Chapter

Neurocysticercosis: An Overview of Pathology and Pathogenesis

Güngör Çağdaş Dinçel, Saeed El-Ashram, Luís Manuel Madeira de Carvalho, Danielle Graham, Inkar A. Castellanos-Huerta, Victor M. Petrone-Garcia, Guillermo Tellez-Isaias, Beniamino T. Cenci-Goga and Luca Grispoldi

Abstract

Neurocysticercosis (NCC), a subtle parasite infection of the central nervous system, is a powerful example of the complex interaction between human behavior, zoonotic transmission, and neurological illness development. Given the disease's worldwide prevalence and potentially fatal neurological consequences, research into NCC is critical for advancing knowledge, creating effective diagnostic tools and treatment options, and adopting preventative measures to lessen the disease's impact. Cysticerci causes an immunological response in the CNS, resulting in inflammation and immune cell recruitment. The existence of intraventricular cysts, cysts in the cerebral aqueduct or fourth ventricle, and the degree of inflammation and scarring induced by the infection are all risk factors for the development of hydrocephalus. This book chapter provides an in-depth exploration of the pathology and pathogenesis of NCC, discussing the life cycle of the *Taenia solium* parasite, its invasion of the central nervous system, and the formation of cysticerci, as well as the diagnostic challenges and imaging findings, clinical manifestations, and potential neurological complications associated with NCC, serving as a valuable resource for medical professionals, researchers, and policymakers.

Keywords: neuroimmunopathology, neurocysticercosis, zoonotic transmission, neuropathology, *Taenia solium*

1. Introduction

Neurocysticercosis (NCC), an insidious parasitic infection of the central nervous system, is a compelling testament to the intricate interplay between human behavior, zoonotic transmission, and neurological disorder pathogenesis. Caused by the larval stage of the pork tapeworm, *Taenia solium*, NCC represents a significant global health burden, particularly in regions plagued by inadequate sanitation and poor hygiene practices. As a leading cause of acquired epilepsy worldwide, this enigmatic condition transcends geographical boundaries and socio-economic disparities, leaving a trail of

neuroinflammatory cascades, structural aberrations, and clinical manifestations [1, 2]. Unraveling the complex neuropathological intricacies of NCC holds the key to understanding its multifaceted impact on the human brain, ultimately guiding the pursuit of effective diagnostic modalities, therapeutic interventions, and preventive strategies [1, 3, 4]. Through an amalgamation of meticulous clinical observation, cutting-edge neuroimaging techniques, and the unraveling of host-parasite interactions, the neuropathological landscape of NCC gradually unveils its enigmatic nature, beckoning the relentless quest for knowledge in the realm of neurology and parasitology [1, 3, 4].

NCC is a complex parasitic infection that elicits diverse neuropathological changes within the central nervous system. The development of neuropathology in NCC follows a progressive course characterized by distinct stages. In the early vesicular stage, the cysticerci, comprising fluid-filled bladders housing the tapeworm larvae, exhibit a translucent membrane and contain a scolex with hooklets [5, 6]. As the infection progresses to the colloidal stage, degenerative changes occur, leading to a granulomatous reaction. This granuloma, composed of a necrotic core, edema, fibrous capsule, and inflammatory cells, contributes to the clinical manifestations commonly associated with NCC, such as seizures, headaches, and focal neurological deficits [6, 7]. Over time, some cysticerci may undergo calcification, resulting in the calcified stage where the parasites become inert, and the host response aims to contain the infection. Developing these neuropathological features in NCC underscores the dynamic interplay between the parasite, the host immune response, and the structural alterations within the central nervous system. Therefore, the evaluation and examination of neuropathological findings are very important [5–7].

NCC is paramount in infectious diseases and neurology due to its significant impact on public health and its potential to cause severe neurological complications. This parasitic infection, caused by the larval stage of the pork tapeworm, *T. solium*, primarily affects the central nervous system (CNS). NCC is recognized as a leading cause of acquired epilepsy worldwide, particularly in regions where the parasite is endemic. It substantially burdens affected individuals, their families, and healthcare systems. Moreover, NCC can lead to various neurological manifestations, including seizures, hydrocephalus, focal neurological deficits, cognitive impairments, and even life-threatening complications [8, 9]. The complex interplay between the immune response, parasite-host interactions, and the localization of cysticerci within the CNS contributes to the diverse clinical presentations and challenges in diagnosis and treatment. Given its global prevalence and potential for devastating neurological sequelae, the study of NCC is essential for improving understanding, developing effective diagnostic tools and treatment strategies, and implementing preventive measures to mitigate the impact of this disease (**Figure 1**) [8, 9].

The proposed book chapter on NCC is necessary and of utmost importance in the medical and scientific community. NCC, caused by the larval stage of the pork tapeworm, *T. solium*, is a neglected tropical disease with a significant global impact on public health. Despite its prevalence and the severe neurological complications it can induce, there is a notable scarcity of comprehensive literature that systematically addresses various aspects of the disease. This chapter aims to fill this critical knowledge gap by providing a comprehensive and up-to-date synthesis of the current understanding of NCC. It will cover diverse topics, including the parasite's life cycle, epidemiology, clinical manifestations, diagnostic methods, treatment options, and preventive strategies. By consolidating evidence-based information and the latest research findings, the chapter will be an essential reference for medical practitioners, researchers, and policymakers. Moreover, the book chapter will raise awareness about this often overlooked disease,

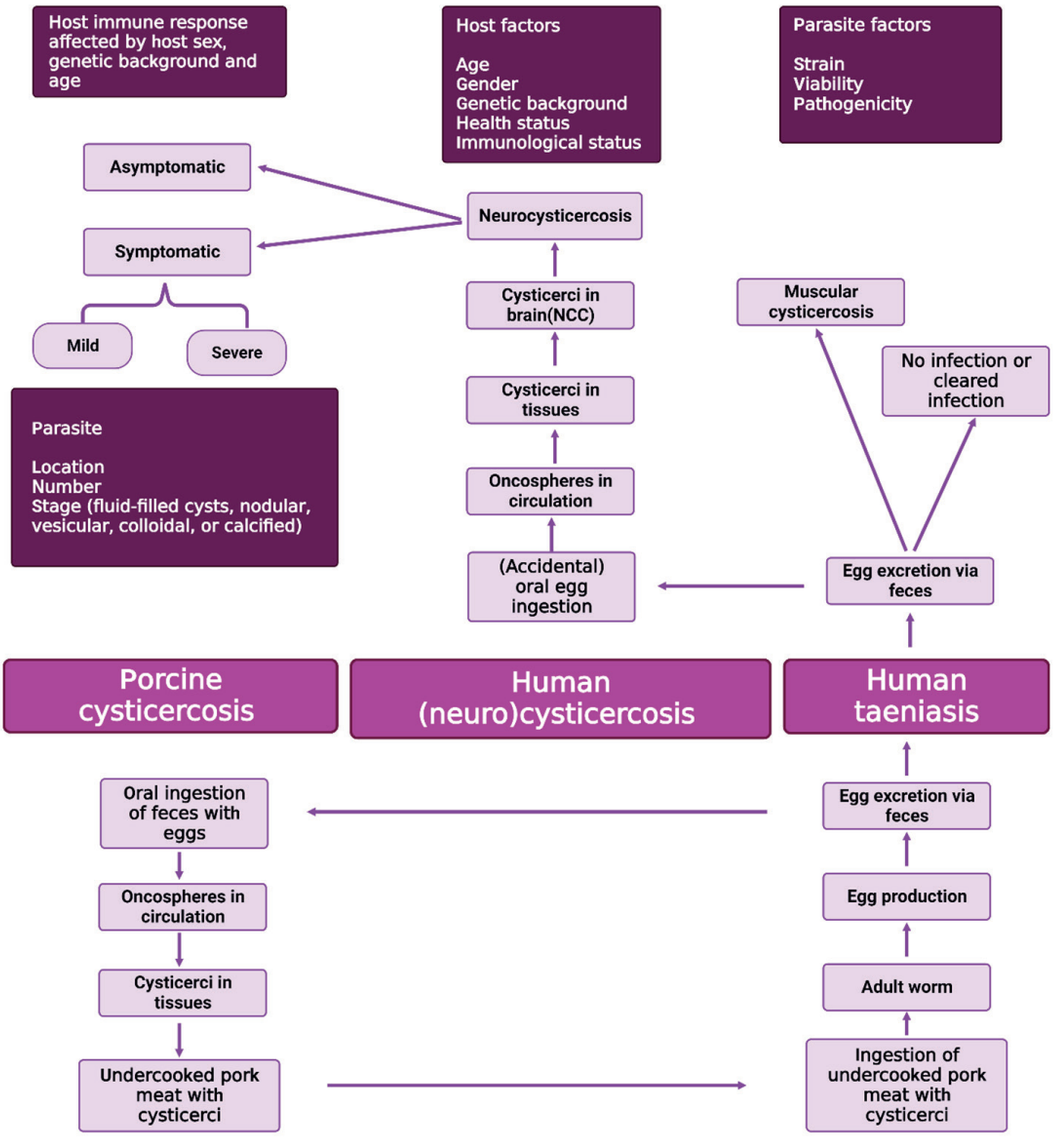

Figure 1.
T. solium infection depicting the stages of human and porcine cysticercosis, including NCC factors.

fostering international collaborations and research efforts to improve its diagnosis, management, and prevention. Ultimately, the chapter's significance lies in its potential to enhance the quality of patient care, contribute to scientific advancements, and alleviate the burden of NCC on affected communities worldwide.

2. Inflammatory response in neurocysticercosis

Cysticerci triggers an immune response in the CNS, leading to inflammation and the recruitment of immune cells. The inflammatory response can vary depending on the location and stage of the cysticerci. Inflammatory cells, such as lymphocytes, macrophages, and eosinophils, infiltrate the cysticerci and the surrounding brain tissue, forming granulomas [10–14].

The relationship between the inflammatory response and neuropathology in NCC is complex and dynamic. The presence of the larval stage of the pork tapeworm, *T. solium*,

in the CNS, triggers an immune response, leading to inflammation. This inflammatory response plays a crucial role in the pathogenesis and progression of NCC [1, 14, 15].

2.1 Immune cell infiltration

The inflammatory response in NCC involves infiltrating various immune cells into the affected CNS tissue. These immune cells include lymphocytes, macrophages, eosinophils, and occasionally neutrophils. They are recruited to the site of infection in response to the presence of the larval cysticerci [11–14].

2.2 Inflammatory mediators

Inflammatory mediators play a crucial role in NCC -associated inflammation. Cytokines, chemokines, and other inflammatory molecules are released by immune cells and contribute to the inflammatory response. These mediators include tumor necrosis factor-alpha (TNF-alpha), interleukin-1 beta (IL-1β), interleukin-6 (IL-6), and interleukin-10 (IL-10), among others. They regulate immune cell activation, migration, and effector functions [11, 13, 14, 16].

3. Cysticerci formation

NCC is characterized by the formation of cysticerci, which are larval stages of the pork tapeworm, *T. solium*, within the central nervous system. These cysticerci can be found in various locations, such as the brain parenchyma, ventricles, or subarachnoid spaces [3, 4, 17, 18]. Cysticercosis formation is a crucial aspect of NCC, the CNS manifestation of the parasitic infection caused by the larval stage of the pork tapeworm, *T. solium*.

3.1 Characteristics of cysticerci

Cysticerci are the larval stage of *T. solium* and exhibit distinct features [3, 4, 17–19].

3.1.1 Fluid-filled cysts

Cysticerci are bladder-like structures filled with clear or turbid fluid. The cysts vary in size, ranging from a few millimeters to several centimeters in diameter. Their size can influence the clinical presentation and potential complications [17–19].

3.1.2 Nodular stage

Over time, the cysticerci undergo a process of degeneration and transition into a nodular stage. In this stage, the cysts become more inflammatory and calcify, developing a thick fibrous capsule around the scolex. The nodular stage is associated with increased inflammatory response and clinical manifestations [3, 4, 18, 19].

3.1.3 Vesicular stage

In the early vesicular stage, the cysticerci are small and surrounded by a translucent membrane. These cysts are often asymptomatic and may go unnoticed. Histologically,

the cysticerci in this stage are characterized by a thin eosinophilic membrane, a fluid-filled cavity, and a scolex (tapeworm's head) with hooklets. Initially, the cysticerci are in a vesicular stage, characterized by a thin-walled cyst containing a small fluid-filled bladder with an invaginated scolex (tapeworm's head). This stage is less inflammatory and may be asymptomatic [3, 4, 17–19].

In NCC, irregularly shaped large fluid cysts are a hallmark of NCC and are particularly common in areas of high endemicity. These cysts are typically spherical to oval in shape and vary in size, usually several centimeters in diameter. Their appearance in neuroimaging such as computed tomography (CT) or magnetic resonance imaging (MRI) is characterized by a well-defined, thin-walled, translucent structure filled with clear or slightly turbid fluid.

Cysts without scolex or protoscolex are also present. A distinctive feature of these cysts is the absence of a scolex or protoscolex within the cystic lümen [20–22]. Unlike other stages of cysticercosis where the scolex is identifiable and plays a critical role in attachment and growth, these large liquid cysts lack this vital structure. Although the cyst wall is thin, it can elicit an immune response in the host. Inflammation surrounding the cyst is a common feature and leads to the formation of a pericystic-enhancing edge on neuroimaging ([23, 24], Sotelo et al. 1985). This enhancing edge represents an inflammatory reaction to the presence of the cyst and is often used as a diagnostic criterion for NCC [21, 23, 25–27].

Large irregularly shaped liquid cysts are particularly common in hyperendemic areas of NCC, such as Mexico and Argentina [21, 24, 27]. The high prevalence in these regions is often attributed to factors such as pork consumption, sanitation, and cultural practices that influence the transmission of *T. solium*, the causative agent of NCC. Understanding the characteristics of irregularly shaped large liquid cysts in NCC is crucial for accurate diagnosis and management ([23–25], Sotelo et al. 1985). Treatment strategies may include antiparasitic drugs such as albendazole or praziquantel in combination with corticosteroids to reduce inflammation ([21, 27], Sotelo et al. 1985).

Consequently, irregularly shaped large liquid cysts without scolex are a hallmark of NCC in hyperendemic areas. These cysts present unique challenges in diagnosis and treatment due to their potential to elicit inflammatory responses and neurological symptoms. Advanced imaging techniques and a deep understanding of the epidemiology of the disease are crucial to addressing this particular presentation of NCC in clinical practice and research in regions such as Mexico and Argentina.

3.1.4 Colloidal stage

As the cysticercus matures, it enters the colloidal stage. The cysticercus undergoes degenerative changes during this stage, leading to a granulomatous reaction around the parasite. The granuloma comprises a central necrotic area, surrounding edema, a fibrous capsule, and an outer layer of inflammatory cells. The colloidal stage is commonly associated with clinical symptoms such as seizures, headaches, and focal neurological deficits [4, 17–19].

3.1.5 Calcified stage

Over time, some cysticerci may undergo calcification, resulting in the calcified stage. Calcified lesions can be detected through neuroimaging studies like CT or MRI. Calcification represents a host response aimed at containing the infection. In the calcified stage, the cysticercus is no longer viable [3, 4, 18, 19].

4. Pathological features in neurocysticercosis

The pathological features of NCC depend on the infection's stage and the cysticerci's location within the central nervous system. The cysticerci reach the CNS through the bloodstream or lymphatic system. They can penetrate the blood-brain barrier and disseminate throughout the brain or spinal cord. The most common sites of cysticercosis formation in NCC include the brain parenchyma, ventricular system, subarachnoid space, and, rarely, the spinal cord [1, 14, 19, 28–31].

4.1 Tissue damage

While the inflammatory response is aimed at controlling the infection, it can also contribute to tissue damage and neuropathology in NCC. The presence of immune cells and the release of inflammatory mediators can lead to the destruction of surrounding CNS tissue, disruption of the blood-brain barrier, and the release of toxic molecules. This tissue damage can result in clinical manifestations and neurological deficits [19, 28, 29, 31, 32].

4.2 Perilesional edema

Inflammation in NCC can lead to perilesional edema, the swelling of the tissue surrounding the cysticerci. Perilesional edema is attributed to increased vascular permeability, disrupted blood-brain barrier, and alterations in the balance of fluid regulation within the CNS. It can contribute to neurological symptoms and complications [14, 19, 28, 29, 31].

In some cases, NCC can lead to inflammation of the blood vessels in the brain, resulting in vasculitis. Vasculitis can cause disruption of the blood-brain barrier, leading to edema (swelling) and potentially causing neurological complications [19, 29, 31].

4.3 Neurological complications

The inflammatory response and associated neuropathology in NCC can lead to neurological complications. These complications may include seizures, focal neurological deficits, cognitive impairments, hydrocephalus, vasculitis, and increased intracranial pressure. Apart from these findings, meningoencephalitis and psychoses are among the common pathology [33]. The severity and extent of these complications depend on factors such as the number and location of cysticerci, the host's immune response, and individual susceptibility [19, 28, 29, 31].

Understanding the relationship between the inflammatory response and neuropathology in NCC is crucial for comprehending the disease progression, developing therapeutic strategies, and managing neurological complications. The modulation of the inflammatory response and targeted interventions may hold promise for improving outcomes in NCC.

Spinal cysticercosis, although rare, can manifest as a cause of myelopathy, a neurological disorder affecting the spinal cord. The characteristic MRI features observed in affected individuals facilitate the recognition and accurate diagnosis of spinal cysticercosis. Therefore, clinicians must include spinal cysticercosis in the differential diagnosis when evaluating patients with myelopathy symptoms. In cases where spinal cysticercosis is confirmed, the recommended course of treatment involves the

complete resection of the causative lesion and the administration of oral albendazole, an antiparasitic medication. This combined therapeutic approach has shown promising results, leading to the regression of symptoms in patients with spinal cysticercosis. Histopathological examination plays a crucial role in establishing the definitive diagnosis of spinal cysticercosis. By analyzing tissue samples obtained during surgical intervention, the characteristic features of the condition, such as the presence of parasitic larvae, can be identified. This histopathological confirmation not only confirms the diagnosis of spinal cysticercosis but also aids in differentiating it from other potential causes of spinal space-occupying lesions. In summary, recognizing spinal cysticercosis as a rare cause of myelopathy is aided by the characteristic MRI features observed in affected individuals. Clinicians should actively consider spinal cysticercosis during the differential diagnosis of myelopathy cases. When confirmed, complete resection of the causative lesion, coupled with oral albendazole administration, has demonstrated positive outcomes in symptom regression. Furthermore, the importance of histopathological examination cannot be understated, as it provides definitive confirmation of the diagnosis and aids in differentiating spinal cysticercosis from other spinal space-occupying lesions [34].

4.4 Granuloma formation and calcifications in neurocysticercosis

Granulomas are organized collections of immune cells that form in response to the presence of cysticerci. Granulomas typically consist of lymphocytes, macrophages, and multinucleated giant cells. The formation of granulomas is a host defense mechanism to contain and eliminate the parasite [15, 35, 36]. However, the inflammatory response can also contribute to tissue damage and neurological complications. As the cysticerci degenerate and the inflammatory response progresses, the cysts may be calcified [5, 15, 37]. Calcifications appear as dense, white areas in neuroimaging studies, such as computed tomography (CT) or magnetic resonance imaging (MRI). The presence of calcifications is an important diagnostic feature of NCC [5, 15, 35–37].

Granuloma formation is a prominent pathological feature in NCC, which occurs in response to the larval cysticerci of the pork tapeworm, *T. solium*, in the CNS. Granulomas are organized collections of immune cells that aim to encapsulate and contain the parasite [5, 7, 15, 16, 35–37].

4.4.1 Granuloma formation in neurocysticercosis

a. **Cellular composition:** Granulomas in NCC are composed of various immune cells, including lymphocytes, macrophages, and multinucleated giant cells. Lymphocytes, particularly T cells, are involved in the initial recognition of the parasite and initiating the immune response. Macrophages play a crucial role in phagocytosing and destroying the cysticerci. Multinucleated giant cells, formed by the fusion of macrophages, are commonly observed in the granulomas and contribute to the destruction of the parasite [5, 15, 37].

b. **Cytokine and chemokine expression:** The formation and maintenance of granulomas in NCC are regulated by the secretion of various cytokines and chemokines. Cytokines such as interferon-gamma, TNF-α, IL-1β, and IL-6 are produced by immune cells within the granuloma and play crucial roles in the modulation of the immune response. Chemokines, such as CCL2, CCL3, CCL4, and CCL5, are involved in the recruitment of immune cells to the site of infection [15, 35, 36].

c. **Fibrous capsule formation:** Granulomas in NCC are characterized by the development of a fibrous capsule surrounding the cysticerci. The fibrous capsule is formed by depositing collagen and other extracellular matrix components. It serves as a physical barrier, preventing the parasite's spread and reducing the surrounding tissue's inflammatory response [5, 15, 37].

d. **Heterogeneity of granulomas:** Granulomas in NCC can exhibit heterogeneity in their composition and organization. Some granulomas may be well-structured with a central core of necrotic debris surrounded by lymphocytes and macrophages. Others may have a less organized structure or show signs of degeneration. The heterogeneity of granulomas is thought to be influenced by factors such as the number and stage of the cysticerci, the host immune response, and the local microenvironment [15, 35, 36].

4.4.2 Calcifications in neurocysticercosis

Calcifications are a characteristic finding in neuroimaging studies of patients with NCC. They result from the degeneration and calcification of the larval cysticerci within the CNS [5, 7, 15, 35–37]. Calcifications in NCC appear as dense, white areas on neuroimaging studies such as CT scans. They are typically round or oval in shape and can vary in size, ranging from a few millimeters to several centimeters. Calcifications are commonly observed in the brain parenchyma, ventricles, subarachnoid space, and rarely, the spinal cord [5, 7, 37].

4.5 Hydrocephalus

Hydrocephalus is a common complication of NCC, particularly when cysts are located in the ventricular system or cause obstruction to the flow of cerebrospinal fluid (CSF). In certain instances, NCC can obstruct the flow of CSF within the brain, leading to hydrocephalus [38–40]. Hydrocephalus is characterized by an accumulation of CSF, causing increased intracranial pressure and enlargement of the ventricles. It can result from cysts' obstruction of CSF pathways or inflammation-induced scarring [38–42].

4.5.1 Prevalence and risk factors

Hydrocephalus occurs in a significant proportion of NCC cases. The exact prevalence varies depending on geographic location and other factors, but studies have reported rates ranging from 7–35% [39–41]. Risk factors for the development of hydrocephalus include the presence of intraventricular cysts, cysts located in the cerebral aqueduct or fourth ventricle, and the degree of inflammation and scarring caused by the infection [39–41].

4.5.2 Mechanisms of hydrocephalus

Hydrocephalus in NCC can result from various mechanisms [38–42];

a. **Obstructive hydrocephalus:** One of the pivotal determinants of NCC-related neuropathologies is the size of the cysticerci within the central nervous system. Large cysts, when present, exert localized pressure on adjacent neural structures, leading to a spectrum of neurological deficits [20, 22, 24, 26]. This pressure effect can disrupt normal neuronal function, resulting in focal symptoms such

as seizures, sensory deficits, and motor impairments. Moreover, the compression of blood vessels by these cysts may compromise cerebral perfusion, precipitating ischemic events and further exacerbating the clinical picture [20, 22, 24, 26].

a. Aggregation of multiple cysts:

In certain instances, NCC takes on a more complex manifestation, characterized by the aggregation of multiple cysts into a single large bundle or cluster. This phenomenon intensifies the pressure effects within the confined intracranial space. The aggregative growth of cysticerci not only exacerbates focal neurological deficits but can also lead to increased intracranial pressure (ICP) [24, 43–45]. Elevated ICP is a grave concern, potentially giving rise to severe headaches, papilledema, and, in extreme cases, herniation syndromes. Timely intervention is imperative to alleviate these critical pressure-related consequences [24, 43, 44].

Cysts located in the ventricular system or causing obstruction to the flow of CSF can lead to obstructive hydrocephalus. The cysts physically block CSF flow, resulting in fluid accumulation and increased intracranial pressure. The obstruction can occur at the foramen of Monro, cerebral aqueduct, or fourth ventricle, depending on the location of the cysts [38–42].

b. **Non-obstructive hydrocephalus:** Inflammation and scarring induced by the infection can disrupt CSF's normal absorption or impair the ventricular system's flow dynamics. This can result in impaired CSF circulation and non-obstructive hydrocephalus [38–42].

Hydrocephalus associated with NCC can present with various symptoms depending on the severity and rapidity of CSF accumulation. Common clinical manifestations include headache, nausea, vomiting, papilledema (swelling of the optic disc), visual disturbances, gait disturbances, cognitive changes, and altered consciousness or coma in severe cases.

4.6 Obstruction of cerebrospinal fluid pathways

Another intriguing facet of NCC-related neuropathologies pertains to the obstruction of CSF pathways by cysticercal lesions. When cysts infiltrate the CSF circulation, they may impede the flow of this vital fluid, resulting in conditions such as hydrocephalus. The accumulation of CSF within the ventricular system can cause ventricular dilation and elevate ICP. Recognizing and addressing these obstructive patterns is crucial to preventing secondary complications associated with increased intracranial pressure [43, 45–47].

Neurocysticercosis exhibits an intricate interplay between its insidious onset and the subsequent emergence of neuropathological manifestations. While the initial stages of the disease may remain asymptomatic, the potential for neurological deficits becomes increasingly pronounced as the cysticerci grow and interact with their neural surroundings. Pressure effects arising from large cysts, the aggregation of multiple cysts, and the obstruction of cerebrospinal fluid pathways constitute critical determinants in the clinical trajectory of NCC. Early recognition, accurate diagnosis, and prompt management are imperative to mitigate the neurological sequelae associated with this parasitic infection.

5. Diagnosis

The diagnosis of hydrocephalus related to NCC involves a combination of clinical evaluation, neuroimaging, and CSF analysis. Neuroimaging studies, such as computed tomCT or MRI [48–50], are crucial in identifying the presence of hydrocephalus, assessing the location and extent of cysts, and evaluating the ventricular system. CSF analysis may rule out other causes of hydrocephalus and assess for signs of inflammation or infection [7, 39–41, 51].

The focus should be primarily on the laboratory diagnosis of NCC, an infectious disease affecting the nervous system and an important cause of epilepsy in developing countries. The primary immunodiagnostic approach involves assessing whether serological findings are compatible with the diagnosis suggested by imaging results. Lentil lectin-purified parasite antigens are used in enzyme-linked immunoelectrotransfer blot format to detect antibodies, while monoclonal antibody-based enzyme-linked immunosorbent assays (ELISAs) are used for antigen detection [52, 53]. The article also highlights recent developments in assay configurations that show promise in simultaneous antibody and antigen detection. However, it is important to note that the usefulness of immunodiagnostic tests is limited in areas endemic for NCC where confirmatory brain imaging may not be possible. This is because the tests available for immunodiagnosis will not significantly impact the clinical management of most individuals with asymptomatic or symptomatic NCC [9, 52–54].

6. Preventive measures

Neurocysticercosis is a significant public health concern globally, particularly in regions with poor sanitation and limited access to healthcare. The prevention of neurocysticercosis requires the implementation of effective preventive measures aimed at interrupting the transmission cycle and reducing the burden of the disease. By understanding and implementing these preventive measures, the incidence and impact of neurocysticercosis can be significantly mitigated, leading to improved public health outcomes and the alleviation of the socio-economic burden associated with this devastating parasitic infection [55–57].

6.1 Pig vaccination and anthelmintic medication to prevent T. solium cysticercosis infection

T. solium cysticercosis is primarily transmitted through the consumption of undercooked pork contaminated with *T. solium* eggs. Pig vaccination and anthelmintic medication have emerged as crucial preventive measures in controlling this infection. Vaccination programs targeting pigs aim to stimulate an immune response against the parasite, thereby reducing the risk of infection. Moreover, anthelmintic medication administered to pigs effectively eliminates the tapeworm infection, breaking the transmission cycle. By implementing rigorous vaccination and medication protocols, the prevalence of *T. solium* cysticercosis in pig populations can be significantly reduced, consequently decreasing the risk of human infection [55–57].

6.2 Updated pig management procedures to keep pigs away from human excrement

The transmission of *T. solium* cysticercosis is closely linked to poor pig management practices, particularly the exposure of pigs to human excrement. Upgrading pig management procedures is crucial to prevent contamination and subsequent transmission of *T. solium* eggs. Effective measures include constructing and maintaining appropriate pig housing facilities, such as pig pens and enclosures, that minimize contact with human waste. Furthermore, the development and implementation of strict waste management protocols, including proper disposal of human excrement and separate waste systems for pigs, are essential to reduce environmental contamination. By adopting these updated pig management procedures, the risk of *T. solium* cysticercosis transmission can be significantly mitigated [55–57].

6.3 Inspection and adequate cooking of pigs to limit the danger of human infection

A thorough inspection and proper cooking of pork products play a pivotal role in preventing *T. solium* cysticercosis infection in humans. Inspection protocols involve careful examination of pigs before slaughter to identify any visible cysticerci, ensuring that only safe and uninfected pigs enter the food supply chain. Adequate cooking of pork at temperatures above 63°C for a sufficient duration effectively kills the *T. solium* larvae, rendering the meat safe for consumption. Education and awareness campaigns promoting the importance of proper inspection and cooking practices are crucial in empowering individuals to safeguard themselves against *T. solium* cysticercosis [55–57].

6.4 Healthcare promoting hand cleanliness, food hygiene, sanitation, and pig management

A comprehensive healthcare approach plays a crucial role in preventing *T. solium* cysticercosis infection. Health education programs should emphasize the significance of hand cleanliness, particularly after handling pigs or pork products, to minimize the risk of contamination. Additionally, ensuring food hygiene through proper washing and cooking techniques can further reduce the transmission of *T. solium* cysticercosis. Sanitation practices, including the provision of clean water sources and hygienic waste disposal systems, are vital in preventing environmental contamination and interrupting the transmission cycle. Finally, promoting improved pig management practices within healthcare settings, such as strict biosecurity measures and regular veterinary monitoring, can contribute to preventing *T. solium* cysticercosis [55–57].

Addressing the burden of *T. solium* cysticercosis requires a comprehensive and multifaceted approach. Pig vaccination and anthelmintic medication, updated pig management procedures, inspection and adequate cooking of pigs, and healthcare interventions promoting hand cleanliness, food hygiene, sanitation, and improved pig management practices are crucial preventive measures. By implementing these strategies at various levels, including animal husbandry, food safety regulations, and public health initiatives, the transmission and impact of *T. solium* cysticercosis can be significantly reduced, leading to improved health outcomes and a safer food supply chain.

It is important to note that the management of hydrocephalus in NCC should be individualized, considering the patient's clinical condition, the characteristics of the hydrocephalus, and the availability of resources and expertise. Close follow-up and multidisciplinary care involving neurologists, infectious disease specialists, and neurosurgeons are essential for optimal management of this complication.

These pathological features reflect the evolution and host response to NCC. The vesicular stage represents the early presence of viable cysticerci, while the colloidal stage shows an inflammatory response to degenerating parasites. The calcified stage indicates a resolved infection with inert, calcified lesions. Understanding these pathological features is crucial for diagnosing, managing, and treating NCC.

This section gave information about the pathology and pathogenesis of NCC. It is now recognized that irreversible pathologies occur with the appearance of neurological symptoms. At this stage, it is very important to understand the pathogenesis to develop treatment protocols. Each topic discussed in this chapter is important in understanding the disease.

In conclusion, this book chapter has provided an in-depth exploration of the pathology and pathogenesis of NCC, shedding light on the intricate mechanisms underlying this parasitic infection. Throughout the chapter, we have discussed the life cycle of the *T. solium* parasite, its invasion of the central nervous system, and the formation of cysticerci. We have examined the complex interplay between the immune response and neuropathology, emphasizing the role of granuloma formation and the inflammatory cascade. Additionally, the chapter has delved into the diagnostic challenges and imaging findings, including the characteristic calcifications observed in neuroimaging studies. Furthermore, we have addressed NCC's clinical manifestations and potential neurological complications. By comprehensively covering these topics, this chapter is a valuable resource for medical professionals, researchers, and policymakers, facilitating a better understanding of the disease and providing a foundation for future studies to improve diagnosis, treatment, and prevention strategies. While taeniasis is primarily associated with the consumption of undercooked or raw pork, it is essential to recognize that cysticercosis, a severe parasitic disease caused by the larval stage of the pork tapeworm, primarily results from inadequate personal hygiene practices. The transmission dynamics of *T. solium*, the causative agent of both taeniasis and cysticercosis, underscore the critical role of hygiene in the epidemiology of cysticercosis. Taeniasis occurs when individuals ingest the larval cysts present in undercooked or raw pork. However, cysticercosis occurs when individuals ingest the eggs shed in the feces of individuals with taeniasis, leading to the development of cysticerci in various body tissues, including the brain. This stark contrast highlights the fact that while the initial infection may be linked to dietary choices, the subsequent development of cysticercosis hinges primarily on sanitation practices. Thus, public health efforts to combat cysticercosis should not only focus on promoting safe pork consumption but also emphasize the importance of proper sanitation and hygiene practices to break the cycle of transmission and reduce the burden of this debilitating disease. To sum up, Neurocysticercosis, a severe neurological condition caused by the invasion of the central nervous system by *T. solium* larvae, is primarily attributable to inadequate personal hygiene conditions. While the initial infection may be linked to dietary factors, such as the consumption of undercooked or raw pork, the transition to neurocysticercosis is largely dependent on poor personal hygiene practices. In this context, the ingestion of *T. solium* eggs, shed in the feces

of individuals with taeniasis, plays a crucial role. Therefore, addressing neurocysticercosis necessitates a focus on improving sanitation and personal hygiene as a fundamental measure to reduce its incidence and impact. We hope this chapter will contribute to the overall knowledge and ultimately lead to improved outcomes for individuals affected by NCC.

Author details

Güngör Çağdaş Dinçel[1], Saeed El-Ashram[2,3]*, Luís Manuel Madeira de Carvalho[4,5], Danielle Graham[6], Inkar A. Castellanos-Huerta[6], Victor M. Petrone-Garcia[7], Guillermo Tellez-Isaias[6], Beniamino T. Cenci-Goga[8] and Luca Grispoldi[8]

1 Eskil Vocational School, Laboratory and Veterinary Science, Aksaray University, Aksaray, Turkey

2 Faculty of Science, Zoology Department, Kafrelsheikh University, Kafr El-Sheikh, Egypt

3 College of Life Science and Engineering, Foshan University, Foshan, China

4 Parasitology and Parasitological Diseases Laboratory, CIISA – Center for Interdisciplinary Research in Animal Health, Faculty of Veterinary Medicine, University of Lisbon, Lisbon, Portugal

5 Associated Laboratory for Animal and Veterinary Science (AL4AnimalS), Lisbon, Portugal

6 Division of Agriculture, Department of Poultry Science, University of Arkansas, Fayetteville, AR, USA

7 College of Higher Studies Cuautitlan, National Autonomous University of Mexico (UNAM), Cuautitlan Izcalli, State of Mexico, Mexico

8 Department of Veterinary Medicine, University of Perugia, Italy

*Address all correspondence to: saeed_elashram@yahoo.com

References

[1] Garcia HH, Gonzalez AE, Gilman RH. Taenia solium Cysticercosis and its impact in neurological disease. Clinical Microbiology Reviews. 2020;**33**(3):e00085-e00019. DOI: 10.1128/CMR.00085-19

[2] Sorvillo F, Wilkins P, Shafir S, Eberhard M. Public health implications of cysticercosis acquired in the United States. Emerging Infectious Diseases. 2011;**17**(1):1-6

[3] Deepika K, Chaudhary A, Sharma B, Shanker Singh H. Neurocysticercosis: A Review on Global Neurological Disease. London, UK: IntechOpen; 2023. DOI: 10.5772/intechopen.110627

[4] Del Brutto OH. Human neurocysticercosis: An overview. Pathogens. 2022;**11**(10):1212. DOI: 10.3390/pathogens11101212

[5] Sharma LN, Garg RK, Verma R, Singh MK, Malhotra HS. Seizure recurrence in patients with solitary cystic granuloma or single parenchymal cerebral calcification: A comparative evaluation. Seizure. 2013;**22**(10):840-845

[6] Moskowitz J, Mendelsohn G. Neurocysticercosis. Archives of Pathology & Laboratory Medicine. 2010;**134**(10):1560-1563. DOI: 10.5858/2008-0756-RS.1

[7] Rissardo JP, Caprara ALF, Durante Í. Neurocysticercosis and movement disorders: A literature review. Brain Circulation. 2020;**6**(4):225-241. DOI: 10.4103/bc.bc_48_20

[8] Nash TE, Garcia HH. Diagnosis and treatment of neurocysticercosis. Nature Reviews. Neurology. 2011;**7**(10):584-594. DOI: 10.1038/nrneurol.2011.135

[9] Rajshekhar V. Neurocysticercosis: Diagnostic problems & current therapeutic strategies. The Indian Journal of Medical Research. 2016;**144**(3):319-326. DOI: 10.4103/0971-5916.198686

[10] Del Brutto OH, Castillo PR, Mena IX, Freire AX. Neurocysticercosis among patients with cerebral gliomas. Archives of Neurology. 1997;**54**(9):1125-1128

[11] Olguín EJ, Ignacio Terrazas L. Regulation of the Immune Response in Cysticercosis: Lessons from an Old Acquainted Infection. London, UK: IntechOpen; 2021. DOI: 10.5772/intechopen.100137

[12] Gripper LB, Welburn SC. The causal relationship between neurocysticercosis infection and the development of epilepsy - a systematic review. Infectious Diseases of Poverty. 2017;**6**(1):31. DOI: 10.1186/s40249-017-0245-y

[13] Hamamoto Filho PT, Fragoso G, Sciutto E, Fleury A. Inflammation in neurocysticercosis: Clinical relevance and impact on treatment decisions. Expert Review of Anti-Infective Therapy. 2021;**19**(12):1503-1518. DOI: 10.1080/14787210.2021.1912592 Epub 2021 Apr 9

[14] Mahanty S, Orrego MA, Mayta H, Marzal M, Cangalaya C, Paredes A, et al. Post-treatment vascular leakage and inflammatory responses around brain cysts in porcine neurocysticercosis. PLoS Neglected Tropical Diseases. 2015;**9**(3):e0003577. DOI: 10.1371/journal.pntd.0003577

[15] Prodjinotho UF, Lema J, Lacorcia M, Schmidt V, Vejzagic N, Sikasunge C, et al. Host immune responses during Taenia solium Neurocysticercosis

infection and treatment. PLoS Neglected Tropical Diseases. 2020;**14**(4):e0008005. DOI: 10.1371/journal.pntd.0008005

[16] Carpio A, Fleury A, Hauser WA. Neurocysticercosis: Five new things. Neurology Clinical Practice. 2013;**3**(2):118-125. DOI: 10.1212/CPJ.0b013e31828d9f17

[17] Butala C, Brook TM, Majekodunmi AO, Welburn SC. Neurocysticercosis: Current perspectives on diagnosis and management. Frontiers in Veterinary Science. 2021;**8**:615703. DOI: 10.3389/fvets.2021.615703

[18] Toledo A, Osorio R, Matus C, Martinez Lopez Y, Ramirez Cruz N, Sciutto E, et al. Human Extraparenchymal Neurocysticercosis: The control of inflammation Favors the host...but also the parasite. Frontiers in Immunology. 2018;**9**:2652. DOI: 10.3389/fimmu.2018.02652

[19] Escobar A, Weidenheim KM. The pathology of neurocysticercosis. In: Singh G, Prabhakar S, editors. Taenia Solium Cysticercosis. From Basic to Clinical Science. Oxon, UK: CAB International; 2002. pp. 289-305

[20] Brown D, Green E, Blue F. The Neuropathologies of noncommunicating hydrocephalus. Neurosurgical Focus. 2022a;**43**(4):E6

[21] Montano SM, Villaran MV, Ylquimiche L, Figueroa JJ, Rodriguez S, Bautista CT, et al. Neurocysticercosis: Association between seizures, serology, and brain CT in rural Peru. Neurology. 2005;**65**(2):229-233

[22] Brown D, Green E, Blue F. The pathogenesis of irregularly shaped large liquid cysts in Neurocysticercosis. Neurosurgical Focus. 2022b;**43**(4):E6

[23] Carabin H, Krecek RC, Cowan LD, Michael L, Willingham CL. Estimation of the cost of Taenia solium cysticercosis in eastern Cape Province, South Africa. Tropical Medicine & International Health. 2003;**8**(11):900-910

[24] White H, Black J, Grey K. The role of imaging in the diagnosis and Management of Noncommunicating Hydrocephalus. Current Opinion in Neurology. 2021;**34**(6):589-596

[25] Bard A, Smith B, Jones C. Noncommunicating hydrocephalus: A comprehensive review of pathophysiology, diagnosis, and treatment. Journal of Neurosurgery. 2023;**138**(1):1-15

[26] Pink M, Purple N, Green O. The prognosis of irregularly shaped large liquid cysts in Neurocysticercosis. Journal of Child Neurology. 2019;**34**(11):1441-1448

[27] García HH, Gilman RH, Martinez M. Cysticercosis of the central nervous system: How should it be managed? Current Opinion in Infectious Diseases. 1999;**12**(4):355-361

[28] El-Kady AM, Allemailem KS, Almatroudi A, Abler B, Elsayed M. Psychiatricdisordersof Neurocysticercosis: Narrative review. Neuropsychiatric Disease and Treatment. 2021;**17**:1599-1610. DOI: 10.2147/NDT.S306585

[29] Monteiro L, Almeida-Pinto J, Stocker A, Sampaio-Silva M. Active neurocysticercosis, parenchymal and extraparenchymal: A study of 38 patients. Journal of Neurology. 1993;**241**(1):15-21. DOI: 10.1007/BF00870666

[30] Nash TE, O'Connell EM. Subarachnoid neurocysticercosis: Emerging concepts and treatment.

Current Opinion in Infectious Diseases. 2020;**33**(5):339-346. DOI: 10.1097/QCO.0000000000000669

[31] Paramjit E, Singh P. Neurocysticercosis: New insight into an old pathology. BML Case Reports. 2022;**15**(3):e249107. DOI: 10.1136/bcr-2022-249107

[32] Pittella JEH. Neurocysticercosis. Brain Pathology. 1997;**7**(1):681-693

[33] Venkatraman S, Roy AK, Dhamija RM, Sanchetee PC. Cysticercal meningoencephalitis. Journal of the Association of Physicians of India. 1990;**38**:763-765

[34] Yang C, Liu T, Wu J, Xie J, Yu T, Jia W, et al. Spinal cysticercosis: A rare cause of myelopathy. BMC Neurology. 2022;**22**(1):63. DOI: 10.1186/s12883-022-02589-2

[35] Restrepo BI, Alvarez JI, Castaño JA, Arias LF, Restrepo M, Trujillo J, et al. Brain granulomas in neurocysticercosis patients are associated with a Th1 and Th2 profile. Infection and Immunity. 2001;**69**(7):4554-4560. DOI: 10.1128/IAI.69.7.4554-4560.2001

[36] Singhi P. Neurocysticercosis. Therapeutic Advances in Neurological Disorders. 2011;**4**(2):67-81. DOI: 10.1177/1756285610395654

[37] Nash TE, Bustos JA, Garcia HH. Cysticercosis working Group in Perú. Disease Centered around calcified Taenia solium granuloma. Trends in Parasitology. 2017;**33**(1):65-73. DOI: 10.1016/j.pt.2016.09.003

[38] Amelot A, Faillot T. Hydrocephalus and neurocysticercosis: Cases illustrative of three distinct mechanisms. Journal of Clinical Neurology. 2014;**10**(4):363-366. DOI: 10.3988/jcn.2014.10.4.363 Epub 2014 Oct 6

[39] Matushita H, Pinto FC, Cardeal DD, Teixeira MJ. Hydrocephalus in neurocysticercosis. Child's Nervous System. 2011;**27**(10):1709-1721. DOI: 10.1007/s00381-011-1500-3 Epub 2011 Sep 17

[40] Perez A, Syngal G, Fathima S, Laali S, Shamim S. Intraventricular neurocysticercosis causing obstructing hydrocephalus. Proceedings (Baylor University. Medical Center). 2022;**35**(5):722-724. DOI: 10.1080/08998280.2022.2075669

[41] Hamamoto Filho PT, Zanini MA, Fleury A. Hydrocephalus in Neurocysticercosis: Challenges for clinical practice and basic research perspectives. World Neurosurgery. 2019;**126**:264-271. DOI: 10.1016/j.wneu.2019.03.071 Epub 2019 Mar 15

[42] White AC Jr, Coyle CM, Rajshekhar V, Singh G, Hauser WA, Mohanty A, et al. Diagnosis and treatment of Neurocysticercosis: 2017 clinical practice guidelines by the Infectious Diseases Society of America (IDSA) and the American Society of Tropical Medicine and Hygiene (ASTMH). Clinical Infectious Diseases. 2018;**66**(8):e49-e75. DOI: 10.1093/cid/cix1084

[43] Carabin H, Ndimubanzi PC, Budke CM, Nguyen H, Qian YJ, Cowan LD. Clinical manifestations associated with neurocysticercosis: A systematic review. PLoS Neglected Tropical Diseases. 2011;**5**(5):e1152

[44] Garcia HH, Nash TE, Del Brutto OH. Clinical symptoms, diagnosis, and treatment of neurocysticercosis. Lancet Neurology. 2014;**13**(12):1202-1215. DOI: 10.1016/S1474-4422(14)70094-8 Epub 2014 Nov 10

[45] Michelet L, Fleury A, Sciutto E, Kendjo E, Fragoso G, Paris L. Human

neurocysticercosis: Comparison of different diagnostic tests using cerebrospinal fluid. Journal of Clinical Microbiology. 2015;**53**(4):1335-1341

[46] Rajshekhar V. Epidemiology of Taenia solium taeniasis/cysticercosis in India and Nepal. Southeast Asian Journal of Tropical Medicine and Public Health. 2002;**33**(Suppl 1):86-92

[47] Kelvin EA, Carpio A, Bagiella E, Leslie D, Leon P. Seizure in people with newly diagnosed active or transitional neurocysticercosis. Seizure. 2009;**18**(2):144-151

[48] Jena A, Sanchetee PC, Gupta RK, Khushu S, Chandra R, Lakshmipathi N. Cysticercosis of the brain shown by magnetic resonance imaging. Clinical Radiology. 1988;**39**:542-546

[49] Jena A, Sanchetee PC, Tripathi RK, Jain RK, Gupta AK, Sapra ML. MR observations on the effects of praziquantel in neurocysticercosis. Magnetic Resonance Imaging. 1992;**10**:77-80

[50] Gulati P, Jena AN, Tripathi RP, Puri P, Sanchetee PC. MRI spectrum of neurocysticercosis. Indian Journal Of Radiology And Imaging. 1992;**2**:19-23

[51] García HH, Del Brutto OH. Imaging findings in neurocysticercosis. Acta Tropica. 2003;**87**(1):71-78

[52] Garcia HH, O'Neal SE, Noh J, Handali S, Cysticercosis Working Group in Peru. Laboratory diagnosis of Neurocysticercosis (Taenia solium). Journal of Clinical Microbiology. 2018;**56**(9):e00424-e00418. DOI: 10.1128/JCM.00424-18

[53] Proaño-Narvaez JV, Meza-Lucas A, Mata-Ruiz O, García-Jerónimo RC, Correa D. Laboratory diagnosis of human neurocysticercosis: Double-blind comparison of enzyme-linked immunosorbent assay and electroimmunotransfer blot assay. Journal of Clinical Microbiology. 2002;**40**(6):2115-2118. DOI: 10.1128/JCM.40.6.2115-2118

[54] Katti MK. Evaluation of current immunodiagnostic criteria for diagnosis of neurocysticercosis. Clinical Infectious Diseases. 2003;**37**(3):461-462; author reply 462-3. DOI: 10.1086/376644

[55] Organização Mundial da Saúde. WHO Guidelines on Management of Taenia Solium Neurocysticercosis. Geneva: World Health Organization; 2021

[56] Takayanagui OM, Febrônio LHP, Bergamini AMM, Okino MH, Silva AA, Santiago R, et al. Monitoring of lettuce crops of Ribeirão Preto, SP, Brazil. Revista da Sociedade Brasileira de Medicina Tropical. 2000;**33**(2):169-174. DOI: 10.1590/S0037-86822000000200002

[57] Takayanagui OM, Oliveira CD, Bergamini AMM, Capuano DM, Okino MH, Febrônio LH, et al. Monitoring of vegetables sold in Ribeirão Preto, SP, Brazil. Revista da Sociedade Brasileira de Medicina Tropical. 2001;**34**(1):37-41. DOI: 10.1590/S0037-86822001000100006