Proposition of Fine Needle Aspiration Cytology as a Diagnostic Tool in Cases of Cysticercosis by *Taenia solium*

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ABSTRACT

INTRODUCTION: Cysticercosis in humans caused by the larval stage of *Taenia solium* is quite common in developing countries, including South Asia, and poses a serious health challenge in these countries. This study was mainly undertaken to prove the utility of fine needle aspiration cytology (FNAC) in the diagnosis of cysticercosis.

MATERIALS AND METHODS: The study included cases diagnosed with cysticercosis by FNAC from January 2008 to December 2015 who were reviewed for clinical data, cytomorphologic findings, and, when available, histopathologic findings.

RESULTS: The study included 24 cases, the majority being women (67%) with a median age of 28 years. Most cases presented with head and neck swelling which was firm and nontender. Aspiration yielded a clear fluid aspirate in most cases (33%). Cytology revealed the presence of wall of parasite in all cases, with the presence of hooklets in 3 cases.

CONCLUSIONS: This study reinforces that in cases where a definite parasitic parenchymal layer can be seen, FNAC eliminates even the need for biopsy for confirmation.

KEYWORDS: *Taenia solium*, diagnosis, FNAC

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Introduction

The larval stage of *Taenia solium* is the causative agent of the parasitic disease cysticercosis in humans.[1] Various organs, such as the brain, eye, heart, and lung, can be affected by this disease; however, it is usually seen as a palpable or visible nodule within subcutaneous tissue or muscle.[2] More than 50 million people are infected, making it the most common parasitic disease worldwide.[3] The number of people infected by *T solium* infection cysticercosis is estimated to be 20 million, and approximately 50 000 people die worldwide. The highest incidence of cysticercosis was in Latin America, namely, some regions of Mexico, where the prevalence is about 3.6%; in Asia, where it is 3.2%; and in the Caribbean (Haiti), where it is around 2.8%. In some regions of Africa, mainly in Western Africa, it ranges from 1.3% to 2.4%.[4] Several countries, such as Vietnam, China, Korea, and Indonesia, seem to have a high exposure to the parasite as indicated by seroprevalence studies, ranging from 0.02% to 12.6%. Also, infection rates determined by the examination of stool for ova and parasite range from 0.1% to 6% in India, Vietnam, and Indonesia. The most astounding number comes from Nepal in an area populated by farmers rearing mainly pigs, where it is as high as 50%.[5]

The preoperative diagnosis of cysticercosis can be made by radio imaging (computed tomographic [CT] scan, magnetic resonance imaging [MRI], and ultrasonography [USG]) and serological tests, such as enzyme-linked immunosorbent assay (<0.75 antibody not detected, ⩾0.75 antibody detected).[6] Although CT scans and MRI are very efficient in detecting these lesions, they are mostly not available or very expensive in these endemic areas. To travel to a tertiary health care center where these facilities are available may even take several days at times, thus adding to an already expensive diagnostic procedure.[4] The sensitivity and specificity of serological tests for the detection of antibodies against cysticercosis are 41.5% and 98.4%, respectively, with a positive and negative predictive value of 92.3% and 81.8%, respectively; although useful if positive, a negative test result does not necessarily rule out the disease in a patient.[7] Past infection by *T solium* itself or even cross-reactivity with other helminths can give a false-positive result,[8] and despite the presence of infection, if the lesion is solitary or is old and calcified, antibodies may not even be detected by serology.[9] Moreover, in muscular lesions, the scolex of the cyst may sometimes be better appreciable by USG than MRI[9]; however, in the evaluation of porcine *T solium* infection by Flecker et al,[10] a high false-positive rate was detected using ultrasound.

However, fine needle aspiration cytology (FNAC) has emerged as a cheap and widely acceptable method for the

diagnosis of cysticercosis[8] and can even be guided by USG when needed, further increasing the yield, eliminating false positives, and facilitating a correct diagnosis.

This study is being undertaken to describe the role of FNAC in diagnosing cysticercosis and also to study the cytological morphology of the parasite and associated cytological findings, as well as to correlate the clinical diagnosis with FNAC and histopathologic diagnosis when available.

Materials and Methods

The study included data from patients after taking informed consent from the patient or next of kin, with the inclusion criteria being patients with subcutaneous or palpable swelling in whom FNAC was performed and used as the diagnostic test for the diagnosis of cysticercosis. Data were collected over an 8-year period from January 2008 to December 2015. Other tests, such as USG, performed as an additional diagnostic tool were available only in a selected number of patients (Table 1). The clinical data and cytomorphologic findings and, when available, the histopathologic findings of these cases were reviewed by an expert pathologist and double-checked by at least 2 pathologists in a double-blind manner.

Fine needle aspiration cytology was performed using a 22- to 23-gauge needle and a 10-mL disposable syringe in all these cases. Slides were then prepared, both air-dried and wet-fixed in 95% ethyl alcohol, and stained with Giemsa and Papanicolaou stains, respectively.

Criteria necessary for the cytological diagnosis included demonstration of fragments of larval cuticle and parenchyma,[8] which consisted of a "reticulum of loose fibrillary stroma and round to oval nuclei,"[11] with suspicion raised if the smears contained eosinophils, neutrophils, epithelioid granuloma, or giant cells.

Histopathologic criteria essential for diagnosis were demonstration of a "multilayered cyst wall, with the outer, cuticular layer, smooth and hyalinised"[12] and "a row of tegumental cells beneath the tegument with the inner layer or parenchyma loose or reticular containing mesenchymal cells and calcareous corpuscles."[13]

Those cases that were eventually diagnosed with cysticercosis were reviewed for the associated cytological findings, nature of the lesion, presenting symptoms, and kind of material aspirated in each case. These cytological findings were correlated with the clinical findings and, when available, the histopathologic findings as well. All histologic specimens were fixed in 10% formalin, embedded in paraffin blocks, and cut and stained with conventional hematoxylin-eosin.

Results

The study included 24 patients, most of them being women (67%) in the age group ranging from 5 to 75 years. The mean age at diagnosis was 25 ± 17.6 years. Most of the patients experienced swelling in the head and neck area (29.2%; 7 of 24) (Figure 1). The lesions were mostly firm and nontender swellings (50%; 12 of 24) (Figure 2).

Table 1. Number of patients recruited and tests previously conducted.

NO. OF PATIENTS (TOTAL = 24)	RADIOLOGICAL DIAGNOSIS (USG)	OTHER TESTS
6	Cysticercosis	NA
18	NA	NA

Abbreviations: NA, not applicable; USG, ultrasonography.

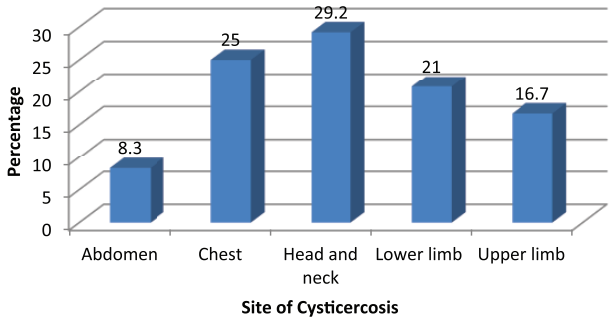

Figure 1. Site of cysticercosis.

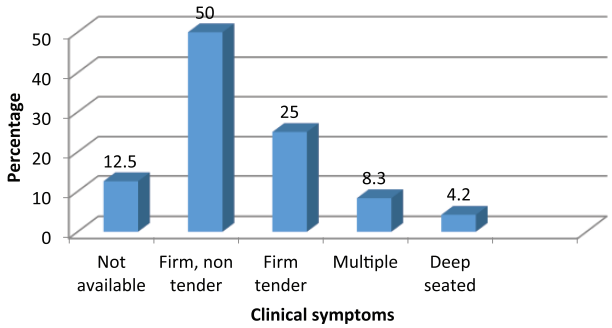

Figure 2. Clinical presentation of cysticercosis.

These cases were mostly clinically misdiagnosed as lipoma (29.2%; 7 of 24). Only 4 cases (16.7%) were correctly diagnosed as cysticercosis.

Aspiration mostly yielded a clear fluid aspirate (33%; 8 of 24). All aspirations were performed without complications (Figure 3).

The diagnosis of cysticercosis was made by FNAC on the basis of visualizing parasitic parenchyma in all the cases (Figures 4 to 7). However, the accompanying features and background infiltrates showed variations. The smears showed a mixed inflammatory infiltrate comprising neutrophils, lymphocytes, eosinophils, histiocytes, and giant cells (in varying proportions in different cases). Three (12.5%; 3 of 24) of these cases showed the presence of hooklets. In 3 (12.5%; 3 of 24) other cases, epithelioid granulomas along with multinucleated giant cells were also visible (Figure 8; Table 2).

A follow-up biopsy was done in 4 (4 of 24) cases, among which 1 was diagnosed with cysticercosis and the other 3 cases revealed no definite evidence of parasite (Figure 9A and B).

Discussion

The larval stage of the tapeworm *T solium*, *Cysticercus cellulosae*, is endemic in the developing world and is a major health challenge.[3] Cysticercus can affect various organs of the body; however, involvement of skeletal muscles and soft tissue is relatively rare.[14] Presentation as subcutaneous swellings, as seen in our series, leads to misinterpretation of mesenchymal lesions[8]; as seen in this study, most of the cases were misinterpreted as lipoma.

The mean age at diagnosis was 25 ± 17.6 years. Cysticercosis seems to be predominantly a disease of the young as the mean age in the study by Adhikari et al[11] was 26.4 years, whereas Handa et al[8] showed cysticercosis to be the commonest in the first 3 decades of life. Supporting the same was another study by Kodiatte et al[15] where the mean age at diagnosis was 25.77 ± 20.81 years.

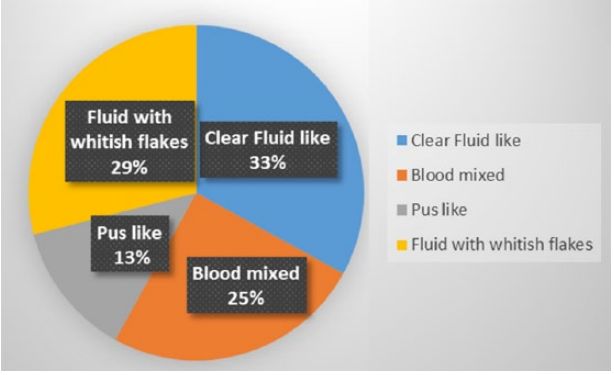

Figure 3. Characteristics of the aspirate.

Cysticercosis can present as a subcutaneous palpable nodule or be found in other areas such as the eye and central nervous system. In our study, the most common location was the head and neck area (7 of 24), similar to the findings by Kodiatte et al[15] (57%). However, there seems to be no pattern of predominance as Handa et al[8] found upper limb to be the commonest site and Rajwanshi et al[16] found trunk to be the commonest. In the study by Ghimire et al,[14] arm was the commonest site.

Most of these patients were clinically diagnosed with lipoma (7 of 24), followed by soft tissue tumor, lymph node, and even dermoid cyst. The same findings were appreciated in a study done in mid and far western regions of Nepal, where again lipoma was the most common misdiagnosis.[14] In some other studies within the subcontinent, tuberculous lymphadenitis was the commonest clinical diagnosis, given the heavy burden of tuberculosis in the region.[15] Some cases in our study were also correctly diagnosed as having cysticercosis (4 of 24); however, these were cases in which a radiological diagnosis suggestive of cysticercosis by USG had already been given.

The aspirate was clear and fluid-like in most cases (8 of 24), with even the presence of whitish flakes along with

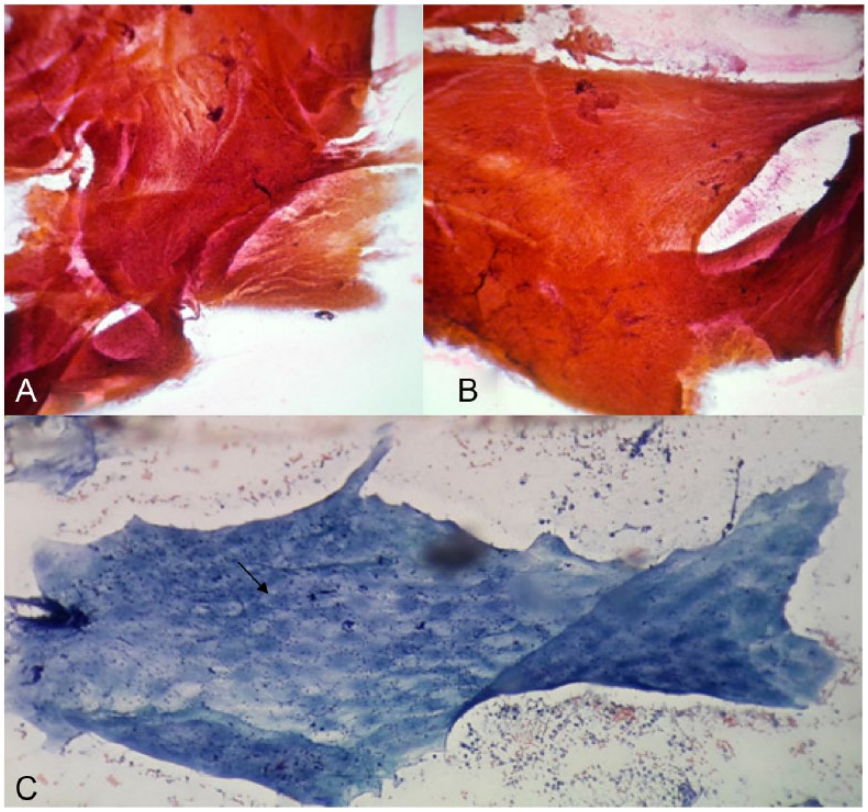

Figure 4. Photomicrograph of aspiration smear revealing a loose fibrillary stroma making up the parenchymal layer of the larva with numerous interspersed nuclei (arrow): (A) and (B) Papanicolaou test, ×40 and (C) Papanicolaou test, ×100.

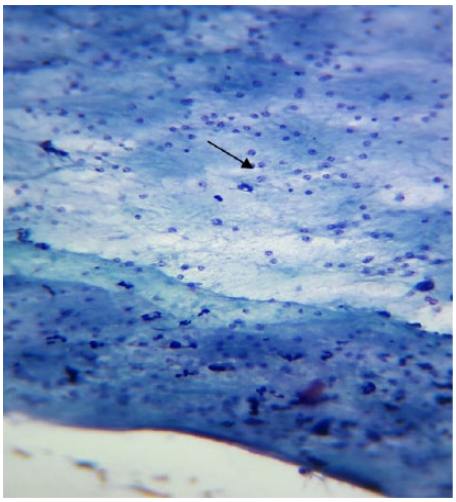

Figure 5. Photomicrograph of aspiration smear in high magnification showing pyknotic nuclei of subcuticular cells (arrow) of cysticercus (Papanicolaou test, ×400).

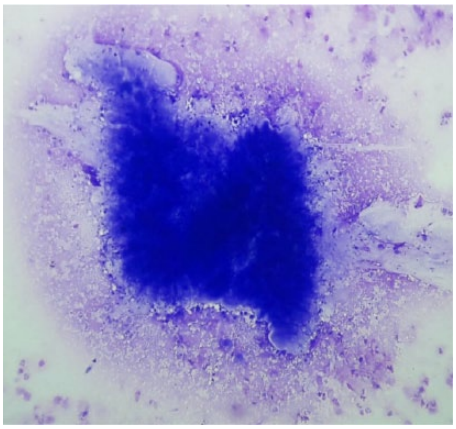

Figure 6. Photomicrograph of aspiration smear showing low-power magnification of the parasite showing an amorphous mass of parenchyma with granular and fibrillar material (Giemsa, original magnification ×100).

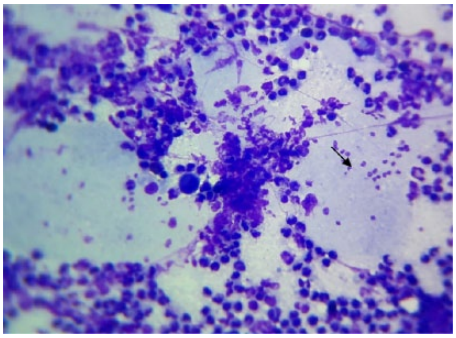

Figure 7. Photomicrograph of aspiration smear showing inflammatory reaction surrounding the fragment of bladder wall (arrow) (Giemsa, original magnification ×400).

fluid-like materials in some (7 of 24). This finding was largely similar to another study where most cases yielded a clear fluid as well (38 of 125),[8] with yet another study revealing that

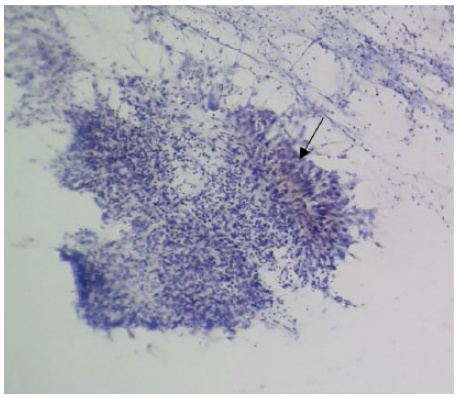

Figure 8. Photomicrograph of aspiration smear showing a collection of epithelioid cells (arrow) (Papanicolaou test, original magnification ×100).

Table 2. Microscopic features using FNAC.

MICROSCOPIC FEATURES USING FNAC	NO. (%) OF CASES
Mixed inflammation with wall of parasite	17 (70.8)
Suppurative inflammation with wall of parasite	1 (4.2)
Granulomatous inflammation with wall of parasite	3 (12.5)
Mixed inflammation, hooklets with wall of parasite	3 (12.5)

Abbreviation: FNAC, fine needle aspiration cytology.

almost all the cases yielded a few drops of clear, pearly white fluid with chalky membranous pieces which were difficult to spread on the slide (29 of 30).[15] These findings point toward a common trend of a clear fluid-like aspirate in most of these cases, which could thus be an indicator of a parasitic infection; nevertheless, a purulent and hemorrhagic aspirate does not rule out the possibility of a parasitic infection, as this was also seen in a significant number of cases.[8] This was supported by the findings by Gill et al where 7 cases (7 of 22) yielded a clear fluid.[18] However, findings by Adhikari et al[11] were different, as most of their cases had a blood-mixed aspirate.

An epithelioid cell and giant cell reaction, as well as an inflammatory reaction, can be evoked by the parasite.[16,18] In our study, a granulomatous inflammation with the presence of epithelioid cell granulomas and multinucleated giant cells was seen in 3 cases, the findings being similar to another study (3 of 10),[11] thus indicating that a foreign body giant cell reaction may not be as common as expected.

The cytomorphologic features seen in all our cases were fragments of larvae of cysticercus, which comprised the parenchymal layer made up of a reticulum of loose fibrillary stroma and round to oval nuclei. Hooklets were seen in only 3 cases. Similarly, hooklets were seen in 6 cases in the study done in far Western Nepal (6 of 27).[14] This differs from another study done in Nepal where hooklets were seen in none of the cases.[11] However, in a study by Handa et al,[8] hooklets were seen in only

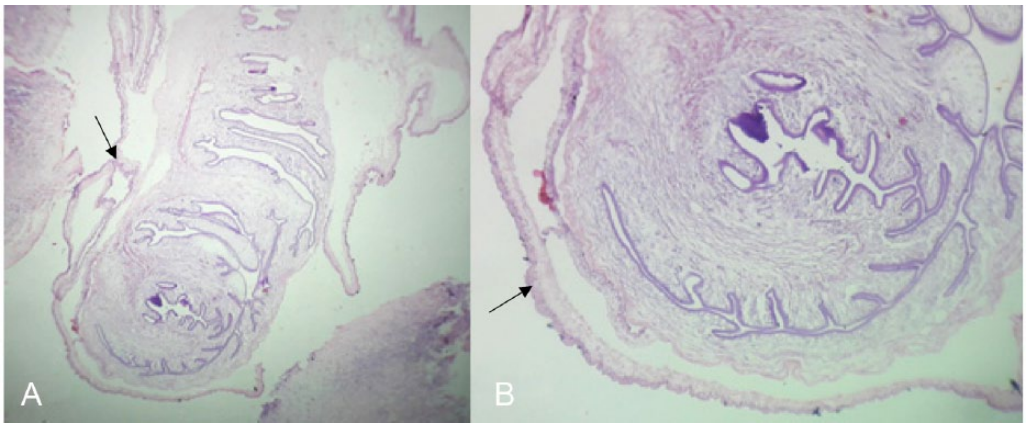

Figure 9. Photomicrograph of tissue section under low and higher magnification, showing a thin fibrous cyst wall within which the cysticercus larva lies enclosed (arrow): (A) ×40 and (B) ×100 (hematoxylin-eosin).

1 case among 125 cases, and Kodiatte et al[15] found hooklets in just 1 case as well. This indicates the rarity of finding hooklets of cysticercus in cytological specimens.

Of the 4 cases that were biopsied, cysticercosis was seen in only 1 (1 of 4) case, whereas others revealed histologic features supporting the likelihood of a parasitic lesion, with presence of epithelioid cell granulomas, multinucleated giant cells, as well as eosinophils in the histopathology specimens. Similar findings have been seen in other studies as well.[8,11] The reasons for a negative follow-up biopsy could be aspiration of the entire parasite and therefore its absence in the biopsy specimen. It may also be possible that portions of the parasitic fragment are lost during surgical removal or grossing procedures owing to cyst rupture.

Conclusions

The excellent performance of FNAC, as seen in this study, in diagnosing cysticercosis obviates the need for lengthy histopathology for diagnosis. Although not very common according to the findings in our study, the differential diagnosis of cysticercosis has to be kept when dealing with subcutaneous nodules, especially in our part of the world, as *T solium* is endemic in some of the ethnic communities in the eastern part of Nepal, where it is not uncommon to find cohabitation with pigs.[7] This study and a number of other studies done within the subcontinent[8,11,14,16,17] reinforce the fact that FNAC is a minimally invasive, rapid, and reliable diagnostic test for the diagnosis of cysticercosis.

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Author Contributions

NS conceived and designed the experiments and wrote the first draft of the manuscript. DRM analyzed the data, contributed to the writing of the manuscript, and jointly developed the structure and arguments for the paper. SP and SD agree with manuscript results and conclusions. SP, SD, SK, and PU made critical revisions and approved the final version. All authors reviewed and approved the final manuscript.

Disclosures and Ethics

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