ORIGINAL RESEARCH PAPER

Pathology

CYTOLOGICAL DIAGNOSIS OF FOLLICULAR DENDRITIC CELL SARCOMA WITH REVIEW OF LITERATURE - STUDY OF FOUR CASES

KEY WORDS: FDCS, Sprinkling of lymphocytes, CD21, CD23

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ABSTRACT

Objective: Follicular dendritic cell sarcoma (FDCS) is a rare neoplasm arising from follicular dendritic cells of germinal centres. The most common site of origin is lymph nodes and it may mimic a variety of tumours at that location, including metastatic carcinomas and sarcomas. Diagnosis is frequently missed on cytology as there are very few case reports describing the cytological characteristics of the lesion. Here we report four cases highlighting the utility of FNA and cell block in the diagnosis of FDCS.

Materials and Methods: Four cases of FDCS diagnosed on cytology were retrieved from the cytology register during the period 2015-2017. FNA was performed from the following sites - tonsil, cervical lymph node, liver and abdominal lymph node .Age ranged from 25-55yrs . Three were males & one female. IHC study was done on formalin fixed cell block tissue.

Results: Cytomorphology showed plump ovoid to spindle cells, in vague swirling / whorl pattern and also discohesive cells, with vesicular nucleus, small distinct nucleoli .Numerous lymphocytes were sprinkled in between the tumour cells. On IHC study the tumour cells were positive for CD 21, 23 in all 4 cases .

Conclusion: This study emphasizes the importance of FNAC which is less invasive, cheap and cost effective method to diagnose this rare neoplasm with cell block and IHC as ancillary tests.

INTRODUCTION:

Follicular dendritic cell sarcoma (FDCS) is a rare neoplasm with follicular dendritic cell of lymphoid follicle as the postulated normal counterpart. FDCS are classified under histiocytic and dendritic cell neoplasms by the WHO classification of tumours (1) .They occur in both nodal and extra nodal sites. There is neoplastic proliferation of spindle to ovoid cells with morphological and immunophenotypic features similar to normal follicular dendritic cells.

The diagnosis of this uncommon tumour requires a high degree of suspicion even on histomorphology. There are only few case reports of this tumor on cytology. Though the histomorphology is reflected on cytology it is quite challenging to diagnose on FNAC. FDCS has low to intermediate grade sarcoma behaviour. Accurate characterization of this neoplasm is important in planning optimal treatment given its potential for recurrence and metastasis. We describe four cases of FDC diagnosed on cytology with ancillary tests like cell block and IHC.

MATERIALS AND METHODS:

Four cases of Follicular dendritic cell sarcoma from the tertiary cancer centre were retrieved from cytology register during the period of 2015-2017. The clinical and radiological details of the patients were obtained from the medical records department. The cytomorphological features on FNA smears that were stained with Papanicolaou and Maygrunwald Giemsa stains were reviewed along with cell block slides. The material for cell block was fixed in 10% neutral buffered formalin and processed. Ancillary tests like immunohistochemistry was done on the cell block sections for two cases and the diagnosis was confirmed. Two of the cases were confirmed on biopsy with IHC.

RESULTS:

CASE 1

A 55 years old male patient presented with complaints of pain during swallowing of 1month duration. On examination he had a 4 x 3 cm, proliferative growth with narrow peduncle attached to right posterior tonsillar pillar with central ulceration. His other tonsil was normal. There was no other lymphadenopathy. CT of head and neck showed a homogenous soft tissue density lesion in the right lateral pharyngeal wall measuring 4.3x2.5x2.6 cm involving tonsil, soft palate and post pharyngeal wall. The biochemical parameters were within normal limits. FNA of the mass exhibited cellular smears with plump ovoid to spindle cells in vague swirling / whorl pattern and also discohesive cells with vesicular nuclei and small distinct nucleoli. Numerous lymphocytes were sprinkled in between with focal aggregates & a few giant cells were noted (Fig 1, 2) .A possibility of FDCS with a differential of lymphoepithelial lesion was given on smears. Biopsy of the tonsillar lesion (Fig 3) was done and subjected for a panel of IHC markers. Tumour cells were immunoreactive for CD21 and CD23, focally positive for EMA and negative for CK and CD68. LCA and CD 20 stained reactive B lymphocytes. Diagnosis of FDCS was confirmed on biopsy (Fig 4, 5) and patient was given radiotherapy. However, he was lost to follow up.

CASE 1:

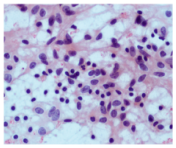


Fig 1 PAP 100X show spindle to ovoid tumour cells with sprinkling of lymphocytes

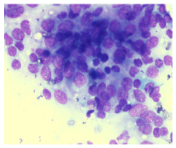


Fig 2 MGG 100X

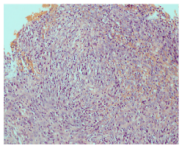
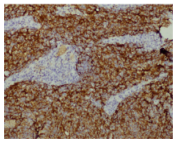


Fig 3 H&E 40X shows tumour cells arranged in whorls in the biopsy



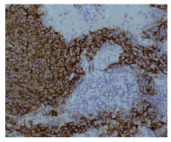


Fig 4&5 IHC 100X show CD 21 and CD 23 positivity in tumour cells in the biopsy

CASE 2

A 30 years old male patient presented with a swelling on the right side of the neck since six months. On examination he had a 10x5cm large nodular lesion occupying the whole of the half of the right neck. CT scan of head and neck revealed a heterogenous enhancing lesion measuring 10.3x5.7cm with central rim of calcification and encasing vascular structures. CT thorax revealed multiple lung nodules. Haemogram, biochemical parameters, USG abdomen were within normal limits. FNAC of the neck mass displayed large cells having round to oval hyperchromatic nuclei seen in clusters as well as singly scattered cells (Fig 6, 7). Sprinkling of lymphocytes were noted. A diagnosis of poorly differentiated malignant tumour with possibility of follicular dendritic cell sarcoma was given. However, considering the site and the cytomorphology a differential of metastatic carcinoma was given. IHC on cell block (Fig 8, 9) revealed tumour cells to be positive for CD23, CD21 (Fig 10, 11) and negative for LCA, CK, CK7, CK5/6, EMA, TTF1, S100, P63, Chromogranin, CD68. Diagnosis of FDCS was established and patient was given chemotherapy for which he had clinically good response with stable disease.

CASE 2:

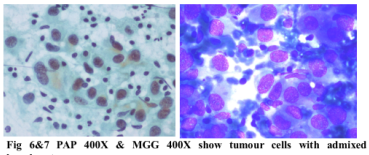


Fig 6&7 PAP 400X & MGG 400X show tumour cells with admixed lymphocytes

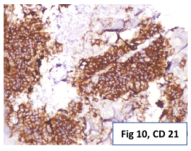


Fig 10, CD 21

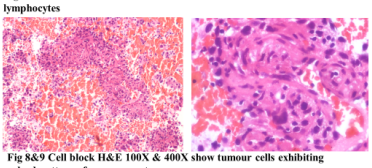


Fig 8&9 Cell block H&E 100X & 400X show tumour cells exhibiting whorl pattern of arrangement

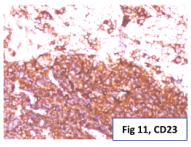


Fig 11, CD23

CASE 3

46 years old female patient presented with complaints of difficulty in swallowing for 3 months. She was referred as metastatic carcinoma diagnosed on FNAC of cervical lymphnode which was done outside. On examination she had 4x3cm cervical lymphnode in the right neck. The FNAC slides were reviewed in our hospital which exhibited characteristic cytomorphological features with clusters of spindle to ovoid cells with focal whorls and sprinkling of lymphocytes. Biopsy of the cervical lymphnode was done and the tumour cells in the biopsy were immunopositive for CD21 and immunonegative for CK, EMA (non specific staining), LCA, p63, S100. Diagnosis of FDCS was confirmed. Patient was given chemotherapy for 1 year. Then on follow-up she had a 3x3 cm mass involving right anterior tonsillar pillar with extension into soft palate. FNA of the mass was done which revealed similar morphology and was consistent with recurrence. The patient underwent surgical excision of the mass and was started on radiotherapy but lost to follow-up.

CASE 4

37 years old male patient presented with complaints of abdominal pain for 2 months. CT abdomen revealed multiple hypoechoic liver nodules largest measuring 1.6x1.6 cm with peripancreatic, periportal and paraaortic lymphnodes largest measuring 3x2.2 cm. USG guided FNA of the par aortic lymph nodal mass and liver lesion were done. Smears had discohesive cells with moderate nuclear pleomorphism and prominent nucleoli. Necrosis was observed. A diagnosis of poorly differentiated malignant tumour was given with possibility of malignant lymphoma and cell block was processed from both sites material and IHC was done. Tumour cells were positive for LCA and negative for other lymphoid and carcinoma markers. Meanwhile biopsy of liver lesion was also done and further IHC on cell block & biopsy confirmed as metastatic FDCS. The patient was started on chemotherapy but he was lost to follow-up.

DISCUSSION:

Follicular dendritic cell sarcoma is an uncommon neoplasm derived from follicular dendritic cells. Follicular Dendritic Cells (FDC) is non-lymphoid, non-phagocytic cells in the stroma of lymph nodes. FDCs are critical mediators of adaptive humoral immune response through antigen presentation and regulate the germinal centre reaction in primary and secondary follicles(2)(3). This neoplasm in lymphnodes was first described by Monda et al., in 1986 and later by Nayler et al., in 1996(4)(5). The extra nodal counterpart was first reported by chan et al in 1994(6).

FDCS mostly affects young to middle-aged adults of both sexes(7) .The commonest site involved is lymphnode. They can also occur in extra nodal sites like the gastrointestinal Tract (GIT), pharynx, mediastinum, skin, liver, spleen etc but rarely(8)(9). There are quite a few case reports and case series enumerating the histomorphological aspects of this tumour. However there are only very few case reports on the cytological diagnosis of this rare neoplasm in literature(10).

In our series three cases were male and one was female. The age range was between 25-55 years. Two of them had nodal presentation with two at extra nodal site. Two of them had recurrence/metastasis.

All four cases had cytomorphological findings which consisted of cellular smears with syncytial arrangement of cells having spindle to ovoid nuclei as described in literature (11)(12)(13)(14) (fig1,2). The nuclei had fine chromatin, delicate nuclear membrane, and prominent nucleoli with occasional pseudonuclear inclusions. The cells had abundant pale cytoplasm with indistinct cell borders. The characteristic swirling/whorl pattern was appreciated in two of the cases (fig 3)

The tumour cells showed mild to moderate degree of nuclear pleomorphism and the appearance of nucleoli also varied from inconspicuous to prominent, similar to a study reported by yuen shan fan et al(15) .

There would be a characteristic biphasic pattern which would be the classic morphology of FDCS which includes syncytial distribution of epithelial cells with sprinkling of lymphocytes. These lymphocytes were usually reactive and T cell type. In our series there was sprinkling of lymphocytes in all the cases which gave a clue to the underlying diagnosis(fig 1,2,6,7) According to some studies by Ren and Vicandi et al plasma cells and eosinophils can also be observed in the background along with reactive T cells(14)(13). In our series plasma cells were noted and eosinophils were not seen.

Necrosis was seen in the abdominal lymph nodal case with liver metastasis which indicated the aggressive nature of the tumour (16). Binucleated and multinucleated giant cells are also noted.

On cytology smears it would be really challenging to make a diagnosis of FDCS. Lymphoepithelial carcinoma, Undifferentiated carcinoma(Nasopharynx),Metastatic poorly differentiated carcinoma,Meningioma,Malignant melanoma, Inflammatory myofibroblastic tumour are the differentials to be considered depending on the site particularly in head and neck region. Thymoma and interdigitating dendritic cell sarcoma also come in the differentials (15). Cell block and immunohistochemistry play a significant role in establishing and confirming the diagnosis. If adequate FNA material is available, the cell block with IHC can obviate the need for biopsy. The follicular Dendritic cells are positive for CD21,CD23,CD35 and variably positive for EMA,S-100,CD68 and negative for cytokeratins,HMB 45,CD3,CD79a (1). In our study we processed cell block for two cases with IHC. In these two cases, the tumour cells were positive for CD21, CD23 (fig 8, 9, 10, 11) and negative for other markers.

One of the cases had metastasis to liver which is a rare occurrence. The usual sites of metastasis described include lung and lymphnodes with liver being less common (17) .The tumor usually pursues an indolent protracted course and is considered to be a low-grade sarcoma with an overall mortality of 17% (14) However in few cases of intraabdominal sites the tumour can have aggressive behaviour with fatal course.

CONCLUSION: FDCS is a rare neoplasm which requires high index of suspicion on cytology smears especially in head and neck region. Clue to diagnosis could be sprinkling of lymphocytes amidst tumour cells. This study highlights the significance of ancillary tests like cell block and immunohistochemistry which help to establish the diagnosis of this uncommon tumour by fine needle aspiration.

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