Cytological diagnosis of parasites presenting as superficial nodular swelling: report of 35 cases

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Received: 29 October 2011 / Accepted: 28 December 2011 / Published online: 20 January 2012
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Abstract Parasitic infestation often present with superficial nodular swelling. Fine needle aspiration cytology plays an important role in prompt diagnosis of the disease. To study the role of FNAC in the diagnosis of parasites presenting as skin or subcutaneous nodules. Total 361 cases of superficial swellings at various sites were subjected to fine needle aspiration cytology. Out of the 361 cases, 35 cases were diagnosed as suggestive of parasitic infestation. These 35 cases form the study group. In 14 cases out of 35 cases, a definitive diagnosis of parasitic infestation was made as parasite or fragments of parasite were seen in the aspirate. In 21 cases, neither parasite nor fragments could be identified on the aspirates and a diagnosis of parasitic inflammation was suggested on the basis of other cytomorphological findings. In 17 of these cases, a biopsy correlation was available, which revealed definitive parasite in 8 cases and the remaining 9 were reported as suggestive of parasitic cyst. The cytological diagnosis was confirmatory in cases where the parasite fragment were identified in the smears. However, in other cases, clear aspirate, presence of eosinophils, macrophages and typical granular dirty background are the features which should prompt the cytologist to the possibility of parasitic infestation.

Keywords Cytodiagnosis · Parasite · Superficial swelling

Introduction

Fine needle aspiration cytology (FNAC) is a well-recognized diagnostic procedure for evaluation of inflammatory nodules caused by parasites. Specific parasites causing diseases such as filariasis, hydatid disease, and cysticercosis have been detected by this technique (Verma and Kapila 1989; Kung et al. 1989; Jayaram 1989; Hofman and Huerre 2002). The diagnosis can be confirmed by the histopathological examination of the excised specimen. The present study was done to analyze the role of FNAC in the diagnosis of parasites along with the cytomorphology of actual parasite and to study the cytological features suggestive of parasitic infestation in those cases where the actual parasite could not be demonstrated.

Materials and methods

Out of the 361 cases presenting with palpable superficial nodules at different sites, 35 cases with age ranging from 4 to 66 years, having swelling at various sites with cytological diagnosis of parasitic lesion or suspicious of parasitic lesion were included in the present study. FNAC was performed with a 22-gauge needle. Aspiration was made by technique of Martin and Ellis (1930) and the aspirated material was smeared on the glass slides. In case of cystic lesions, cyst content was aspirated and smears prepared from cyst fluid after cytocentrifugation were studied along with the aspiration performed from cyst wall. The smears were stained with Papanicolaou stain after fixation in 95% alcohol and with May-Grunewald-Giemsa stain after air drying. Subsequent excision biopsy was also evaluated wherever possible. The sections were reviewed and findings were correlated with the cytological findings.

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Results

The study included 35 patients in the age group 4–66 years with cytological diagnosis of parasitic lesion or suspicious of parasitic lesion. Out of 35 cases, 31 cases were confirmed on cytology and/or histopathology as parasitic lesions. The rest of the 4 cases responded to treatment so biopsy was not performed. Among 35 patients in the present study 16 were females and 19 were males. 12 cases

presented with arm swelling, 8 with neck swelling, 4 with abdominal wall swelling, 3 with back swelling, 2 with swelling on shoulder and scrotum, 1 with breast, axilla, mandible and fore head swelling. The clinical and cytological features of all patients were tabulated (Table 1). All the patients presented with slow growing nodule, soft to firm in consistency, and the provisional clinical diagnoses were lipoma, neurofibroma, tuberculous and reactive lymphadenopathy, epididymal cyst, benign soft tissue tumor,

Table 1 Showing the clinico-cytological features of all the cases

Case	Age/sex	Site	Clinical diagnosis	Cytological findings		
				Aspirate	Parasite	Associated cytological findings
1	19/F	Right arm	Lipoma	Purulent	Bladder wall cysticercosis	N, L, M, DGB, C
2	22/F	Left arm	Neurofibroma	Clear fluid	Nil	M, L, ECG, Eo, H, G
3	26/M	Left neck	TB lymphadenitis	Purulent	Nil	N, M, L, Eo, DGB
4	25/F	Right neck	TB lymphadenitis	Purulent	Bladder wall cysticercosis	L, ECG, DGB, H, C
5	32/F	Abdominal wall	Lipoma	Purulent	Nil	N, M, L, Eo
6	24/M	Scrotal swelling	Epididymal cyst	Clear fluid	Microfilaria	M, L, DGB
7	21/M	Left axilla	Reactive lymphadenitis	Clear fluid	Nil	M, L, ECG, Eo, G
8	18/M	Left arm	Parasitic cyst	Clear fluid	Bladder wall cysticercosis	N, M, L, Eo
9	36/M	Right neck	Reactive lymphadenitis	Hemorrhagic	Nil	N, M, L, Eo
10	31/F	Right arm	Benign soft tissue tumor	Clear fluid	Bladder wall cysticercosis	N, M, L, H
11	28/F	Left neck	TB lymphadenitis	Clear fluid	Nil	L, PC, ECG, G
12	32/F	Right breast swelling	Benign breast disease	Hemorrhagic	Microfilaria	ECG, M, L, H
13	27/F	Left back	Benign soft tissue tumor	Purulent	Nil	N, M, L, PC, DGB
14	35/M	Left mandible	Benign soft tissue tumor	Hemorrhagic	Nil	M, L, Eo, DGB
15	40/M	Right lower back	Parasitic cyst	Clear fluid	Bladder wall cysticercosis	M, L, C
16	4/F	Abdominal wall	Benign soft tissue tumor	Hemorrhagic	Nil	N, M, L, Eo
17	30/M	Left arm	Benign soft tissue tumor	Purulent	Bladder wall cysticercosis	M, L, C, DGB
18	9/F	Left fore head	Lipoma	Clear fluid	Nil	L, Eo, ECG
19	29/M	Left neck	Reactive lymphadenitis	Purulent	Nil	N, M, L, DGB
20	18/F	Right neck	Reactive lymphadenitis	Purulent	Bladder wall cysticercosis	M, L, DGB
21	28/M	Left shoulder	Benign soft tissue tumor	Purulent	Nil	N, M, L, ECG, DGB
22	20/F	Right back	Lipoma	Purulent	Bladder wall cysticercosis	M, L, DGB, H, C
23	26/M	Abdominal wall	Inflammatory swelling	Purulent	Hydatid cyst wall	M, L
24	22/M	Scrotal swelling	TB epididymitis	Purulent	Microfilaria	N, M, L, Eo
25	19/M	Right shoulder	Benign soft tissue tumor	Purulent	Nil	L, ECG, DGB, H, PC, G
26	23/F	Left arm	Benign soft tissue tumor	Clear fluid	Bladder wall cysticercosis	M, L, Eo
27	40/F	Right neck	Benign soft tissue tumor	Hemorrhagic	Nil	M, L, DGB
28	44/M	Left arm	Parasitic cyst	Purulent	Bladder wall cysticercosis	N, M, L, DGB, C
29	22/M	Right arm	Neurofibroma	Purulent	Nil	N, M, L, Eo, DGB
30	64/M	Abdominal wall	Epidermal inclusion cyst	Purulent	Nil	N, M, L, DGB, C
31	55/F	Left arm	Benign soft tissue tumor	Purulent	Nil	L, ECG, DGB, H, C, G
32	32/M	Right neck	TB lymphadenitis	Purulent	Nil	N, M, L, DGB
33	39/F	Left arm	Benign soft tissue tumor	Purulent	Nil	M, L, ECG, Eo, H, G
34	52/F	Left neck	Reactive lymphadenitis	Purulent	Nil	N, M, L, DGB
35	55/M	Right arm	Epidermal inclusion cyst	Purulent	Nil	N, M, L, DGB, C

N neutrophil, L lymphocyte, Eo eosinophil, M macrophages, H histiocytes, PC plasma cell, ECG epithelioid cell granuloma, G giant cell, C calcification, DGB dirty granular background, M male, F female

epidermal inclusion cyst and parasitic lesion. In 21 cases aspiration yielded purulent fluid, in 9 cases, the aspiration yielded clear fluid in and in the rest of the 5 cases yielded hemorrhagic fluid. All aspirations were performed without complications.

In 14 cases on FNAC, actual parasite structures were demonstrable in the smears which included 10 cases of cysticercus, 3 cases of filariasis and one case of hydatid cyst. In 10 cases parts of cysticercus cellulosae were identified. The larval part included the ciliated wall of the larvae and the parenchymal reticulin of thin fibril with characteristic nuclei and calcareous spherules (Fig. 1a, b). The nuclei characteristically had prominent chromatin condensation on their nuclear membrane. Follow-up biopsy confirmed the diagnosis (Fig. 2).

In 3 cases gravid adult filarial worm was identified containing coiled form of microfilarial larvae (Fig. 3) along with neutrophils, eosinophils and few lymphocytes. One hydatid cyst was aspirated from the abdominal wall swelling showed fragments of hyaline, lamellated cyst wall membrane (Fig. 4). Hooklets were not seen in any case. In 17 cases, the cytological findings were very much suggestive of a parasitic cyst; however, no parasite could be seen. The smears showed a mixed inflammatory infiltrate comprising neutrophils, lymphocytes, eosinophils, macrophages in a dirty granular background. Epithelioid non-necrotising granuloma was seen in 9 out of 35 cases. In these cases Ziehl Neelson staining was done which came out to be negative. No actual parasite structure could be demonstrated in any of these cases. A cytological diagnosis of parasitic cyst was suggested and excision was advised. Follow-up biopsy of 17 suggestive cases confirmed the diagnosis of parasite which included 1 case of hydatid cyst and 16 cases of cysticercus (Figs. 5, 6).

Fig. 2 Photomicrograph of tissue section showing cysticercosis larva enclosed in a thin fibrous cyst wall

Fig. 3 FNAC smear showing adult gravid worm containing coiled form of microfilarial larvae

Fig. 1 a, b FNAC smears demonstrating wall of cysticercus cellulosae with calcareous spherule (arrow) surrounded with inflammatory cells

Fig. 4 FNAC smear demonstrating fragments of lamellated membrane

Fig. 5 Smear shows non necrotizing epithelioid cell granuloma in a dirty granular background

Fig. 6 Smear shows degenerating muscle fragment (mimicking parasitic fragment) against a dirty background

Discussion

A wide range of parasitic infections can present as superficial nodule. Various parasites pass through the skin on its migration to the blood stream or the infestation may be localised to the skin and subcutaneous tissue. The parasites causing diseases such as filariasis, hydatid disease, and cysticercosis have been detected by FNAC (Verma and Kapila 1989; Kung et al. 1989; Jayaram 1989; Hofman and Huerre 2002).

Human cysticercosis is the larval infestation of the cestode *Taenia solium*. The cysticercus can be found in any organ, but is common in skeletal muscle, subcutaneous tissue, eyes and the central nervous system. Fully developed cysticerci are about 1 cm in diameter.

Hydatid cyst is one of the most serious helminthic diseases of human being with worldwide distribution, caused by larval form of the cestode worm of *Echinococcus*. It may develop in almost any part of the body. The most common location is liver (75%), followed by lung (15%) and only 10% occur in rest of the body (Kiresi et al. 2003). Hydatid cystic disease of the soft tissues is uncommon, accounting for only 2.3%, according to the largest published series that consists of 24 cases in 1,056 patients (Abu-Eshy 1998).

There are an estimated 60 million people infested with filariasis in Southeast Asia Region and about 31 million people having clinical manifestation of filariasis (Chowdhary et al. 2008). The spectrum of illness in filariasis is wide and varied but asymptomatic microfilaremia is the most common manifestation (Sharma et al. 2005). The classical clinical features of lymphatic filariasis include lymphangitis, lymphadenitis, hydrocoele, elephantiasis, chyluria, allergic manifestations, and tropical eosinophilia. Other less frequent presentations include recurrent inflammatory lesions, localized nodules in the breast, scrotum, and subcutaneous tissue (Jain et al. 2001).

Although not common, hydatid cyst may also occur in subcutaneous tissue, and it bears many similarities to cysticercus. Both the parasites have a bladder wall, have scolices with hooklets, and can incite an inflammatory response but cytomorphological details help to distinguish the two. The bladder wall is thin, membranous in cysticercus but thicker acellular lamellated in a hydatid cyst (Arora et al. 1994). Hydatid cysts have multiple daughter cysts within a parent cyst and hence may yield many scolices in an aspirate. In contrast, cysticercus has only one scolex. The scolex of cysticercus is large, almost 1 mm diameter with two rings of alternating large and small hooklets measuring 170 and 130 μ m, respectively. The scolex, although an uncommon finding in cytology smears, if present is visible to the unaided eye and is recognized at scanning magnification (Arora et al. 1994). In contrast, multiple scolices suspended in clear fluid

are aspirated from viable hydatid cysts. In echinococcus, individual scolices are small and the hooklets measure 22 and 40 μm and can be appreciated at higher magnification (Singh et al. 2006). The calcareous corpuscles are a unique feature of cestode tissue are not seen in hydatid cyst. These spherical, non-cellular masses occur in the parenchyma and are especially seen in larval cestodes. The corpuscles take on a bluish purple color in hematoxylin and eosin stain (Ash and Orihel 1990).

The diagnosis of cysticercus is usually made when fragments of larval cuticle and parenchyma are identified. The presence of scolex in cytology smears is an uncommon finding (Verma and Kapila 1989; Kumar and Misra 1991; Rajwanshi et al. 1991). No scolex or hooklets were seen in any of our aspirates. In most of our cases diagnosis of cysticercosis was made because of finding of wall of cysticercus cellulosa and calcareous spherules. The diagnosis of hydatid cyst is usually made when the fragments of hyaline lamellated cell wall membrane, scolices, hooklets and brood capsules are seen in the smears (Leiman 1999).

In our case only lamellated membrane was aspirated, confirmatory diagnoses could only be made on histopathology.

Though there are eight species of filarial worm which infect humans, *Wuchereria bancrofti* and *Brugia malayi* are responsible for most of the cases in India (Chowdhary et al. 2008). Microfilariae of *W. bancrofti* are characterized by a sheath, which is longer than the larval body, hence tail tip is free of nuclei. On the other hand, microfilariae of *B. malayi* are smaller in size and nuclei extend up to the tail tip (Chowdhary et al. 2008). Various reports in the literature describe the tissue reaction as ranging from an intense inflammatory reaction of neutrophils, lymphocytes, eosinophils, epithelioid cells, and foreign body giant cells surrounding dead worm (Arora et al. 1996). Liquefaction necrosis, Charcot Leyden crystals, and degranulated eosinophils have also been described (Kumar and Misra 1991). Many authors have reported microfilariae in breast lumps by FNAC smears (Yenkeshwar et al. 2006; Varghese et al. 1996; Pandit et al. 1997; Bapat and Pandit 1992; Kapila and Verma 1996; Rukmangadha et al. 2006). The most common stage, according to researchers, found in cytological smears is microfilaria (62.3%), the adult worm being seen less commonly (13.7%) (Jain et al. 2001). One of our cases presented with breast swelling, showed microfilaria. The granulomatous response was seen, the clinical suspicion was that of a benign breast disease. Our Two cases presented with scrotal swellings showed microfilariae on aspiration. The lymphatic vessels of spermatic cord appear to be common and perhaps the principal site of adult *W. bancrofti* in men with asymptomatic microfilaremia. Noroes et al. (1996) demonstrated occurrence of living *W. bancrofti* in scrotal area of men.

In 13 out of our 35 cases, that is 37.15%, showed eosinophils. In 19 out of 35 cases, that is 54.29%, showed dirty granular background. Therefore finding of eosinophils and dirty granular background indicates parasitic lesion. 5 out of 9 clear aspirates, that are 55.56%, showed actual parasite as compared with 8 out of 21 purulent aspirates and 1 out of 5 hemorrhagic aspirates. This indicates that chances of finding of actual parasite are more in clear aspirate.

The cytological diagnosis is quite straightforward in cases where actual parasite structure (parasite fragment, calcareous corpuscles and detached single hooklets) is identified in the smears. However Suspicion about a parasitic lesion starts with the presence of eosinophils, neutrophils, palisading histiocytes and giant cells in an aspirate from superficial nodule (Hofman and Huerre 2002; Bapat and Pandit 1992). When parasites degenerate, there is an infiltration of inflammatory cells, associated with the development of foreign body granulomas. These types of cells in variable composition along with typical granular dirty background and clear aspirate are the features which should always indicate the pathologist to the possibility of parasitic infestation. FNAC is a low-cost outpatient procedure. It is one of the tools for preoperative diagnosis and may even obviate the need for open biopsy (Adhikari et al. 2007).

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