Fine Needle Aspiration Cytology of Metastatic Renal Cell Carcinoma - A Case Report

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ABSTRAK

Sitologi sedutan jarum halus di bawah panduan radiologik untuk mendiagnosa karsinoma sel renal telah diterima pakai dan digunakan secara meluas. Ini adalah kerana karsinoma sel renal mempamirkan ciri sitologi yang karakteristik yang membolehkan ianya di identifikasi secara sitologi dengan tepatl. Kami membentangkan kes seorang lelaki berumur 66 tahun yang menghidap karsinoma sel renal peringkat lanjut dimana telah terdapat penyebaran sel kanser ke kelenjar limfa aorta dan servikal, peparu dan hepar. Sitologi sedutan jarum halus dari massa para-aortik menunjukkan gugusan terlekat sel malignan dengan sitoplasma yang banyak dan bervakuol konsisten dengan diagnosis karsinoma sel renal. Histologi dari kelenjar limfa servikal dan dengan penemuan ujian imunohistokimia, diagnosisnya adalah konsisten dengan karsinoma sel renal metastatik. Pesakit meninggal dunia tiga tahun tahun selepas diagnosis dibuat.

Kata kunci: karsinoma sel renal, sitologi sedutan jarum halus

ABSTRACT

Fine needle aspiration cytology under radiologic guidance for diagnosis of renal cell carcinoma is well established and is increasingly utilized. This is because renal cell carcinoma displays fairly characteristic cellular features permitting correct cytologic identification. We present a case of a 66-year-old man who had advanced renal cell carcinoma with spread to aortic and cervical lymph nodes, lungs and liver. Fine needle aspiration cytology of the para-aortic mass showed tight clusters of malignant cells with abundant and vacuolated cytoplasm consistent with renal cell carcinoma. Histology of the left cervical lymph nodes together with immunohistochemistry findings were consistent with the cytologic diagnosis of metastatic renal cell carcinoma. The patient succumb to his illness three years after the diagnosis was made.

Keywords : renal cell carcinoma, fine needle aspiration cytology

INTRODUCTION

Renal cell carcinoma is a relatively rare tumour accounting for less than three percent of all adult cancers (Bennington JL and Beckwiht JB. 1975, Javadpour N. 1984). It is generally a tumour of adults where the average age at diagnosis is

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between 55 to 60 years (Bennington JL and Beckwiht JB. 1975, Javadpour N. 1984). The clinical diagnosis of renal cell carcinoma is difficult since its clinical manifestations are quite variable; about 30 percent of patients have distant metastasis when the tumor is diagnosed (Bennington JL and Beckwiht JB. 1975, Javadpour N. 1984). The most common site of metastasis include lung, liver, bone, lymph nodes, adrenal and brain (Bennington JL and Beckwiht JB. 1975). These metastases may readily become targets for fine needle aspiration.

In this case report we present a 66-year-old gentleman with advance renal cell carcinoma in whom the diagnosis was made on fine needle aspiration cytology of para-aortic nodes containing metastatic deposits of renal cell carcinoma, and further supported by tissue biopsy of a cervical lymph node.

CASE HISTORY

A 66-year-old Chinese gentleman who was a known case of non insulin dependent diabetes mellitus for 14 years and hypertension, complained of intermittent left lumbar pain radiating to the left iliac fossa for two years. He was diagnosed to have lumbar spondylosis and treated with analgesics. He also complained of loss of appetite for two weeks before coming to the hospital but there was no weight loss. He had shortness of breath after climbing up four flights of stairs but there was no orthopnoea, paroxysmal nocturnal dyspnoea or chest pain. He had nocturia every two hours but no haematuria, poor flow or hesitation. There was no bowel symptoms, night sweats and fever. He was a chronic heavy smoker for about 40 years and smoked thirty cigarettes per day. On physical examination, the patient showed signs of heart failure with ankle oedema and basal end inspiratory crepitations. Abdominal examination revealed a non tender mass which was ballotable on the left lumbar region with ascites. Urine examination showed protein 4+, glucose 4+ and red blood cells 3+. The diagnosis of diabetic nephropathy with left renal tumour was made based on the above findings. Abdominal X-ray showed micro-calcifications at the lower pole of the left kidney which was consistent with scarring from a previous infection. Computed Tomography Scan showed multiple masses in the para-aortic region extending into the left renal hilum involving the upper pole of the left kidney. The radiologic impression was left renal lymphoma.

A left cervical lymph node measuring 2 x 1 cm which was firm and mobile was noted. Fine needle aspiration cytology of the para-aortic nodes was performed under ultrasound guidance using a 22-gauge, 20-cm-long-spinal-type needle which was connected to a 20-ml plastic syringe placed in a syringe holder.

Cytologic examination showed a cellular aspirate comprising of cohesive clusters of malignant cells with some attached to fibrin strands. The cells exhibit abundant cytoplasm with fine vacuolations (Figure 1). Occasional cells showed granular cytoplasm (Figure 2). The nuclei were moderately pleomorphic with some showing prominent nucleoli. Abnormal mitotic figures were also noted.

Excision biopsy of the left cervical lymph node showed infiltration by malignant cells forming multiple lobules in cohesive sheets separated by thin fibrous septae (Figure 3). Focal areas showing tubulopapillary arrangements were present. The cells displayed abundant pink to clear cytoplasm with distinct cytoplasmic border. The nuclei were large round and vesicular with prominent nucleoli and several mitotic figures were seen. Immunohistochemical study showed tumour cells were positive for cytokeratin, epithelial membrane antigen and vimentin. Marker for leucocyte common antigen was negative. A diagnosis of metastatic renal cell carcinoma of clear cell type was made.

X-ray of the lung showed nodules at the left lower zone adjacent to the lower rib, most likely a metastatic deposit. Ultrasound of the liver showed multiple nodules

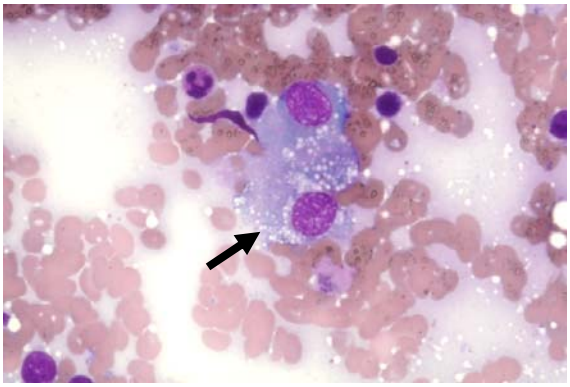

FIGURE 1: FNA of paraaortic lymph node showing cells displaying abundant cytoplasm with fine vacuolations and eccentric nucleus. May-Grunwald Giemsa stain, original magnification x 200

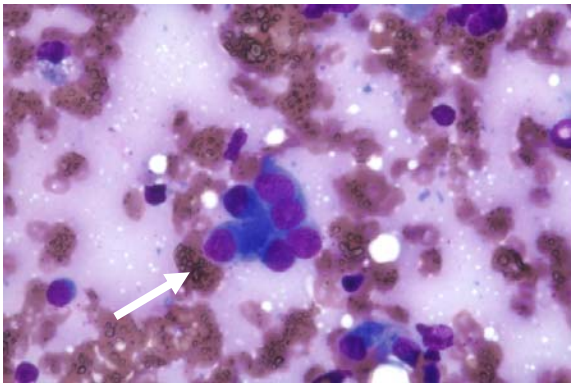

FIGURE 2: FNA smear showing neoplastic cells displaying granular cytoplasm. May-Grunwald Giemsa stain, original magnification x 200.

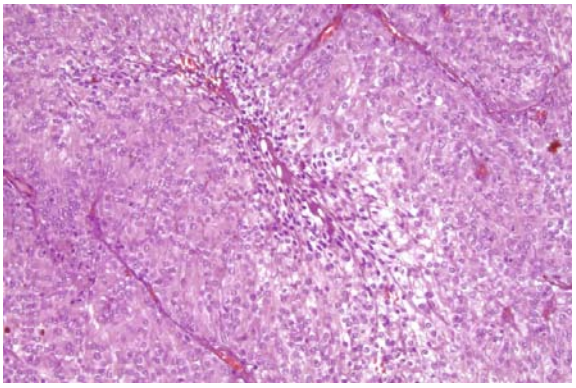

FIGURE 3: Histological section of lymph node showing sheets of malignant cells separated by fine fibrous septae, displaying clear cytoplasm in areas. H&E, original magnification x 100

consistent with metastases. There was no plan for surgery for him as the tumour was inoperable. The patient was referred to oncology unit for further management. He was admitted to the ward several times with the problem of widespread metastases including to the gut and lungs. He also presented with lower gastrointestinal bleeding and difficulty in breathing. He succumbed to his illness three years after the diagnosis was made.

DISCUSSION

Renal cell carcinoma is a rare tumour occurring more commonly in adults. Its usual presentations are haematuria (59%), flank pain (41%) and abdominal mass (45%). However, the combination of these three features, classically regarded as the diagnostic triad of renal cell carcinoma, occur in only nine percent of the patients and are usually a late manifestation (Skinner DG et al 1971). As many as 25 percent of renal cell carcinoma is asymptomatic, with discovery of the tumour being incidental to a routine physical examination and unrelated radiological study (Peterson RO 1986).

With the recent technologic advances in diagnostic radiology, percutaneous aspiration of renal lesions can be guided by several radiologic techniques include selective arteriography (Boijsen E and Link DP 1977), ultrasound (Holm HH et al 1975, Kristensen JK et al 1974), and CT scan techniques (Sundram M et al 1982) in an attempt to obtain diagnostic cytologic material. This radiologically guided aspiration was first introduced by Lindblom (Karp W and Ekelund L 1979) in 1952 and since then, fine needle aspiration biopsy for cytologic evaluation of renal masses has been performed more or less routinely. This minimally invasive diagnostic procedure is safe, economical and able to give fast diagnosis obviating open biopsy for tissue diagnosis.

Several studies had proven that fine needle aspiration cytology of a renal mass is a useful diagnostic procedure. With reference to malignancies, the usefulness of the method is related to its high sensitivity, 0.93, and high degree of typing accuracy(Murphy WM et al 1984, Pilotti S et al 1988). Reported success rates are 87 to 100 percent (mean of 93.5 percent) for renal tumours(Murphy WM et al 1984, Sundram M et al 1982).

The cytologic diagnosis of renal cell carcinoma by fine needle aspiration cytology poses no diagnostic difficulties whether the aspirates are from the primary site or metastatic deposits (Linsk JA and Franzen S 1984). This is because renal cell carcinoma displays fairly characteristic cellular features permitting their correct cytologic identification (Linsk JA and Franzen S 1984).

Aspirates from renal cell carcinoma are usually cellular even though in some cases the difficulty arises because of inadequate sampling or the presence of much necrotic debris and haemorrhage within the aspirates, obscuring the cellular details. This condition is particularly true for papillary variant of renal cell carcinoma because of the perculiar features of this variant that show presence of cystic and extensive degenerative changes (Pilotti S et al 1988).

Tumour cells may be single, or are arranged loosely in flat sheets, clusters, papillary fronds or an alveolar pattern. The smear pattern may occasionally be mixed. Three distinct cell types have been described on fine needle aspiration cytology (Koss LG et al 1984) , the clear cell, the granular cell and the oncocytic cell types, occurring either excusively or admixed together. The clear cells of renal cell carcinoma have abundant, fragile, finely vacuolated cytoplasm, best appreciated on the Diff-Quik stain. The cytoplasm is highly characteristic (Linsk JA and Franzen S 1984), as seen in this case particularly with Romanovsky stain and is termed ‘opaque with or without vacuolization and granulation’ to distinguish it from the so-called clear cell of

histopathology, which has been denuded of its cytoplasmic content by the histologic process. Cytoplasmic vacuoles are punched out, bubbly or lacy. The partially extruded nucleus is a useful identifying feature (Linsk JA and Franzen S 1984). The cell borders may be well defined but are usually indistinct. Granular cells have eosinophilic or cyanophilic cytoplasm, which is moderately dense and granular. Oncocytic cells have extremely dense, eosinophilic, compact cytoplasm with well-defined cell borders. Rarely, renal cell carcinoma may show a diffuse spindled appearance.

A nuclear grading system based on four nuclear grades defined in order of increasing nuclear size, irregularity and nucleolar prominence, proposed by Furhman et al (1982) showed that nuclear grade was effective in predicting survival and development of metastasis after nephrectomy (Amtrup F et al 1974). This grading system has been popular in routine surgical material of renal cell carcinoma and could readily be applied to fine needle aspiration cytology material. Several studies using Furhman's nuclear grading system showed high concordance between nuclear grading in fine needle aspiration material and histologic specimens (80 – 92%) (Nurmi M et al 1984). These findings were further supported by the high interobserver and intraobserver reproducibility. Multiple grades coexist in about 15 percent of all renal cell carcinomas.

Even though most renal cell carcinomas are identified without much difficulties from fine needle aspirates; there are few diagnostic pitfalls that one may encounter especially when the aspirates are from metastatic sites. Renal cell carcinoma may metastasize to any site in the body including salivary gland, thyroid, ovary and soft tissue (Bennington JL and Beckwiht JB 1975). Therefore, cells of metastatic carcinoma should be distinguished from those of other tumours containing clear or granular epithelial cells that may arise in these organs (Bennington JL and Beckwiht JB 1975, Lever WF and Schaumberg-Lever G 1983, Nguyen GK 1986). The differential diagnosis of tumours with vacuolated (clear) cells includes acinic cell carcinoma and mucoepidermoid carcinoma of the salivary gland, clear cell thyroid carcinoma, clear cell tumour of the lung and mesonephric (clear-cell) carcinoma of the ovary. However, cells of renal cell carcinomas contain intracytoplasmic fat; therefore an oil-red-O staining of an air-dried aspiration smear is very helpful in their identification.

Metastatic renal cell carcinoma in the adrenal gland may pose a special problem since histologic differential diagnosis between renal cell carcinoma invading or metastasizing to the adrenal gland and a primary adrenal cortical carcinoma is very difficult if not impossible on the light microscopic level (Bennington JL and Beckwiht JB 1975). A similar degree of difficulty is to be expected in aspiration cytology of tumour cells aspirated from a renal cell carcinoma and those of adrenal cell carcinoma. However, adrenal cortical carcinoma tend to show more cellular anaplasia than do renal cell carcinomas (Bennington JL and Beckwiht JB 1975, Weiss LM 1984). Electron microscopic study of tumour tissue may be helpful in making a correct diagnosis.

In our case, the diagnosis was made on the aspirates taken from the para-aortic lymph node which was supported further with the biopsy of the cervical lymph node. Radiological imaging showed a right renal mass that gave a clue to the origin of the tumour.

In short, the presence of malignant epithelial cells arranged in cohesive clusters or sheets displaying vacuolated and granular cytoplasm in a patient with a previous history of radical nephrectomy for renal cell carcinoma is highly suggestive of metastatic renal cell carcinoma. The presence of a solid renal mass demonstrated by radiological imaging techniques and/or a vascular renal tumour

demonstrated by angiography would also lend support to the diagnosis of a metastatic renal cell carcinoma.

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