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CASE REPORT

Stereotactic ablative radiotherapy to the lower limb for metastatic melanoma

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Introduction

Stereotactic ablative radiotherapy is a highly precise form of image-guided radiotherapy in which high doses of radiation are delivered per fraction, over a short treatment time, to extracranial sites. It aims to provide local control while sparing adjacent organs.

In 2020, stereotactic ablative radiotherapy was commissioned in the UK for use in metachronous oligometastatic disease for up to three disease sites, as studies suggested that stereotactic ablative radiotherapy to these sites can improve local control, progression-free survival and reduce time to next systemic anticancer therapy.

This article presents a case demonstrating stereotactic ablative radiotherapy to be effective and safely deliverable to treat melanoma that had metastasised to the lower limb lymph nodes.

Case report

A 54-year-old patient with a background of chronic obstructive pulmonary disease and postoperative right leg deep vein thrombosis was diagnosed with melanoma (BRAF mutant) in 1996; the primary lesion was excised from the right ankle. Disease recurred locally in the right lower limb in 2014 and progressed on multiple occasions despite different sequential lines of therapy. These included systemic anticancer therapy (vemurafenib, dabrafenib, pembrolizumab), electrochemical therapy, surgical excision of skin metastases, and right-sided inguinal lymphadenectomy.

While under active surveillance, having most recently received pembrolizumab, restaging positron emission tomography computed tomography imaging in 2021 showed a popliteal fossa lymph node with high standardised uptake value (SUV) (max 4.4) and no other sites of disease (Figure 1).

Treatment options were discussed by the melanoma multidisciplinary team. The lymph node was too deep and too close to surrounding blood vessels for electrochemical therapy. The patient preferred to avoid surgery, having developed lymphoedema following her inguinal lymphadenectomy. The patient was therefore referred for stereotactic ablative radiotherapy and accepted by the stereotactic ablative radiotherapy multidisciplinary team.

Contrast-enhanced computed tomography with 2 mm slices was used for planning. The setup was supine, legs extended and abducted, right foot and ankle fixed in position with a thermoplastic mould. A lead block was not used to reduce the dose to the contralateral leg, because of concern about potential bowing of the treatment couch after block positioning resulting in setup uncertainty, as the block cannot be in place during cone beam computed tomography imaging.

The gross tumour volume was delineated using planning computed tomography and diagnostic magnetic resonance and positron emission tomography computed tomography imaging. Planning target volume margins were 5 mm.

6MV FFF photons were used with a single partial arc for delivery of the planned regimen. A dose of 40 Gy in three fractions was prescribed to the tumour volume, plus a margin for error (planning target volume). This was achievable because of the lack of nearby organs at risk. Steps were taken to limit the potential for late side-effects; a lymphovascular corridor was spared to reduce the risk of lymphoedema. Doses to the knee and weight-bearing bones were minimised to reduce the risk of fractures (Figure 2).

Acute side effects included grade 1 fatigue. Three months post-treatment, positron emission tomography computed tomography imaging showed a good response to treatment in the right popliteal fossa node (Figure 3). No late side effects have been reported, although further follow up is required.

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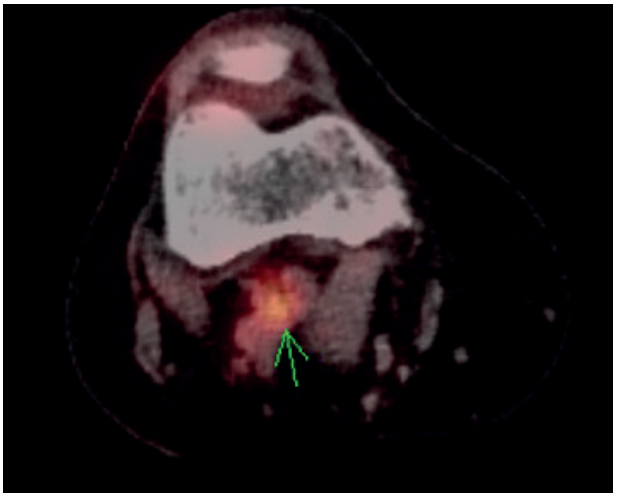

Figure 1. Axial fused positron emission tomography computed tomography scan showing the popliteal fossa lymph node with high standardised uptake value.

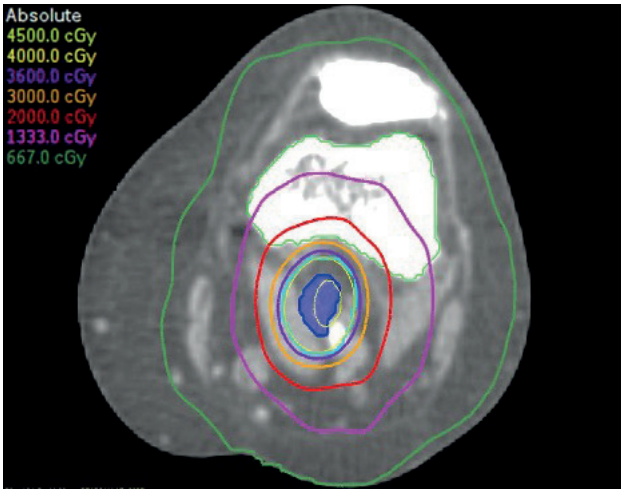

Figure 2. Axial slice of the radiotherapy plan with isodose lines. Gross tumour volume dark blue. Planning tumour volume cyan blue.

Discussion

Stereotactic ablative radiotherapy was first described in the 1990s (Blomgren et al, 1995), and followed the development of stereotactic radiosurgery for neurological disease (Leksell, 1951).

For extracranial malignancies, stereotactic ablative radiotherapy has been used extensively in the treatment of early stage, inoperable non-small-cell lung cancers (Zheng et al, 2014). However, it has attracted research in other clinical scenarios as a result of its hypothesised radiobiological advantages over conventional radiotherapy (Bernstein et al, 2016).

In April 2020, the NHS commissioned the use of stereotactic ablative radiotherapy for metachronous, extracranial metastatic sites in patients with up to three locations of metastasis, including lymph nodes. This followed a study supporting its use in this setting, which provided evidence of improved overall- and progression-free-survival when stereotactic ablative radiotherapy was used in addition to standard of care treatment (Palma et al, 2020). Furthermore, a large-scale observational trial in the UK showed desirable outcomes and a good safety profile for the use of stereotactic ablative radiotherapy in oligometastatic cancer patients (Chalkidou et al, 2021).

A literature search of PubMed using appropriate terminology did not reveal any published research specifically regarding stereotactic ablative radiotherapy and its application to limb

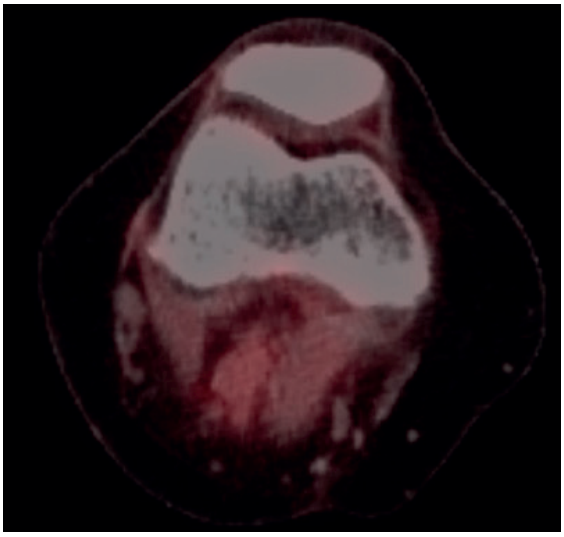

Figure 3. Axial slice of positron emission tomography computed tomography scan 3 months post-treatment showing treatment response and reduction in standardised uptake value of the right popliteal fossa node.

Learning points

- Stereotactic ablative radiotherapy can be safely applied to limb lymph nodes using this protocol, with limited early toxicity.
- Ongoing research and follow up is required to further study the long-term effectiveness and tolerability of stereotactic ablative radiotherapy in this context.
- Stereotactic ablative radiotherapy can act as a suitable alternative to surgery and electrochemical therapy when such treatments are declined or not achievable/safe.
- Phase 3 randomised evidence is awaited to confirm the improved progression-free and overall survival rates, and the freedom from systemic anticancer therapy intervals that stereotactic ablative radiotherapy may offer, in addition to standard of care treatment in metachronous extracranial oligometastatic disease.

lymph node oligometastases. A number of articles discuss applying stereotactic ablative radiotherapy to multi-site lymph node oligometastases (Franzese et al, 2020a,b), as well as those of the pelvis, mediastinum and retroperitoneum (Burkoň et al, 2020). One article cites the axilla as a target (Teh et al, 2007).

This case provides evidence that stereotactic ablative radiotherapy can be safely and effectively applied to more unusual oligometastatic sites, such as peripheral limb lymph node basins. To the authors' knowledge, this is a novel use of stereotactic ablative radiotherapy. The patient will require clinical follow up to assess outcomes, including late effects. Ongoing phase 3 trials will help to provide stronger evidence for the use of stereotactic ablative radiotherapy in the oligometastatic setting.

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