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Cercariform Cells – A Clue to the Cytological Diagnosis of Urothelial Carcinoma Metastasis to an Unusual Site

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Abstract
Cervical lymph node metastases of urothelial carcinoma are very rare and indicate widespread disease with poor prognosis. The presence of certain peculiar shaped malignant epithelial cells, termed as cercariform cells, are considered to be of diagnostic importance in the cytological diagnosis of metastatic urothelial carcinoma. These cells have a nucleated globular body and a unipolar nontapering cytoplasmic process. We report a case of ureteral urothelial carcinoma metastasis to left cervical lymph node which was diagnosed on cytology after a period of 3 years post surgery for the primary tumour.
Keywords: *urothelial carcinoma, cervical lymph node, cercariform cells.*

Introduction

Identification of metastatic disease is important for the correct staging and management of any cancer. Aspiration cytology of metastatic urothelial carcinoma is encountered less frequently in routine cytology practice. This partly accounts for the difficulty in recognizing the cytomorphological features
of this condition especially in case of metastasis to unusual sites.[1] However, literature shows that there are certain peculiar shaped malignant epithelial cells, termed as "cercariform cells", which are considered to be of diagnostic importance in the cytological diagnosis of metastatic urothelial carcinoma.[2,3]
We report a case of ureteral urothelial carcinoma metastasis to left cervical lymph node which was diagnosed on cytology after a period of 3 years post surgery for the primary tumour.

Case Report

A 52 years old male presented with a swelling over left lower cervical region for 1 month duration. On examination, it was a 1.5 x 2 cm firm, mobile, non tender lymph node, which on aspiration yielded scanty colourless material. Two smears were made and stained with giemsa and pap stains repectively. FNA smears were highly cellular with cells arranged in sheets, small clusters and discretely. Cells are plump oval to plasmacytoid with round / ovoid dense nuclei and moderate amount of cytoplasm. Scattered cells with peculiar morphology resembling cercariform cells were noted. (Fig 1 &2)Hence a provisional diagnosis of metastasis to lymph node possibly from urothelial carcinoma was given.

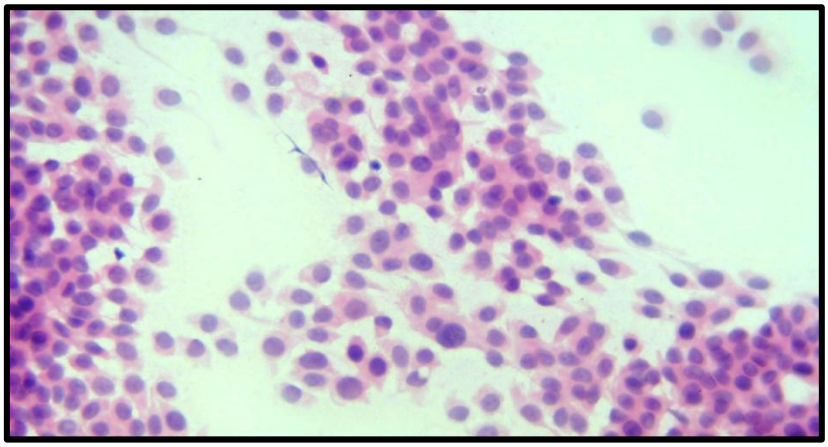

Fig 1: 40X pap stained cellular smears showing clusters, sheets and discrete malignant cells with plasmacytoid and cercariform morphology.

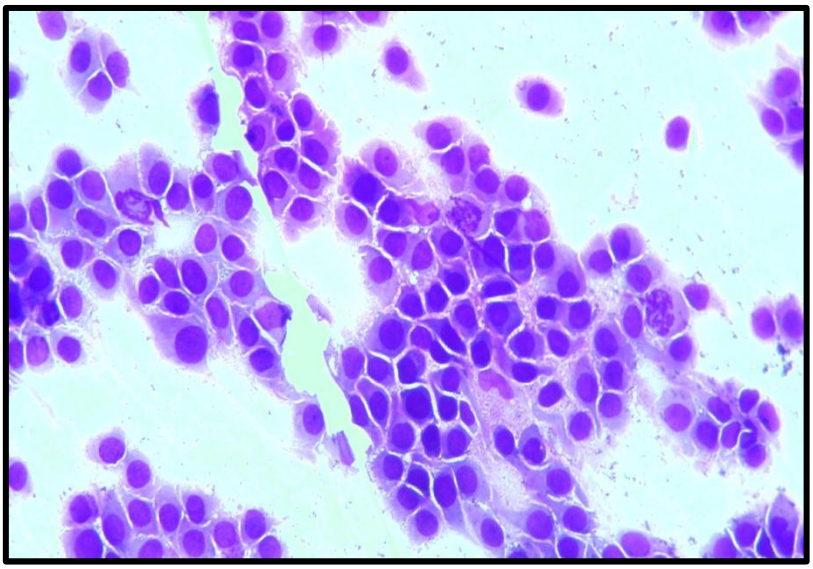

Fig 2: 40X giemsa stained cellular smear with malignant cells and a few showing nucleated globular body with single non tapering cytoplasmic process.

On further interrogation, he had a history of left nephroureterectomy in 2016. Histopathological examination of which showed invasive papillary urothelial carcinoma low grade involving mid ureter. (Fig 3)

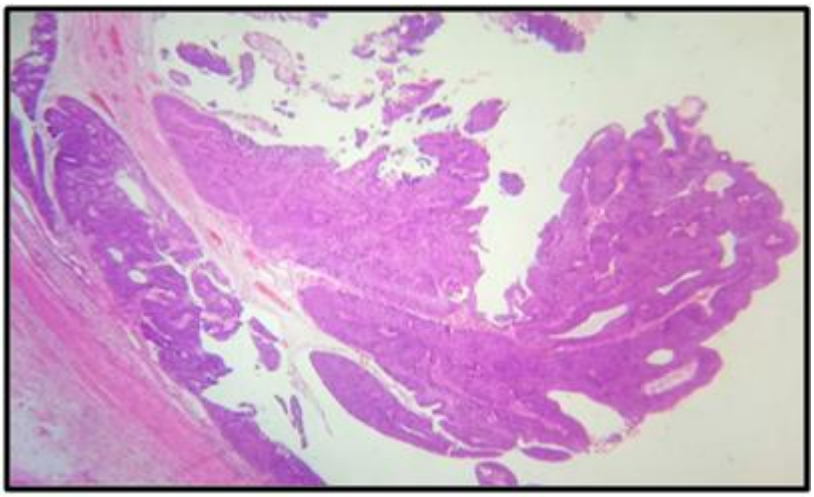

Fig 3: 10x H&E. Histopathology of left nephroureterectomy showing invasive papillary urothelial carcinoma low grade involving mid ureter.

F-FDG PET/CT for assessment of his disease status revealed moderate to intensely FDG concentrating retroperitoneal, bilateral retrocrural, abdominal, left hilar, left supraclavicular and left cervical level II and III lymph nodes suggesting lymph nodal metastases. (Fig 4)

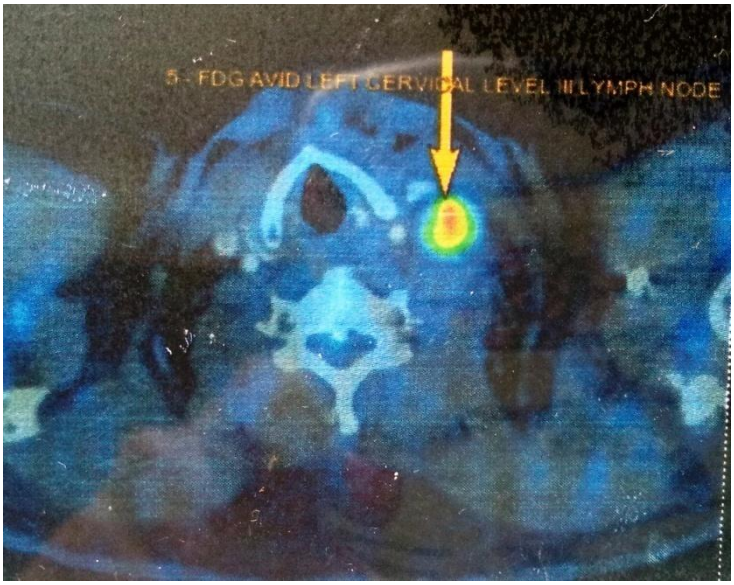

Fig 4: F-FDG PET/CT showing moderate to intensely FDG left cervical level II lymph nodes suggesting lymph nodal metastases.

This confirmed the diagnosis of metastasis from urothelial carcinoma of relatively a rare primary site to an unusal site like cervical lymph node. Patient also had family history of malignancy. His brother and sister survived colon cancer, the details of which were not available. On follow up, he had 6 cycles of chemotherapy and unfortunately succumbed to disease within one year.

Discussion

FNA procedures of enlarged lymph nodes are increasingly being done now a days which helps in the early detection of secondary and primary lymph node malignancy. Cervical lymph node group is the most commonly involved one and the primary is most often from the oral cavity.[4] However, cervical lymph nodal metastasis from remote primary sites should also be considered as differential diagnosis in the workup of cervical lymph node enlargement.[5] A 9 year review of patients with head and neck metastases from 845 urogenital tract tumors (kidney, prostate, bladder, testes, penis, urethra and ureter) showed that only 31 (3.7%) of these tumors developed metastases to the cervical and supraclavicular lymph nodes.[6] Although metastasis of urogenital tract tumors to cervical lymph nodes is rare, the frequent metastasis location is mostly supraclavicular lymph nodes.[7] Metastasis of urothelial carcinoma to head and neck region isassociated with poor prognosis and low survival rate.[8]

The diagnosis of neoplasm with adequate material in the FNA specimen is not difficult usually. However, the definitive characterization of the type of tumor, specifically transitional cell carcinoma, can be challenging.[3] Limited exposure to aspiration cytology of metastatic urothelial carcinoma in routine cytology practice partly accounts for the difficulty in recognizing the cytomorphological features of this condition especially in case of metastasis to unusual sites.[1] However, literature shows that there are certain peculiar shaped malignant epithelial cells, termed as “cercariform cells”, which are considered to be of diagnostic importance in the cytological diagnosis of metastatic urothelial carcinoma. [2,3] The presence of spindled, pyramidal and/or racquet-shaped cells with eccentric nuclei were first identified as distinctive indicators of metastatic transitional cell carcinoma by Johnson *et al.*[1] Some of these malignant cells were later on

designatedby Powers and Elbadawi in view of the characteristic morphology of their cytoplasmic processes .[2] The word "cercaria" has its origin in the Greek word "kerkos" meaning tail. These cells are classically described as malignant cells with a nucleated globular body and a unipolar nontapering cytoplasmic process – the ends of which could be fishtail-like, bulbous or flattened.[2] They found that these cells occurred frequently in normal and low grade neoplastic urothelium, in numerous preparations including urine specimens, smears from FNA preparations, touch smears from excised tumors, and histologic sections of transitional cell neoplasms.[2]

Since cercariform cells are consistently observed on Millipore filter preparations, the characteristic morphology of these cells is not considered as a smearing artifact.[3] Potential mimics of cercariform cells are malignant cells from squamous cell carcinomas. The tapering cytoplasmic processes, hyperchromatic, pyknotic or degenerated nuclei and frequent cytoplasmic keratinization of tadpole cells in squamous cell carcinoma are important distinguishing features. Other mimics include malignant spindle cells of mesenchymal origin with unipolar cytoplasmic processes. However, minimal nuclear atypia and the presence of malignant cells with bipolar cytoplasmic processes, in addition, help in correctly identifying these cells of mesenchymal origin.[1]

The finding of a few cercariform cells is not specific for urothelial carcinoma. In a study performed by Hida and Gupta, it was inferred that the presence of more than 20 cercariform cells per case is significantly more likely to occur in metastasis from transitional cell carcinoma.[3] Another study conducted by Renshaw et al concluded that the presence of numerous cercariform cells (>10 per case) in an aspiration smear favored transitional cell carcinoma.[9] They also found the presence of a small vacuole in the bulbous tail to be a helpful criterion in identifying cercariform cells. Cells in clusters were excluded to avoid counting cells with artifactual cytoplasmic flattening secondary to cell to cell abutment.[9]

Urothelial carcinoma of the upper urinary tract is relatively rare, representing about 5% of all urothelial tumors. Ureteral urothelial carcinoma is even less common than that of the renal pelvis, accounting for about 25% of all upper urinary tract transitional cell carcinomas.[10] Batata et al concluded that among 2566 primary urothelial carcinomas, ureteral cancers accounted for only 2.5%.[11]

Eventhough, upper urinary tract urothelial carcinoma is relatively rare in the normal population, patients with Lynch Syndrome are at increased lifetime risk with an incidence as high as 6%. Urothelial carcinoma is considered part of the classical Lynch-syndrome tumor spectrum.[12] Crockett et al. described that among 39 patients with Lynch Syndrome and urothelial carcinoma, ureteral tumours predominated over tumors of the renal pelvis.[13]

Conclusion

The presence of a few cercariform cells in cytology smears is not specific for urothelial carcinoma. However, cercariform cells if present in adequate numbers in an aspiration smear of a metastatic tumor is a strong indicator towards its transitional cell origin. Cervical lymph node metastases of urothelial carcinoma are very uncommon and indicate widespread disease with poor prognosis. In conclusion, the presence of adequate number of cercariform cells in smears from lymphnode should raise a suspicion of urothelial carcinoma metastasis even if the lymphnodes are in the head and neck region. The presence of urothelial carcinoma in ureter which is a rare primary site, along with the family history of malignancy in first degree relatives create a strong suspicion of a familial tumour syndrome in this patient. The association of upper urinary tract urothelial carcinoma with Lynch syndrome further supports this suspicion.

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