Radiology Case Reports 13 (2018) 1259–1266

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/radcr

Case report

Long-term radiological and histological outcomes following selective internal radiation therapy to liver metastases from breast cancer

Paul C. Lyon, BSc, MSc, MRCS, MRes, DPhil[a,b,c], Helen Winter, BSc, MBBS, MSc, MRCP, FRACP[d], Karin Herbschleb, MRCP[d], Leticia Campo, Diploma[e], Robert Carlisle, PhD[c], Feng Wu, MD, PhD[b], Robert Goldin, MD, MEd, FRCPath[f], Constantin C. Coussios, PhD[c], Mark R. Middleton, BA, MA, PhD, FRCP[d], Fergus V. Gleeson, FRCR, FRCP[a], Philip Boardman, FRCR[a], Ricky A. Sharma, MB, BChir, MA, PhD, FRCP, FRCR[d,g,]*

[a] *Department of Radiology, Oxford University Hospitals NHS Foundation Trust, Churchill Hospital, Old Road, Headington, Oxford OX3 7LE, United Kingdom*

[b] *Nuffield Department of Surgical Sciences, John Radcliffe Hospital, Oxford OX3 9DU, United Kingdom*

[c] *Institute of Biomedical Engineering, University of Oxford, Old Road Campus Research Building, Oxford OX3 7DQ, United Kingdom*

[d] *Department of Oncology, Churchill Hospital, Oxford University Hospitals NHS Foundation Trust, Oxford, OX3 7LE, United Kingdom*

[e] *Good Clinical Practice Laboratories, Oxford Institute for Radiation Oncology, University of Oxford, Old Road Campus Research Building, Oxford OX3 7DQ, United Kingdom*

[f] *Centre for Pathology, Imperial College at St Mary's Hospital, London W2 1NY, United Kingdom*

[g] *NIHR University College London Hospitals Biomedical Research Centre, UCL Cancer Institute, University College London, 72 Huntley Street, London WC1E 6DD, United Kingdom*

ARTICLE INFO

Article history:
Received 23 May 2018
Revised 19 August 2018
Accepted 26 August 2018

Keywords:
Selective internal radiation therapy
SIRT
Transarterial radioembolization
Liver-directed therapy

ABSTRACT

Liver metastasis from breast cancer is associated with poor prognosis and is a major cause of early morbidity and mortality. When liver resection is not feasible, minimally invasive directed therapies are considered to attempt to prolong survival. Selective internal radiation therapy (SIRT) with yttrium-90 microspheres is a liver-directed therapy that can improve local control of liver metastases from colorectal cancer. We present a case of a patient with a ductal breast adenocarcinoma, who developed liver and bone metastasis despite extensive treatment with systemic chemotherapies. Following SIRT to the liver, after an initial response, the patient ultimately progressed in the liver after 7 months. Liver tumor histology obtained 20 months after the SIRT intervention demonstrated the presence of the

* Corresponding author.
E-mail addresses: paul.lyon@nhs.net (P.C. Lyon), helen.winter2@gtc.ox.ac.uk (H. Winter), Karin.Herbschleb@radboudumc.nl (K. Herbschleb), leticia.campo@oncology.ox.ac.uk (L. Campo), robert.carlisle@eng.ox.ac.uk (R. Carlisle), feng.wu@nds.ox.ac.uk (F. Wu), r.goldin@imperial.ac.uk (R. Goldin), constantin.coussios@eng.ox.ac.uk (C.C. Coussios), Mark.Middleton@ouh.nhs.uk (M.R. Middleton), Fergus.Gleeson@ouh.nhs.uk (F.V. Gleeson), phil.boardman@ouh.nhs.uk (P. Boardman), ricky.sharma@ucl.ac.uk (R.A. Sharma).
https://doi.org/10.1016/j.radcr.2018.08.020

resin microspheres in situ. This case report demonstrates the long-term control that may be achieved with SIRT to treat liver metastases from breast cancer that is refractory to previous chemotherapies, and the presence of microspheres in situ long-term.

Background

Breast cancer is a leading cause of mortality worldwide [1]. It represents a heterogeneous group of subtypes with characteristic molecular features, prognosis, and responses to treatment [2]. The development of liver metastasis from breast cancer heralds a poor prognosis [3]. If it is feasible, hepatic resection is of offered to patients, but unfortunately the vast majority are unresectable at the time of diagnosis of liver metastasis [3]. Other liver-directed therapies have been attempted for liver-only disease with the primary aim of palliating and prolonging survival. These treatments include radiofrequency [4,5] and microwave ablation, transarterial chemoembolization [6], selective internal radiation therapy (SIRT) [7], and stereotactic body radiotherapy [8,9].

SIRT was developed as a liver-directed therapy for metastatic colorectal cancer and primary liver cancer [10]. Recently, a randomized multicenter clinical trial has demonstrated an improvement in radiological response rate and hepatic progression-free survival in patients with metastatic colorectal cancer treated with SIRT [11]. In case reports and small case series, SIRT has also been used to treat liver metastases from other primary tumors including breast [12], neuroendocrine [13], and pancreas [14].

SIRT involves the administration of yttrium-90 (^{90}Y) microspheres via the arterial blood supply of liver metastases [15]. The microspheres are typically about 30 μm in diameter. The administered dose is targeted by meticulous angiography of the tumor and its vasculature. Potential adverse events of SIRT therapy include postradioembolization syndrome (PRS) (20%-55% of patients), radioembolization-induced liver disease (REILD), damage to the biliary system including radiation cholecystitis, portal hypertension, radiation pneumonitis, gastroduodenal ulceration, vascular injury, and lymphopenia [10,16,17]. PRS typically consists of mild fatigue, gastrointestinal upset, anorexia, fever, and cachexia and it may require symptomatic management. REILD is defined as jaundice and ascites 1 to 2 months after a radioembolization procedure, in the absence of tumor progression or bile duct occlusion [18]. One prospective study evaluated 45 patients without chronic liver disease who underwent radioembolization for the liver in a single institution and 9 (20%) went on to develop REILD in the first 90 days [19]. All these patients had received chemotherapy preprocedure or postprocedure and population analysis strongly suggested that the syndrome associated with the combined effect of radiation and chemotherapy.

There are some reports of tumur pathology from hepatic resection after SIRT, all of which focus on colorectal liver metastases [20–22]. In colorectal patients, microspheres have been identified in the vascular tumor bed and the portal tract vessels within liver parenchyma following SIRT [20]. These microspheres were typically associated with giant cell reaction or histiocytes. In the tumor bed, the blood vessels and fibroblasts showed changes suggestive of radiation injury. Necrosis, mucin and calcification have also been described. Another study describes a patient with metastatic cholangiocarcinoma, who had a partial response to SIRT and went on to a liver resection and remained disease-free at 9 months [22]. Histology demonstrated residual microspheres with evidence of moderate-to-severe hepatic inflammation and early stage fibrosis, with 50% overall tumor necrosis. In the same study, a patient with metastatic rectal cancer also went on to have a liver resection, and this time histology revealed residual microspheres, moderate-to-severe inflammation with no evidence of fibrosis and 80% tumor necrosis. In addition, the study describes residual microsphere embolization surrounding resected esophageal and cholangiocarcinoma liver metastases with 80% and 45% tumor necrosis, respectively. Another study examined the histology of the nonneoplasic liver in 7 patients 6-23 months following SIRT in metastatic colorectal cancer [3], hepatocellular carcinoma [2], and neuroendocrine tumor [1,23]. Of the 7 tissue samples, 6 were core biopsies and 1 was a wedge resection. Of the biopsies, 5/6 demonstrated microspheres, typically in the portal tracts, and without significant associated inflammation. Mild portal vein dilatation was seen in 3/6, mild portal fibrosis in 2/6, and in 1 case a particle was demonstrated in an artery with associated thrombus. The wedge resection demonstrated extensive coagulative necrosis of hepatocytes due to portal vein thrombosis. The study suggests that SIRT causes little diagnostic pathologic change in the normal liver surrounding the liver metastasis, and that the microspheres are generally found in the portal tracts with little inflammatory reaction.

Publications of long-term outcomes, including histology, in breast cancer patients with liver metastases who have received SIRT are currently lacking, so it is not known what histological changes are observed in breast cancer metastases. This report describes radiological outcomes and histology in an extensively pretreated breast cancer patient who underwent tumor biopsies 20 months after receiving SIRT. It represents the first report of tumor histology so long after SIRT in a patient with metastatic breast cancer, demonstrating the presence of microspheres distributed in the stroma surrounding viable tumor.

Clinical presentation

Written informed consent was obtained from the patient for publication of this case report, including accompanying images. A 49-year-old woman, with no past medical history of note, presented with right-sided grade 2, node positive,