METASTATIC INGUINAL LYMPHADENOPATHY OF UNKNOWN PRIMARY

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Abstract:
Malignant Inguinal lymphadenopathy arises from malignant tumours in the skin of lower limbs, the cervix, the uterine body, the ovary, the perineum, the rectum, the anus, and the remaining 1 was metastatic cancer with unknown primary site. Two cases with metastatic squamous cell carcinoma inguinal lymphadenopathy primary undetected with all routine clinical and imaging evaluation underwent FDG PET CT scan and then treated. FDG PET CT scan showed increased uptake in the metastatic inguinal nodes (SUV- 10.58 and 17.2) with no other significant uptake of tracer. Both the patients are treated with external beam radiation to the pelvis including both inguinal regions for 41 Gy with concurrent weekly cisplatin and boosting the inguinal node up to 60 Gy. There was complete response and the patients are on follow up. Metastatic inguinal lymph node squamous cell carcinoma of unknown origin is a rare entity and PET CT scan can be used as a valuable tool for the meticulous search of the primary.

Keyword: Inguinal lymphadenopathy, FDG - PET CT, cancer of unknown primary, malignant inguinal nodes

The precise clinical definition of carcinoma unknown primary, according to Pavlidis et al refer to patients who present with histological confirmed metastatic cancer in whom medical history, physical examination, full blood count, basic biochemistry battery, urinalysis, stool occult blood testing, immunohistochemistry with specific markers as well as imaging technology with chest X-ray, CT of the chest, abdomen and pelvis or mammography and MR imaging in certain cases have failed to detect the primary tumour [1]. Metastatic inguinal lymphadenopathy most commonly arise from the primary malignancy in the skin of lower extremity, skin of lower half of the trunk, perineum, anal canal, ovary, uterine body, uterine cervix, vagina, vulva and penis. But in 1% of the cases the primary remains undetected by the routine clinical, radiological and endoscopic evaluation and accounts for a separate entity called metastatic inguinal lymphadenopathy of unknown origin.
Primary Interestingly Zaren et al reviewed the medical records at the MD Anderson Hospital from 1944 to 1975 and reported 2232 patients reported with metastatic inguinal lymphadenopathy. Appropriate workup defined primary sites in 2210 of these patients. The remaining 22 patients had inguinal node metastasis from unknown primary sites [2]. $^{18}$F-flouro-2-deoxyglucose positron emission tomography has brought in a new revolution in the diagnosis and management of cancer. With its ability to scan the whole body and to detect metabolically active cancer sites coupled with the precise anatomical delineation with computed tomography, PET-CT scan is the valuable tool in detecting the primary and metastatic sites. Here we report 2 cases of metastatic inguinal lymphadenopathy of unknown primary.

Case 1:

55 years old, postmenopausal woman with no other comorbid illness presented with complaints of lump in right groin for 3 months. Her general and systemic examination including a detailed pelvic examination was normal except for a 4x4.5cm fixed right inguinal nodal mass with ulceration. Aspiration cytology from the nodal mass was reported as malignant epithelial cells of squamous origin. She was further evaluated with colposcopy, proctoscopy, ultrasonogram and other metastatic workup which were normal. Computed tomography of abdomen revealed a 4.4 x1.9cm nodal mass in right inguinal region. No pelvic lymphadenopathy.

**CT scan showing the right inguinal mass**

PET CT scan was done with the idea to detect the primary. PET-CT scan showed Right inguinal nodal mass of SUV 10.58 with focal increased tracer uptake of SUV 5.8 in anal region with no CT demonstrable lesion. Clinically and radiologically no lesion made out at the site of anal region uptake.

**FDG** And the anal uptake was due to physiological sphincter activity.

**PET CT scan of the first patient**

Case 2:

35 years old, premenopausal woman with no other comorbid illness presented with complaints of lump in right groin for 2 months with ulceration of the overlying skin. Her general and systemic examination including a detailed pelvic examination was normal except for a 6x6.5cm...
fixed right inguinal nodal mass with ulceration. Biopsy from the nodal mass was reported as squamous cell carcinoma; grade II-III of high nuclear grade. She was further evaluated with colposcopy, proctoscopy, ultrasonogram and other metastatic workup which were normal. Computed tomography of abdomen revealed 6 x 5.3 cm nodal mass in right inguinal region infiltrating skin and superficial planes.

CT scan showing nodal mass infiltrating the skin
This patient was also evaluated further with PET CT scan which showed mass in the right inguinal region of SUV 17.2, with focal increased tracer uptake in right adnexa of SUV 4.07 with no CT demonstrable lesion.

FDG PET CT scan of the second patient
Treatment and response: As the primary was not detected by the PET-CT scan, we decided to treat both the patients with curative intent. Surgical excision deferred in view of large size of the lesion and infiltration of overlying skin. So they were taken up for radical radiation. As the possible sites of primary are perineum and genitourinary tract, it was decided to treat the whole pelvis with both inguinal regions. They were treated with 6MV x ray therapy to the pelvis including both inguinal regions at 180cGy per fraction up to 4140cGy. The right inguinal region was given electron boost to receive a total dose of 60 Gy. Patient also received 4-5 cycles of weekly cisplatin at a dose of 40mg/m². Both patients tolerated treatment well, with no major toxicity. Patients were assessed periodically, and there was good regression of the metastatic node at the end of therapy. Both the patients are in follow-up for the past 9 months, and they are doing well.

Discussion: Carcinoma unknown primary is a unique subset characterised by presentation of nonspecific symptoms followed by a metastatic disease. The primary remains undetected in most of the cases, and they have an unusual pattern of distant metastasis, marking its poor prognosis. Autopsy studies in these patients draw valuable information regarding the disease biology. The primary was detected only in 50% of all cases commonly arising from the pancreas and lungs. They had unusual metastatic sites like heart, kidney, adrenal gland and skin [3]. It is important to identify patients with favourable factors to aid in the
management. There are many prognostic models to help us; prognostic models by Van der Gaast and Culline were examples. But in this era of advanced molecular techniques, there is always a constant search to identify prognostic factors at genetic level. For carcinoma unknown primary, Tothill et al developed a 79 genes based assay using quantitative polymerase chain reaction to prognosticate this high variable group of malignancy [4]. The possible favourable subsets in carcinoma unknown primary are patients with metastatic squamous cell carcinoma involving cervical lymph nodes, squamous cell carcinoma involving the inguinal lymph nodes, female patients with axillary nodal metastasis, women with peritoneal carcinomatosis, men with skeletal metastasis with raised PSA, poorly differentiated and undifferentiated carcinoma. PET CT scan for detection of primary in carcinoma of unknown origin was first reported by Rege et al in 1994. He detected primary in 2 cases out of 4 cases of secondaries neck [5]. As the survival of the patients in unknown primary can vary when primary detected or primary undetected or other distant metastasis, it is a valuable tool for tailoring the optimal treatment in patients. In 2009, Kwee et al systematically analysed all published data about the role of FDG-PET in carcinoma of unknown primary. 433 patients from 11 studies were included in the systematic review. He concluded that FDG-PET/CT helped in detecting 37% of primary tumours in carcinoma in unknown primary. Both sensitivity and specificity were high around 84%. Lung, oropharynx and pancreatic carcinoma were the most commonly detected primaries Most common cause of false positive FDG uptake include lung and oropharynx. Carcinoma breast accounted for the most common false-negative result accounting for nearly 27%. Kwee et al hence concluded, “FDG-PET/CT can be used as a method for unknown primary detection.”[6]. Metastatic inguinal lymphadenopathy is one of the favourable subset and meticulous search of primary need to be done. History is very important to relate to any significant presenting symptom and it’s always beneficial to rule out any previous surgeries involving the lower limb. All patients should undergo detailed pelvic examination including colposcopy to identify and early cervical lesions. Patients should also undergo colonoscopy to detect any mucosal lesions of anorectum. Routinely these patients should undergo computed tomography of the whole abdomen to detect any pelvic node involvement and also to find any other possible sites of primary. Even after meticulous search, if primary is not detected patient can be subjected to whole body FDG-PET CT scan. PET CT scans not only aides to detect the primary but also helps to evaluate the metastatic extent of the disease. For metastatic inguinal lymphadenopathy, standard therapy used earlier was inguinal nodal dissection with or without chemotherapy. Interestingly Zaren et al reports a overall survival of 55% in this subgroup of patients[2]. In 1987, Guarischi et al reported 56 cases treated for metastatic carcinoma of unknown primary. The results show that with optimal radiation therapy to the locoregional site, patient had better survival. Guarischi et al study showed 3 different field extents either whole abdomen, or whole pelvis or the inguinal nodal region alone. He concludes, “based on the pattern of failure following radiotherapy and that the primary tumours do not manifest themselves subsequently, treating more than the local area of involvement cannot be advocated.”[7].

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Treatment results adapted from Guarischi et al, 1987

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<thead>
<tr>
<th>Treatment</th>
<th>No of cases</th>
<th>3 year</th>
<th>5 year</th>
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<tr>
<td>Local excision</td>
<td>8</td>
<td>35</td>
<td>35</td>
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<tr>
<td>Radiative therapy1</td>
<td>25</td>
<td>35</td>
<td>26</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>5</td>
<td>50</td>
<td>25</td>
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whole pelvis with boost to the inguinal node along with weekly cisplatin. No residue/recurrence on follow up. He used 50Gy to the whole pelvis and the 45 Gy to the inguinal region with 6 cycles of cisplatin chemotherapy at 60mg/m² [8].

Conclusion:
Sung-Ha Lee et al reported a case using PET-CT scan for the evaluation of CUP with inguinal nodes. PET CT scan did not detect the primary. Patient was treated with radiation to the Carcinoma unknown primary with metastatic inguinal node is very rare entity. PET CT might serve to detect the primary site, and help us to plan optimal treatment for these patients. Concurrent chemoradia tion has proved benefit comparable to surgery. Careful followup of these patients is necessary.

References: