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## CASE REPORT

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# Brachial Plexus Metastasis Masquerading as Radiation-induced Brachial Plexopathy

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### ABSTRACT

*Brachial plexopathy is a form of peripheral neuropathy. Cardinal symptoms include pain, paraesthesia, and weakness across C5 to T1 nerve root distribution. The two major causes of brachial plexopathy in breast cancer patients include tumour recurrence along the path of the brachial plexus and radiation damage to the plexus. Differentiation between the two pathologies is important to guide treatment, but is difficult to make clinically. Magnetic resonance imaging with or without fluorine-18 fluorodeoxyglucose positron emission tomography-computed tomography is a standard approach for differentiation. We report the use of this approach to diagnose metastasis of breast cancer at the brachial plexus.*

**Key Words:** Brachial plexus neuropathies; Fluorodeoxyglucose F18; Magnetic resonance imaging; Positron emission tomography computed tomography; Radiation induced brachial plexopathy

## 中文摘要

### 癌轉移臂肌叢神經偽類似輻射引致臂肌叢病

王晉彥、黃思進、李燕蘋、施俊健、魏偉達、楊美雲

臂肌叢病是一種外圍神經病。主要症狀包括C5到T1神經分佈地區疼痛、感覺異常和虛弱。乳腺癌患者臂肌叢病的兩個主要原因包括腫瘤沿臂肌叢路徑復發和放射治療輻射引致的損傷。臨床上區別這兩種病理是困難的，但對指導治療非常重要。使用磁共振成像加或不加上氟-18氟脫氧葡萄糖正電子發射斷層掃描-電腦斷層掃描是區別兩者的標準方法。我們報告使用這種方法去診斷一例乳癌轉移至臂肌叢神經。

### INTRODUCTION

Brachial plexopathy is a form of peripheral neuropathy. Cardinal symptoms include pain, paraesthesia, and weakness across the C5 to T1 nerve root distribution.

The two major causes of brachial plexopathy in breast cancer patients include tumour recurrence along the path of the brachial plexus and radiation damage to the plexus. Differentiation between the two pathologies is

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important to guide treatment, but is difficult to make clinically. Magnetic resonance imaging (MRI) with or without fluorine-18 fluorodeoxyglucose positron emission tomography-computed tomography (<sup>18</sup>F-FDG PET-CT) is the standard approach for differentiation.<sup>1</sup> We report the use of this approach in the diagnosis of recurrent breast cancer at the brachial plexus.

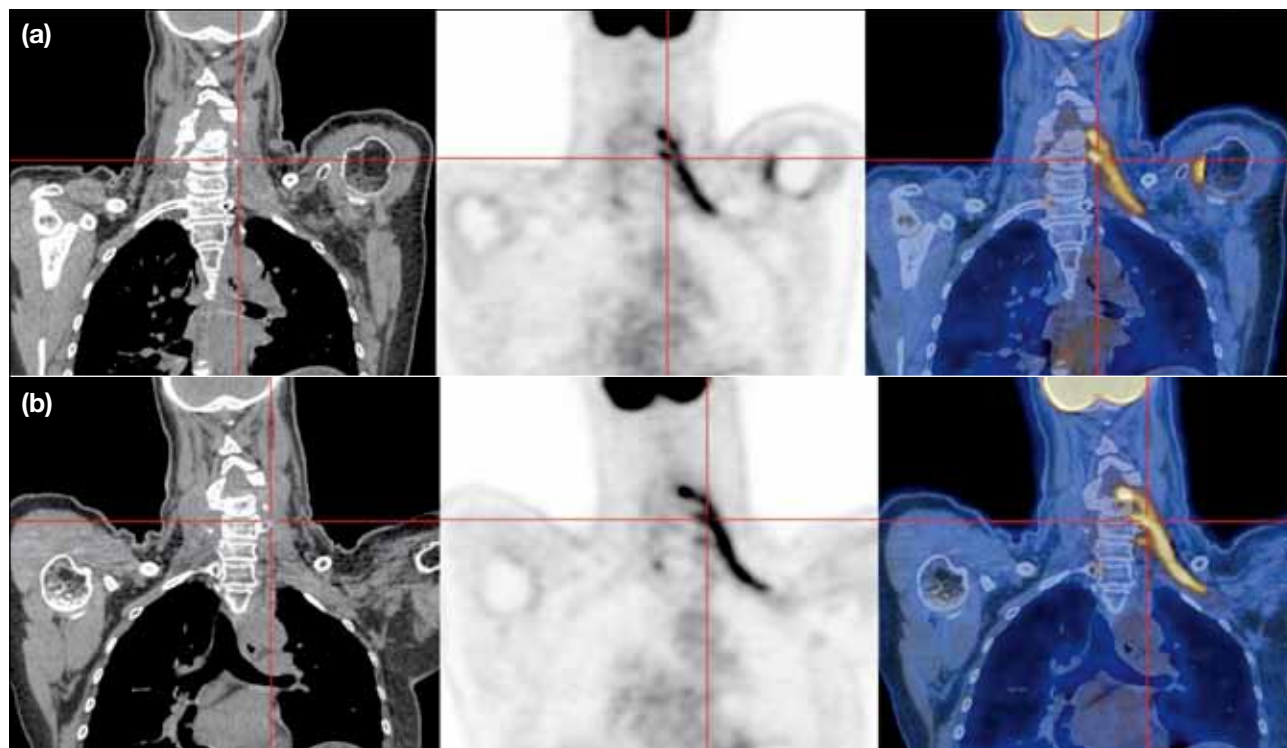
## CASE REPORT

In 2004, a 45-year-old woman was diagnosed with left breast cancer and underwent left lumpectomy and axillary dissection. Pathology confirmed a 0.8-cm primary invasive ductal carcinoma of the breast, with one out of 22 lymph nodes positive for nodal metastasis. Immunohistochemical analysis showed a triple-negative profile with negative oestrogen receptor, progesterone receptor, and human epidermal growth factor receptor 2 status. She then received adjuvant chemotherapy adriamycin / cyclophosphamide for four cycles, followed by docetaxel for four cycles. She also underwent adjuvant radiotherapy to the left breast and left supraclavicular fossa, with tangential opposing

fields treating the left breast, matched with an anterior field treating the left supraclavicular fossa. A total dose of 50 Gy over 25 daily fractions was delivered over 5 weeks, followed by a 10 Gy boost over five fractions to the primary site.

In early 2013, she developed recurrent disease. <sup>18</sup>F-FDG PET-CT showed regional nodal relapse and lung metastasis. No abnormal metabolic activity was noted in the left brachial plexus region. Excisional biopsy of the left interpectoral nodal mass confirmed recurrent triple-negative invasive ductal carcinoma. She was enrolled into a clinical trial and received palliative chemotherapy using weekly paclitaxel plus an investigational targeted therapy or placebo. Interim CT showed complete response with resolution of all the target lesions.

In late 2014, she complained of left upper limb weakness with difficulty in abduction above the shoulder. Physical examination showed weakness of the proximal left upper limb. Distal power was preserved and no sensory deficit was detected. MRI of the cervical spine showed intervertebral disc prolapse from C4/5 to



**Figure 1.** Fluorine-18 fluorodeoxyglucose positron emission tomography-computed tomography (FDG PET-CT) with CT, PET, and fused PET-CT images showing (a) linear increased activity (maximum standardised uptake [SUVmax] of 6.0) in the left apical axillary region extending to left C4-7 nerve roots caused by perineural disease spread in mid 2015, and (b) further increased activity (SUVmax of 6.6) at C4-7 nerve roots with intraspinal extension at C5-6 levels 3 months later.

C6/7 with mild compression of the exiting nerve root. CT showed no evidence of recurrence. She was put on expectant management with interval scans. Her degree of left upper limb weakness remained static.

In mid-2015, <sup>18</sup>F-FDG PET-CT showed linear increased activity in the left apical axillary region extending to the left C4-7 nerve roots, suspicious of perineural spread of breast cancer disease (Figure 1a). Nonetheless, MRI of the cervical spine showed denervation of the left supraspinatus muscle only and no definite mass to suggest disease recurrence. Owing to the uncertain nature of the brachial plexus lesion, a decision was made to monitor it with interval imaging.

Three months later, <sup>18</sup>F-FDG PET-CT showed increased activity at the C4-7 nerve roots with intraspinal extension at C5 and C6 levels (Figure 1b). There were new hypermetabolic left supraclavicular nodal and lung lesions suggestive of metastasis. MRI confirmed perineural thickening and enhancement along the left brachial plexus with intraspinal extension (Figure 2). All suggested recurrence with nerve infiltration. Nonetheless, the left shoulder pain did not progress.

Palliative radiotherapy 30 Gy in 10 fractions was given to the C4-T1 region including the vertebral bodies and the involved nerve roots, with partial overlapping with previous radiotherapy portal, followed by palliative chemotherapy with capecitabine. Four weeks after completion of radiotherapy, the passive range of movement and pain control of the left shoulder improved, but her proximal left upper limb weakness

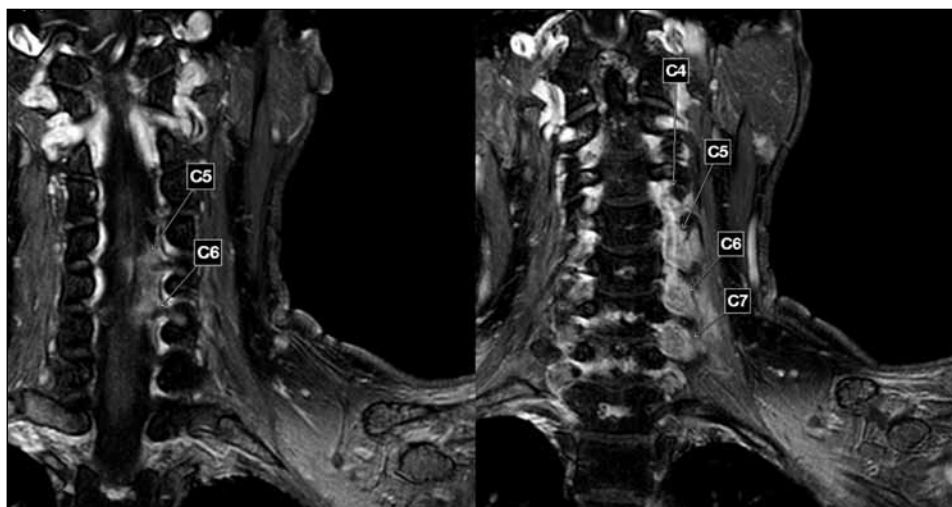
persisted.

## DISCUSSION

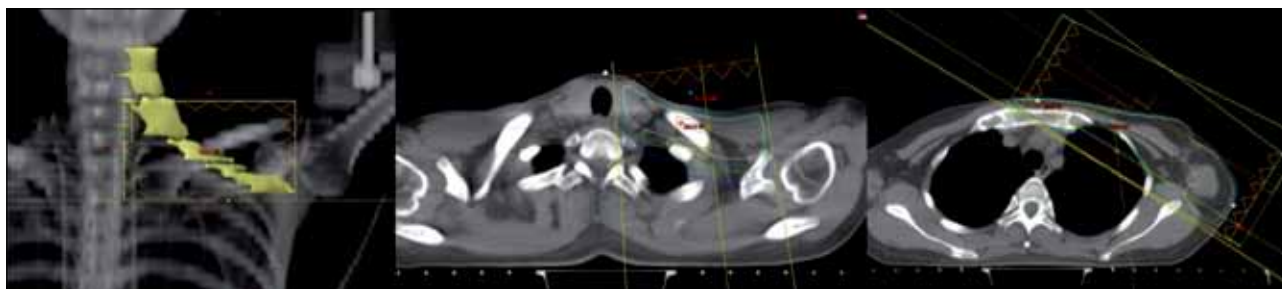
Neoplastic brachial plexopathy (NBP) from breast cancer causes severe pain and disability. Its incidence is 0.5% and it is thought to occur through lymphatic spread.<sup>2</sup> Unrelenting pain is the most common presenting symptom. Later, weakness and focal sensory disturbances occur in distribution of the brachial plexus.<sup>3</sup>

Radiation-induced brachial plexopathy (RIBP) is a major late side-effect of radiotherapy to the breast. Radiotherapy is an established treatment modality to improve loco-regional control of breast cancer and is increasingly used in an adjuvant setting. It is an integral part of breast conservation therapy. Radiotherapy after mastectomy can improve survival in high-risk patients. The addition of regional nodal irradiation to the whole breast or thoracic-wall irradiation reduces the rate of breast cancer recurrence, albeit at the expense of a higher incidence of acute pneumonitis and lymphoedema.<sup>4</sup> Radiation portal typically includes tangential opposing fields for the breast or chest wall, matched with a single anterior beam to encompass the supraclavicular and axillary lymph nodes (Figure 3). The brachial plexus is unavoidably irradiated by the supraclavicular field.

The incidence of RIBP is associated with irradiation technique, ranging from 66% with 60 Gy in 5 Gy fractions in the 1960s<sup>5</sup> to <1% with 50 Gy in 2 Gy



**Figure 2.** Magnetic resonance imaging of the cervical spine showing perineural thickening and enhancement along the left brachial plexus with intraspinal extension.



**Figure 3.** Typical radiotherapy portal for treatment of breast cancer (with brachial plexus contoured as yellow).

fractions nowadays.<sup>6</sup> Radiation causes delayed damage to mature nerve tissue, which is partly attributable to initial microvascular injury, then fibrosis. It is a dynamic process characterised by gradual stepwise worsening over a period of several years.<sup>7</sup> Survival of breast cancer patients improves with the success of multimodality treatment, although this enables late effects of radiotherapy to occur and progress. RIBP is not curable so prevention is vital to spare patients of this dreadful complication. Better radiotherapy technique to avoid hotspots from overlapping fields and daily fractions of >3 Gy is crucial.<sup>8</sup> The Radiation Therapy Oncology Group suggests a maximum point dose of 60-66 Gy to the brachial plexus.<sup>8</sup>

After surgery and radiotherapy, some patients may have morbidity of the upper limb including pain, paraesthesia, oedema, and weakness. In a study of 814 women who underwent breast surgery and adjuvant radiotherapy, up to 20% reported paraesthesia.<sup>9</sup> Vague neuro-vascular complaints are often non-specific and may be disregarded during follow-up. Therefore, the diagnosis of brachial plexopathy is often delayed. Diagnosis is based on analysis of symptoms, electrophysiological findings, MRI, and PET by a multidisciplinary team of neurologist, diagnostic radiologist, and radiation oncologist. The diagnosis of NBP is made when MRI reveals a mass at any site along the course of the brachial plexus.<sup>10</sup> Nonetheless, there is no diagnostic radiological sign for RIBP. Radiation fibrosis surrounding the brachial plexus can have low- or high-signal intensity on T2-weighted images, with or without contrast enhancement.<sup>11</sup> Thickening of cords of the brachial plexus, with or without signal intensity change, may also be present.<sup>12</sup> Diagnosis of RIBP is by excluding the presence of a mass adjacent to the brachial plexus. The use of MRI to diagnose

NBP has demonstrated sensitivity of 96%, specificity of 95%, positive predictive value of 96%, and negative predictive value of 95%.<sup>10</sup> Nonetheless, MRI can result in indeterminate or non-diagnostic findings. The signal characteristics and morphological appearance of diffusely infiltrating tumour sometimes overlap with those of radiation- or surgery-related scarring.<sup>12</sup>

<sup>18</sup>F-FDG PET-CT provides functional information and is a valuable tool to evaluate patients with brachial plexopathy.<sup>13</sup> Metabolically active malignant tumour produces substantially increased radiotracer activity, whereas radiation-induced inflammation produces only minimal-to-mild linear uptake of FDG, allowing differentiation between malignant and benign causes of brachial plexopathy.<sup>14</sup> In a case series of nine patients with confirmed NBP, PET-CT helped to confirm metastasis in patients with indeterminate MRI findings and to provide additional information about disease extent in the rest of the body.<sup>15</sup>

In our patient, <sup>18</sup>F-FDG PET-CT revealed NBP, although histological diagnosis was not obtained. The patient had clinical improvement after radiotherapy and chemotherapy. She had recurrence of symptoms 1 year before a positive <sup>18</sup>F-FDG PET-CT finding. Initial MRI and CT of the cervical spine showed negative results, and subsequent MRI failed to confirm the diagnosis. <sup>18</sup>F-FDG PET-CT appears to be more accurate in detection of NBP. Close monitoring clinically and radiologically is also important to establish the diagnosis.

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