

REVIEW

TAENIASIS/CYSTICERCOSIS IN BALI, INDONESIA

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Abstract. *Taenia solium* and *Taenia saginata* are found in humans in Bali, Indonesia. During a field survey of 660 people in Bali from 2002-2009 of taeniasis/cysticercosis cases using mitochondrial DNA confirmation of the species, we detected 80 cases of *T. saginata* taeniasis, 2 dual *T. saginata*/*T. solium* infections with *T. solium* metacystodes in the brain and 12 neurocysticercosis (NCC) cases at Sanglah Hospital, Denpasar. Although the prevalence of NCC in Bali is low, sporadic cases are still present. There is no *Taenia asiatica* in Bali. We summarize here the field survey findings of taeniasis, including 1 dual infection with taeniasis and cysticercosis in 2007, and the reason why there are no *T. asiatica* cases and we describe 3 NCC cases admitted to Sanglah Hospital, Denpasar, Bali in 2004. Diagnosis was based on anamnesis, clinical examination, including CT Scan, histopathological, serological and mitochondrial DNA examinations. In order to prevent unexpected symptomatic NCC after treatment with praziquantel, we recommend introducing a rapid test to confirm taeniasis carriers and cysticercosis cases as a tool for real time diagnosis.

Keywords: *Taenia solium*, *T. saginata*, taeniasis, cysticercosis, Indonesia

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INTRODUCTION

In Asia, there are 3 human *Taenia* species: *Taenia solium* (pork tapeworm), *Taenia saginata* (beef tapeworm) and *Taenia asiatica* (Chao and Fan, 1986; Fan *et al*, 1987; Fan 1988; 1988; Zarlenga *et al*, 1991; Eom and Rim, 1993; Bowles and McManus, 1994; Hoberg *et al*, 2000; Ito *et al*, 2003; Eom, 2006; Okamoto *et al*, 2010). The taxonomy of *T. asiatica* is still unclear, since hybrid *T. saginata*/*T. asiatica* worms

have been found in Thailand (Okamoto *et al*, 2010) and China (Nkouawa *et al*, in preparation).

Taeniasis in human due to *T. saginata* and *T. asiatica* is caused by eating uncooked or undercooked beef and viscera of swine contaminated with metacestodes of these species, respectively. Metacestodes of *T. asiatica* may develop not only in pigs but also in cattle and goats (Fan *et al*, 1987, 1989). In contrast, *T. solium* only causes two distinct clinical presentations: taeniasis due to the presence of adult tapeworm(s) in the small intestine of humans after eating uncooked or undercooked pork contaminated with the metacestodes of this species, and cysticercosis caused by the presence of metacestode(s) in parenteral tissue after accidental oral ingestion of eggs of the parasite. Cysticercosis caused by metacestode(s) in the central nervous system (neurocysticercosis, NCC) is one of the most important causes of epilepsy, and a leading cause of late-onset epilepsy (Takayanagui and Odashima, 2006; Ito *et al*, 2006).

Cases of *T. solium*, *T. saginata* and *T. asiatica* have been reported from Indonesia. To date, there have been 3 endemic provinces for taeniasis/cysticercosis in Indonesia: North Sumatra, Bali and Papua. North Sumatra is endemic for *T. asiatica* taeniasis (Kosin *et al*, 1972; Fan *et al*, 1990; Wandra *et al*, 2006). Bali is endemic for *T. saginata* taeniasis and *T. solium* taeniasis/cysticercosis (Sutisna *et al*, 1999, 2000; Wandra *et al*, 2006; Sudewi *et al*, 2008). Papua is endemic for *T. solium* taeniasis/cysticercosis (Tumada and Margono, 1973; Handali *et al*, 1997; Simanjuntak *et al*, 1997; Sutisna *et al*, 1999, 2000; Wandra *et al*, 2000, 2003; Subahar *et al*, 2001; Ito *et al*, 2002; Margono *et al*, 2003, 2006; Salim *et al*, 2009). Taeniasis and cysticercosis are reported sporadically in Lampung,

Jakarta, East Java, West Kalimantan, East Kalimantan, North Sulawesi, South Sulawesi, South East Sulawesi, and East Nusa Tenggara Provinces of Indonesia (Simanjuntak *et al*, 1997; Margono *et al*, 2001; Wandra *et al*, 2003; Ito *et al*, 2004; Sudewi *et al*, unpublished).

Epidemiological surveys for taeniasis/cysticercosis were conducted in all 9 districts of Bali from 2002 to 2009. During the field surveys, we examined a total of 660 people and simultaneously collected data regarding NCC cases at Sanglah Hospital, Denpasar. In this review, we summarize 80 cases of *T. saginata* taeniasis, 1 dual infection with *T. solium*/*T. saginata*, in 2007 and 3 NCC cases admitted to the hospital in 2004.

TAENIASIS/CYSTICERCOSIS IN BALI

Taenia saginata taeniasis

During the epidemiological survey in Bali from 2002 to 2009, we detected a total of 80 cases of *T. saginata* taeniasis (32, 24, 7, 3, 3, 4, and 7 cases in 2002, 2004, 2005, 2006, 2007, 2008, and 2009, respectively) using mitochondrial DNA confirmation by multiplex PCR and DNA sequencings (Yamasaki *et al*, 2004; Ito *et al*, 2009). The risk factor for *T. saginata* taeniasis is consumption of "beef lawar", a traditional local food of raw minced beef. Butchers and their family members are often found to be infected with *T. saginata* in Bali and with *T. asiatica* in Lake Toba, North Sumatra (Wandra *et al*, unpublished).

In Gianyar District, *T. saginata* taeniasis cases were found yearly (32, 14, 5, 2, 3, 4, and 7 cases in 2002, 2004, 2005, 2006, 2007, 2008, and 2009, respectively). Approximately 84% of taeniasis cases (67/80) were from Gianyar District. There were no cases of reinfection with *T. saginata* after treatment with tapeworm(s). Once most

people are confirmed to have an infection, the majority will stop eating raw beef. The high number of cases in Gianyar District may be due to the low impact of health education campaigns advising the community to consume cooked beef only in order to prevent taeniasis. Further study is needed to determine the true prevalence of taeniasis in Gianyar District.

Nearly all taeniasis cases were suspected based on a question that asked about the expulsion of proglottids. Most people gave a reliable history, at least for *T. saginata*. *T. asiatica* is morphologically similar to *T. saginata* (Fan, 1988; Eom *et al*, 1993; Ito *et al*, 2003) and is fairly common in North Sumatra, Indonesia (Kosin *et al*, 1972; Fan *et al*, 1990; Wandra *et al*, 2006, 2007), but has never been reported from Bali. We believe the reason why Balinese people are not infected with *T. asiatica* is because they do not eat the uncooked viscera of swine, different from the people of North Sumatra (Wandra *et al*, 2006, 2007).

We found no cases of *T. solium* taeniasis in Bali. However, there are cysticercosis cases in Bali. In order to detect *T. solium*, we would have to develop a rapid diagnostic test to screen for taeniasis carriers. Serum samples of taeniasis cases may be useful for developing screening tests for taeniasis carriers (Wilkins *et al*, 1999; Levine *et al*, 2007; Nakao *et al*, unpublished), but fecal samples are useful to confirm taeniasis carriers and identify the species (Yamasaki *et al*, 2004; Guezala *et al*, 2009; Nkouawa *et al*, 2009).

Dual infection with *T. saginata* taeniasis and *T. solium* neurocysticercosis

In 2007, we found a 47-year-old Balinese male *T. saginata* carrier who appeared to be healthy and had no neurologic symptoms of cysticercosis. We treated him with praziquantel 15 mg/kg BW. A

single worm was expelled, examined morphologically and later confirmed to be *T. saginata* by multiplex PCR in Asahikawa, Japan. Unfortunately, he had seizure within 6 hours of treatment, requiring hospitalization for several days. A CT scan showed multiple cystic lesions in the brain. Serological examination carried out in Asahikawa, Japan, later showed weakly positive antibody responses to both native and recombinant antigens (Sako *et al*, 2000; Sato *et al*, 2006; Ito *et al*, 2009) before treatment, and a stronger response post-treatment (data not shown). This case shows asymptomatic NCC cases may become symptomatic after treatment even with a low dose of praziquantel (Flisser *et al*, 1993; Sarti *et al*, 2000). In 2009, we treated another dual infection case in Bali (Wandra *et al*, in preparation).

Cysticercosis due to *T. solium*

The first record of cysticercosis in Bali was reported from pigs more than 80 years ago (Le Coultre, 1928; Oemijati, 1977). Thirty-two years later, two human cases of subcutaneous cysticercosis (SCC) were reported (Soebroto *et al*, 1960). Since 1971, several cases of *T. solium*, epileptic seizures, SCC and NCC have been reported, including the seroprevalence of cysticercosis in Bali. Between 1960 and 1997, a total of six taeniasis cases due to *T. solium* have been confirmed. In contrast, a total of 44 cysticercosis cases have been reported. Both NCC and SCC are found in Bali, with a ratio of 2.6:1 for NCC (32 cases) and SCC (12 cases). However, there is no information about cases infected with both NCC and SCC (Soebroto *et al*, 1960; Hadidjaya, 1971; Ngoerah, 1975; Simanjuntak *et al*, 1977, 1997; Coker-Vann *et al*, 1981; Bakta *et al*, 1983; Theis *et al*, 1993; Sutisna, 1994, 1999; Sudewi and Nuartha, unpublished quoted from Sutisna *et al*, 2000). The seroprevalence

of cysticercosis in Bali ranged from 5.2 to 21% during 1981-1997 (Sutisna *et al*, 2000). One risk factor was consumption of pork lawar, an uncooked minced pork mixed with fresh pigs blood, a traditional cuisine among the Balinese people (Wandra *et al*, 2006, 2007). Pork lawar is more popular than beef lawar in Bali. This is based on Balinese Hinduism, which differs from Indian Hinduism (Simanjuntak *et al*, 1997; Ito *et al*, 2003; Wandra *et al*, 2007).

The number of cysticercosis cases has decreased dramatically, since only two sero-positive cases were detected from 9 districts in Bali among 660 people during 2002-2009. We did not detect any taeniasis cases due to *T. solium*. The decrease in the number of NCC and SCC cases due to *T. solium* may be due to improvement in household sanitation and pig husbandry through sustainable public health education in Bali and improvement in the economy. Most families have latrines and pigs are generally reared indoors (Wandra *et al*, 2007).

Although the prevalence of cysticercosis is currently low, sporadic cases are still detected at hospitals, especially at Sanglah Hospital, Denpasar. NCC cases included 1 case of disseminated cysticercosis (2003) (Sudewi *et al*, 2008), 3 cases of NCC (2004) summarized in this review, 1 case of NCC (2005), 2 cases of dual infection (2007, 2009), and 5 cases of NCC (2009) (Wandra *et al*, unpublished).

Case 1

A 50-year-old Balinese woman, from a rural village in Karang Asem District, eastern Bali was admitted to Sanglah Hospital on 4 September 2004. She complained of a headache and a history of epileptic seizures for two years duration, and presented with 2 subcutaneous nodules on her body. The subcutaneous nodules

were mobile, non-tender, located at the fossa cubity sinistra and femoralis dextra, measuring 1 and 1.5 cm in diameter, respectively. There were no abnormalities of the respiratory or cardiovascular systems. On neurological examination she was unconscious with a GCS of E2V1M5, pupil anisocore (5 mm/3 mm). The Babinski's sign was positive bilaterally, funduscopy showed papilledema bilaterally. Electroencephalography showed bifrontal slow waves. Laboratory testing, including routine blood tests, eosinophils and fecal examination, were normal. Excision of the subcutaneous nodules was performed and histopathological examination revealed a characteristic structure of a taeniid metacystode (Fig 1a). A CT scan showed an active lesion with surrounding edema of the frontoparietal dextra et sinistra. ELISA results using native antigens for screening and recombinant chimeric antigens for confirmation of cysticercosis, 100% specific to cysticercosis, were positive [(OD values in native and recombinant antigen systems: 0.392 (cut-off value: 0.051) and 0.446 (cut-off value: 0.093), respectively] (Sako *et al*, 2000; Sato *et al*, 2006).

The patient was treated with 10 mg diazepam, 300 mg phenytoin (intravenous) and 50 mg dexamethasone (intravenous) and 800 mg albendazole daily for one month. On the 16th day, the patient was discharged in stable condition without neurological deficit and free from seizures. However, 8 months later (May, 2005), she had a focal seizure. The family stated she stopped taking phenytoin for the previous 4 months. After taking phenytoin orally again, she again became seizure free. A repeated CT scan 3 months later (August 2005) showed a calcified lesion of the frontoparietal dextra et sinistra. The serology results were negative (OD values in native and recombinant antigen

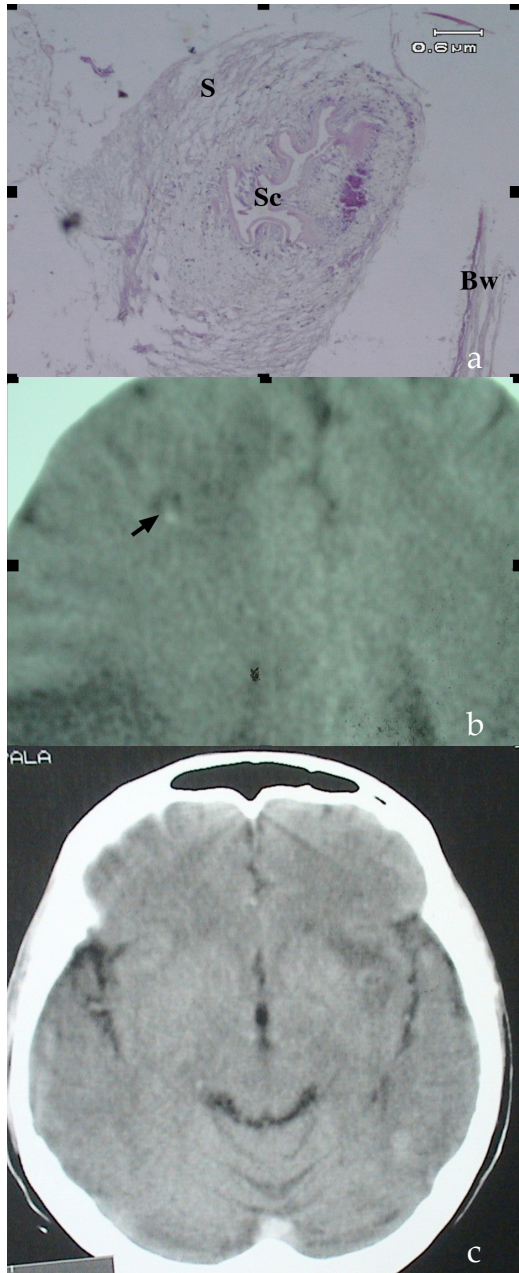


Fig 1–(a) Subcutaneous nodule showing a characteristic structure of a taeniid metacestode, scolex (S), spiral canal (Sc), and bladder wall (Bw). (b) CT scan showing an active lesion with scolex (arrow) with surrounding edema of the frontoparietal dextra et sinistra. (c) A calcified lesion after 3 months.



Fig 2–(a) CT Scan showing multiple cystic lesions with scoleces (arrow) and (b) multiple calcified lesions after 3 months.

systems: 0.027 and 0.034, respectively). Immunoblot also became negative (data not shown).

Case 2

A 31-year-old Balinese man, from a rural village in Gianyar District, Bali was admitted to Sanglah Hospital on 31 October 2004. He complained of headache and gave a history of epileptic seizures for 10 years duration with paresthesias. He had 3 generalized tonic-clonic seizures

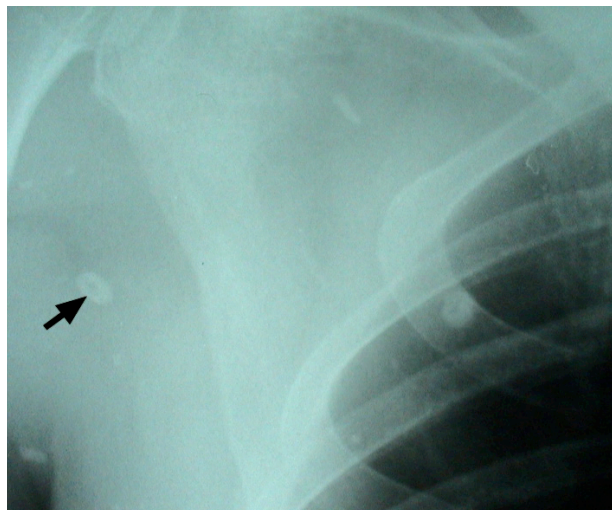


Fig 3—Chest radiograph showing multiple cigar-shaped calcified lesions (arrow).

3 hours prior to admission. On examination, he was conscious and had left sided paresthesia of his whole body. There were no abnormalities of the respiratory or cardiovascular systems. Funduscopy showed papilledema bilaterally. Laboratory data, including routine blood tests for eosinophils and fecal examination, were normal. A CT scan of the brain showed multiple cystic lesions with a scolex and multiple calcified lesions (Fig 2a). ELISA, using native and recombinant antigen systems, was positive (OD values: 0.338 and 0.879, respectively). He was treated with diazepam 10 mg/day orally, followed by phenytoin 300 mg/day (intravenous), albendazole 800 mg/day and dexametasone 40 mg/day for 1 month. He was free of seizures during hospitalization. A CT scan of the brain performed 3 month later showed the cystic lesions had disappeared and there remained multiple calcified lesions (Fig 2b). Antibody responses remained positive after treatment.

Case 3

A 60-year-old Balinese woman from a rural village of Denpasar Municipality,

Bali was admitted to Sanglah Hospital on 29 December 2004. She complained of a headache and a history of 3 focal seizures involving the right side of her body during the previous 3 months. She also had dysarthria and hemiparesthesias of the right side of the body 6 hours prior to admission. She was conscious with right hemiparesis, had muscle strength of 4/4 based on the Medical Research Council (MRC) scale, but had right supranuclear facial and hypoglossal nerve palsies, and right hemiparesthesia. The Babinski sign was negative and she had decreased deep tendon reflexes. Funduscopy showed

bilateral papilledema. Laboratory data, included routine blood tests for eosinophils and fecal examination, were normal. A CT scan showed a calcified lesion with surrounding edema in the parietooccipital region. A chest radiograph showed multiple cigar-shaped calcified lesions (Fig 3). Serological results with ELISA using native and recombinant antigen systems were positive (OD values: 0.092 and 0.371, respectively). She was treated with piracetam 12 grams, dexametasone 10 mg followed by 20 mg daily, and acetosal 100 mg, phenytoin 300 mg daily for one month. She gradually improved and was discharged from the hospital without neurological deficits on 4 January 2005. Antibody responses in this case remained weakly positive after treatment.

These 3 confirmed NCC cases in 2004 showed active *T. solium* cysts in the brain. Several retrospective studies of a Japanese NCC case reveal cysts can survive at least 10 years (Ito *et al*, 1999; Yanagida *et al*, 2010). Therefore, it is important to check antibody responses in NCC suspected or confirmed cases before and after treatment

in order to monitor progression.

CONCLUSION

T. solium and *T. saginata* have been described in Bali. Recent field surveys from 2002 to 2009 showed *T. saginata* taeniasis is still endemic. The prevalence of cysticercosis is now low, but sporadic cases are still detected at Sanglah Hospital, Denpasar, Bali. Clinicians should remember symptomatic NCC may be induced by treatment with low dose praziquantel for the treatment of *T. saginata* taeniasis, some may also have asymptomatic NCC. Cysticercosis outbreaks may occur even with a single taeniasis carrier of *T. solium* in the community (Schantz *et al*, 1992; Hira *et al*, 2004). We need to develop new tools for detection of taeniasis carriers, such as rapid tests to detect taeniasis and cysticercosis during field surveys in endemic areas (Handali *et al*, 2010a, b). In order to prevent unexpected seizures induced after treatment with praziquantel, we need to develop rapid serology to detect cysticercosis. One drug based on pumpkin seeds has been developed for the treatment of intestinal cestode infections in China, and it apparently, does not induce seizures (Li *et al*, in preparation). The recombinant antigens 100% specific for detection of cysticercosis (Sako *et al*, 2000; Sato *et al*, 2006) have been used in Indonesia (Sudewi *et al*, 2008) China, Thailand and Cameroon to detect NCC cases in the community (Li *et al*, 2006; Anantaphruti *et al*, 2010; Nkouawa *et al*, 2010). We need to introduce rapid immunochromatography test kits or other rapid tests to detect cysticercosis and taeniasis (Handali *et al*, 2010a, b) as was done for echinococcosis (Sako *et al*, 2009). Sustainable campaigns to eradicate of cysticercosis are important for people to know the risk factors for this disease.

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