CASE REPORT

Rash and subcutaneous fat necrosis after DEB-TACE with doxorubicin

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SUMMARY

A 73-year-old woman with hepatocellular carcinoma localised to the liver was treated with doxorubicin-loaded drug-eluting beads through transcatheter arterial chemoembolisation (DEB-TACE). She developed subcutaneous, erythematous, tender nodules in her abdomen 3 days after the procedure. PET/CT scan that was done to evaluate for evidence of disease progression showed mild avidity of these nodules. Biopsy showed fatty necrosis. Nodules started to improve spontaneously 2 weeks after onset. At 8 weeks after onset, lesions stabilised in size and the associated tenderness and erythema resolved. This represents a rare side effect of TACE procedure in general. It can happen secondary to non-target embolisation of hepatic falciform artery, planned embolisation of extrahepatic collateral supplies and even when there is no clear cause. Spontaneous resolution of acute symptoms usually occurs over the course of few weeks, though subcutaneous lesions consisting of necrotic fat tissue may persist for longer periods.

BACKGROUND

The incidence of hepatocellular carcinoma (HCC) has been rising in the USA in the last three decades.¹ The prevalence is higher in other parts of the world where there is higher prevalence of chronic viral hepatitis.² Local treatment directed to the liver is usually considered when tumour is confined to the liver with adequate liver function. If resection is not feasible, other modalities of local therapy is usually entertained. Options include

radiofrequency ablation, transarterial chemoembolisation (TACE) and in some cases cryoablation.³ In conventional TACE, chemotherapy, in combination with lipiodol, is usually injected directly into the hepatic artery that feeds the tumour promoting an immediate drug peak in the bloodstream right after the procedure. Drug-eluting beads (DEBs) have now been used in the procedure for more than a decade.⁴ They are capable of occluding the blood flow to the target tissue and delivering a local and sustained dose of the loaded chemotherapy drug directly to the tumour over several days. DEB-TACE is usually associated with high success rate, good tumour response and less systemic toxicity. This case illustrates a rare side effect of this local ablative procedure.

CASE PRESENTATION

A 73-year-old white woman presented with diabetes, coronary artery disease status post-bypass surgery and history of liver cirrhosis secondary to non-alcoholic steatohepatitis. She was found to have a liver mass on a screening ultrasound. CT scan showed 2.6 cm liver lesion confined to segment 4. The lesion had mild heterogeneous enhancement, but did not demonstrate rapid washout on delayed phase imaging. Alpha fetoprotein level was normal. CT-guided mass biopsy showed well-differentiated hepatocellular carcinoma in the background of nodular cirrhosis. At the time of HCC diagnosis, the patient was at Child-Pugh class A. The patient had evidence of portal hypertension with history of oesophageal varices banding. She was not felt to have adequate hepatic reserve, thus was not a candidate for resection. The patient was not felt to be a transplant candidate either secondary to age and comorbidities. She underwent microwave ablation of the liver tumour. MRI 1 month after treatment showed a 13 mm arterial enhancing lesion in segment 7 and 12 mm arterial enhancing lesion in segment 6 with associated washout and T2 signal abnormality. There was also several other small enhancing lesions in both lobes, so she was referred to chemoembolisation. She received two sessions of doxorubicin-loaded DEBs through transcatheter arterial chemoembolisation (DEB-TACE) to the right lobe of the liver and one session to the left lobe. Liquid doxorubicin was used to load beads. Three days after the last session, she developed subcutaneous nodules in her lower abdomen. She presented with a total of five erythematous nodules, with average size of 1.5 cm. Four nodules were on the left lower quadrant and one nodule

Figure 1 Erythematous tender subcutaneous lesions in the left lower quadrant 3 days after last session of drug-eluting beads through transcatheter arterial chemoembolisation.

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Figure 2 Two weeks after onset. Erythema and pain improved but subcutaneous nodules increased slightly in size.

on the right lower quadrant. Lesions were erythematous and tender ([figure 1](#)). The patient was using subcutaneous insulin but reported that her injection sites are usually the arms and thighs. The lesion sites did not correspond to any recent insulin administration. She was prescribed pain medications and had close follow-up.

OUTCOME AND FOLLOW-UP

After 2 weeks, her erythema and pain improved, but the nodules increased slightly in size ([figure 2](#)). PET/CT was performed to evaluate the possibility of subcutaneous spread of HCC, but only showed slight avidity in the subcutaneous nodules ([figure 3](#)). Ultrasound-guided biopsy showed necrotic fat tissue with no evidence of malignancy. After 4 weeks of onset, the subcutaneous lesions decreased in size and the erythema resolved, but lesions remained mildly tender. In 8 weeks, while the skin lesions remained in place, the associated erythema and tenderness resolved completely.

DISCUSSION

Skin rash with fat necrosis after TACE is a rare complication of the procedure. It is a possible complication with embolisation of extrahepatic collateral supplies to HCC.⁵ In some cases, it is

Figure 3 PET/CT showing mild avidity in the subcutaneous nodules in the left lower abdomen.

Learning points

- ▶ Drug-eluting bead implantation through transcatheter arterial chemoembolisation is a successful modality in treating liver malignancy.
- ▶ Skin rash with subcutaneous fatty necrosis is a rare side effect.
- ▶ Self-resolution usually occurs over the course of a few weeks.

secondary to non-target embolisation of hepatic falciform artery (HFA). Few cases were reported in the literature.^{6–8} In our case, the embolisation was targeted and there was no falciform artery identified during the procedure. Retrospective review of the case confirmed the absence of HFA as well.

Doxorubicin is typically mixed with the spheres prior to its embolisation to the tumour. It comes in powder or liquid form. Powder form is usually used in our institution for embolisation purpose. In the presented case, liquid doxorubicin was used as powder form and had limited supply. It is postulated that powder form is less systemically absorbed and hence has less systemic side effects.

Data for more than 800 patients who were treated with DEB-TACE from multiple studies and abstracts were reviewed by Carter and Martin and revealed only one case of skin rash reported after the procedure.⁹ In all reported cases, the condition resolved with conservative measures. Severe cases might require surgical debridement.

Anthracyclines including doxorubicin and epirubicin are vesicants. They cause skin necrosis in iatrogenic subcutaneous administration. They are the most commonly used drugs for TACE procedure. Subcutaneous fat necrosis in the presence of HFA is secondary to high drug concentration in these tissues. HFA runs in the falciform ligament and supplies subcutaneous tissue around the umbilicus. Skin rash might also occur after embolisation of extrahepatic collateral supplies to target lesion. In cases where extrahepatic collaterals were not embolised and had absent HFA radiologically, the pathogenesis of this finding remains unknown. This case suggests the possibility of haematogenous migration of released chemotherapy from the bead to the subcutaneous tissue of the abdomen. The route of haematogenous migration could possibly be at the level of microcirculation and hence not visualised at the time of procedure.

Contributors AGE: prepared the initial draft for the case report, revised the manuscript critically, approved the version to be published and agreed to be accountable for all aspects of the work. TP: revised the manuscript critically, provided some additions and suggestions for many changes, approved the version to be published and agreed to be accountable for all aspects of the work. JMM: provided some pictures with captions, reviewed procedures images retrospectively, revised the manuscript critically, approved the version to be published and agreed to be accountable for all aspects of the work.

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