawanyawisuth K., Graeff-Teixeira C. 2014. Eosinophilic meningitis caused by *Angiostrongylus cantonensis*: an emergent disease in Brazil. *Memórias do Instituto Oswaldo Cruz* 109: 399-407. doi:10.1590/0074-0276140023

[54] Lv S., Zhou X.N., Andrews J.R. 2017. Eosinophilic meningitis caused by *Angiostrongylus cantonensis*. *ACS Chemical Neuroscience* 8: 1815-1816. doi:1021/acschemneuro.7b00233

[55] Qvarnstrom Y., Xayavong M., Aramburu da Silva A.C., Park S.Y., Whelen C., Calimlim P.S., Sciulli R.H., Honda S.A.A., Higa K., Kitsutani P., Chea N., et al. 2016. Real-time polymerase chain reaction detection of *Angiostrongylus cantonensis* DNA in cerebrospinal fluid from patients with eosinophilic meningitis. *The American Journal of Tropical Medicine and Hygiene* 94: 176-181. doi:10.4269/ajtmh.15-0146

[56] Katchanov J., Sawanyawisuth K., Chotmongkol V., Nawa Y. 2011. Neurognathostomiasis, a neglected parasitosis of the central nervous system. *Emerging Infectious Diseases* 17: 1174-1180. doi:10.3201/eid1707.101433

[57] Herman J.S., Peter L., Chiodin P.L. 2009. Gnathostomiasis, another emerging imported disease. *Clinical Microbiology Reviews* 22: 484-492. doi:10.1128/CMR.00003-09

[58] Kamgno J., Boussinesq M., Labrousse F., Nkegoum B., Thylefors B.I., Mackenzie C.D. 2008. Encephalopathy after ivermectin treatment in a patient infected with *Loa loa* and *Plasmodium* spp. *The American Journal of Tropical Medicine and Hygiene* 78: 546-551.

[59] Lukiana T., Mandina M., Situakibanza N.H, Mbula M.M., Lepira B.F., Wobin T., Odio W.T., Joseph Kamgno J., Boussinesq M. 2006. A possible case of spontaneous *Loa loa* encephalopathy associated with a glomerulopathy. *Filaria Journal* 5: 6. doi:10.1186/1475-2883-5-6