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Case Report Open Access

Irreversible Electroporation Ablation of Liver Metastases Adjacent to the Heart Induces Ventricular Tachycardia: A Case Report

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Abstract

Irreversible electroporation (IRE) is a new non-thermal ablation therapy that is currently undergoing clinical investigation for treatment of malignant liver and lung tumors; however, there is emerging evidence that is method can interfere with heart function. Here we report the first case of a 61-year-old Malaysian woman who underwent IRE ablation on liver metastases from pancreatic cancer located adjacent to the heart. During IRE ablation, two electrodes were placed on the liver tumor, with minimum distances from the heart of 5.7 mm. Despite using a cardiac synchronization device during the IRE ablation, paroxysmal ventricular tachycardia was induced in this patient. Therefore, care must be taken when treating lesions located near the heart with IRE.

Keywords: Irreversible electroporation; Ablation; Liver metastases; Ventricular tachycardia; Heart

Introduction

Tumor ablation is a common minimally-invasive treatment for liver tumors and metastases [1]. While tumor ablation using thermal energy is widely used, it is somewhat limited by perfusion-mediated temperature stabilization and the risk of thermal damage to adjacent structures [2,3]. As a result, incomplete tumor ablation with subsequent tumor recurrence and possible thermal injury to vital structures are commonly reported limitations of this therapy.

As an alternative, irreversible electroporation (IRE) is a new non-thermal ablation therapy that creates countless permanent lethal nanopores in the cell membrane [4]. During IRE, the surrounding extracellular matrix structures will remain intact. Due to its precision, the anatomical framework, shape, and strength of vulnerable surrounding structures (bile ducts, blood vessels, and ureters) are not compromised [5]. As such, IRE is undergoing clinical investigation as a local tumor therapy for malignant liver and lung lesions. However, there is emerging evidence that the electroporation pulses used in IRE interfere with heart function and potentially cause arrhythmias, particularly for tumors located close to heart muscle [6]. Therefore, cardiac synchronization is typically employed during IRE.

In this report, we describe the first case of paroxysmal ventricular tachycardia induced by IRE ablation on liver metastases located near the heart, despite employing cardiac synchronization.

Case Report

A 61-year-old woman was referred to our institution in November 2015 after being diagnosed with pancreatic cancer and upper abdominal pain symptoms. Her carbohydrate antigen (CA) 125 level was elevated to 86.14 U/ml (normal range: 0–35 U/ml), while her serum carcinoembryonic antigen (CEA) level and CA 19-9 levels were within normal limits. An electrocardiogram showed sinus bradycardia. Abdominal ultrasonography showed a solid tumor in the left lobe of her liver, considered to be a solid tumor metastasis from pancreatic cancer. An abdomen computed tomography (CT) scan revealed irregular lumps in the left lobe of the liver, with high density, considered to be liver metastases (size 2.0 × 1.8 cm) (Figure 1).

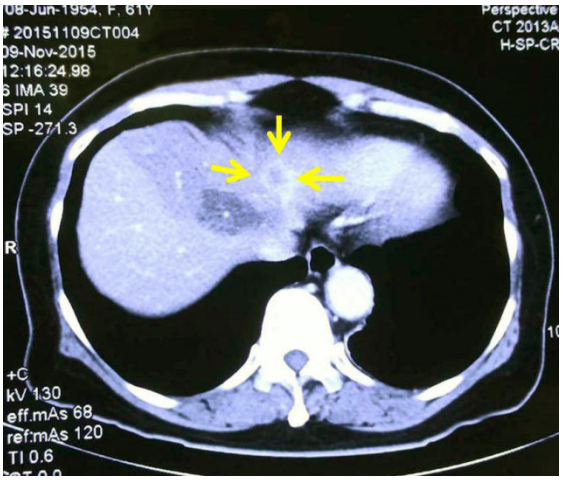

Figure 1: CT image of the patient before IRE treatment. The tumor showed high density, as indicated by the arrows.

Histopathological examination of the liver tumor confirmed moderately differentiated adenocarcinoma of the pancreas. Considering the diagnosis of advanced cancer with a tumor located adjacent to heart, the patient was unsuitable for traditional surgery, radiotherapy, and chemotherapy. Therefore, after comprehensive discussion with different departments, she was considered a candidate for IRE ablation treatment of liver metastases, for palliative control of

tumor growth. After informed consent was obtained from the patient, IRE ablation (Nanoknife, AngioDynamics, Latham, NY, USA) was performed percutaneously under total intravenous anesthesia induced with propofol (2 mg kg^{-1}), sufentanil (0.3 μg kg^{-1}), and rocuronium (0.6 mg kg^{-1}), and was maintained with propofol and sufentanil.

According to the planned target area, two electrodes were placed on both sides of the liver tumor under CT (Somatom Definition AS, Siemens Healthcare, Erlangen, Germany) and ultrasound (IU22, Philips Healthcare, Bothell, WA, United States) image guidance, with minimum distances from the heart of 5.7 mm (Figure 2). The ablation parameters were 2400 volts to 3000 volts (1500 V/cm) between the electrodes given in 70 μs pulses, 2.0 cm exposed, with a total of 70 pulses per ablation. The ablation parameters were determined using preplanning software distributed by the electrode manufacturer, which ensured that the electric field covered the entire tumor. In addition, to prevent pulse-induced arrhythmias, a preprogrammed commercial electrocardiography (ECG) trigger monitor (AccuSync 72; AccuSync Medical Research Corporation, Milford, Connecticut, USA) was connected to a five-lead ECG to synchronize pulse delivery within the refractory period of the heart. An external biphasic defibrillator was also prepared, and was immediately available for the treatment of ventricular arrhythmias. The intraoperative cardiac electrical activity and muscle contraction was observed closely. After a test pulse at 270 V, 10 tentative pulses were delivered via each electrode pair. While these pulses confirmed adequate conductivity, 60 additional pulses were administered to reach a total of 70 pulses per electrode pair.

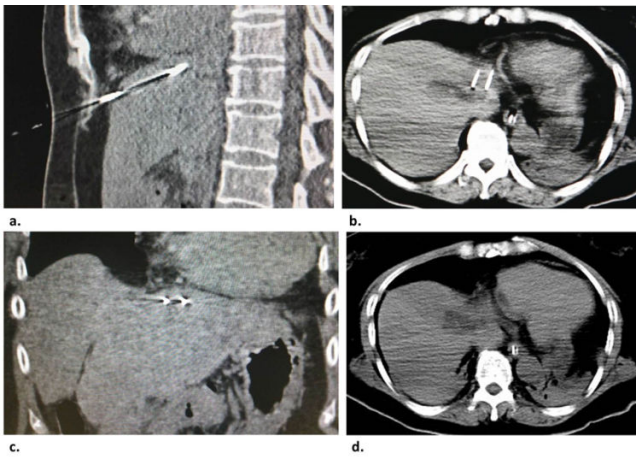

Figure 2: Intraoperative CT images of the patient a: sagittal plane; b: cross-section; c: coronal plane; d: cross-section of immediately after IRE ablation.

During ablation of the lesion, we observed an episode of paroxysmal ventricular tachycardia without hemodynamic changes, and aborted the procedure (Figure 3). The arrhythmias were transient and no cardioversion or other treatment was required. After a period of close observation without recurrence of arrhythmia, we continued IRE ablation. Thereafter, a little ventricular wave without serious arrhythmia was observed. Finally, the electrodes were removed, and CT examination was performed to determine whether the tumor treated area had changed, as well as to ensure no bleeding, exudate, or other intraoperative complications had occurred. There were no obvious postoperative complications, and the patient was discharged on the 9th postoperative day. An enhanced CT scan 8 days after the procedure showed low density in the liver metastasis, indicating that the tumor was under control after IRE ablation (Figure 4).

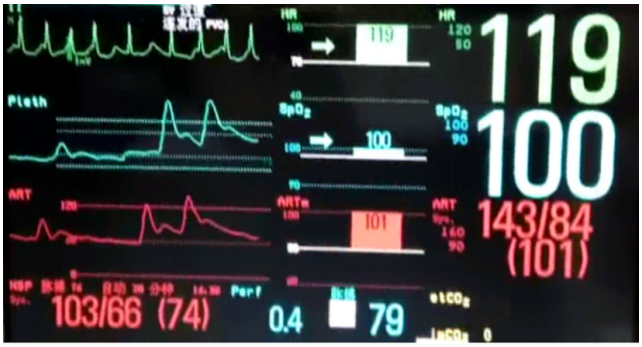

Figure 3: Electrocardiogram of the patient during IRE treatment.

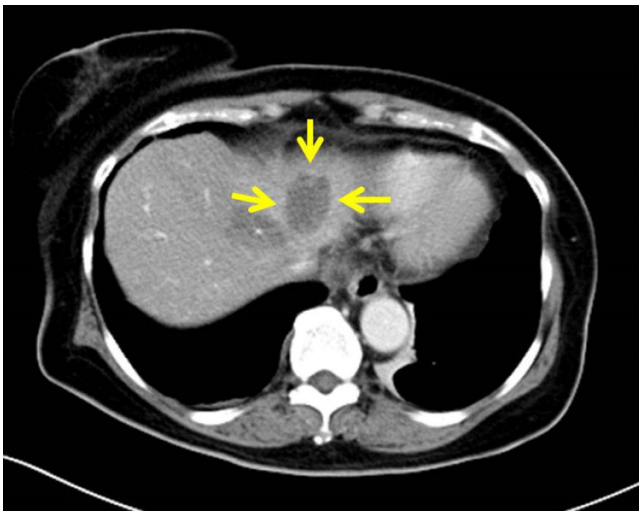

Figure 4: Enhanced CT image of the patient, 8 days after IRE ablation. The tumor showed areas of low density, as indicated by the arrows.

Discussion

IRE delivers powerful electrical pulses to human tissue to induce targeted cell death, but preserve the bile ducts and other vessels. Moreover, IRE can potentially lead to cardiac arrhythmias when it is used in proximity to the heart. Among the possible heart function irregularities arising from the application of electroporation pulses (e.g., atrial and ventricular flutter and fibrillation, premature heartbeats), the most dangerous is ventricular fibrillation [7]. Typically for ventricular myocardium, the vulnerable period coincides with the middle and terminal phases of the T wave [7]. However, higher shock strengths cause the vulnerable period to occur several milliseconds earlier in the heartbeat [8]. Therefore, the whole T wave should be considered to be within the vulnerable period for the ventricles. The vulnerable period for the atria is somewhere in the S wave [7]. Therefore, any externally applied electrical pulses that are delivered

outside these vulnerable periods have an extremely low probability of inducing ventricular fibrillation [7]. Moreover, the likelihood that electroporation influences heart function also depends on applied pulse voltage, duration, number and repetition frequency of electroporation pulses, and electric current pathway [7].

Although fibrillation can occur in normal and healthy hearts, it is more likely in hearts with structural or functional abnormalities [6]. Indeed, during some arrhythmias, the heart becomes more susceptible to external stimuli due to a decreased threshold level for fibrillation. Therefore, electroporation pulses coinciding with some arrhythmias could elicit fibrillation. This potential danger is most significant for premature heartbeats or extrasystoles [7].

As IRE has the potential to cause fatal cardiac arrhythmias, specific precautions are required [9]. Cardiac screening and synchronized pulsing are absolutely necessary during IRE ablation [10]. Indeed, in a previous animal study conducted using a 2-electrode configuration, all cells within a radius of 1.7 cm from each applicator were found to show a transient or permanent increase in cell membrane permeability, suggesting that the delivery of IRE pulses within 1.7 cm of the myocardium could induce arrhythmias [10]. Moreover, this study indicated that unsynchronized IRE close to the heart can cause fatal ventricular arrhythmias, while synchronizing IRE pulse delivery with an absolute refractory period could avoid significant cardiac arrhythmias [10]. The study concluded that when performing IRE ablation, the distance from the heart should be greater than 1.7 cm, or IRE should be performed in synchronized mode to avoid inducing ventricular arrhythmias [10]. Indeed, in an initial clinical study where IRE ablation was performed with cardiac synchronization, only atrial arrhythmias occurred (four cases), and these resolved either spontaneously or within 24 hours after therapy [11].

Based on these early studies, IRE is considered to be safe when it is combined with ECG-synchronized delivery [11]. However, Sugimoto et al. reported that a number of transient ventricular extrasystoles occurred when the synchronization device failed to operate properly (unsuccessful synchronization with the R wave). As a result, some pulses were delivered during the vulnerable period of the ventricular myocardium, which corresponds to almost the entire T wave as seen on the ECG [12]. As rhythmic cardiac contraction is governed by the discharge of electrical impulses (action potentials) by the sinoatrial node [13], external electrical stimuli can lead to localized depolarization through the opening of non-specific ion channels [14-16]. Moreover, electrical stimuli that exceed the threshold excitation potential may cause localized depolarization to build into an action potential [17]. Therefore, as IRE delivers powerful electrical pulses to human tissue, it may trigger a premature action potential in a cardiac myocytes, and has the potential to causing fatal cardiac arrhythmias [10]. However, previous studies have found that if IRE pulse delivery is adjusted to fall during the absolute refractory period (before the vulnerable period of the myocardium), this arrhythmogenic potential is minimized [6,18,19].

Unlike these previous studies, we found that paroxysmal ventricular tachycardia was still induced when treating lesions located near the heart by IRE combined with cardiac synchronization. However, we also observed that the patient can recover rhythm to normal on their own, without cardioversion or other treatment, after an episode of paroxysmal ventricular tachycardia without hemodynamic changes. Moreover, we could continue IRE treatment after the patient recovered rhythm, and no other serious arrhythmias reoccurred.

In summary, our experience suggests that severe arrhythmias can be induced when treating lesions located near the heart even when synchronizing the irreversible electroporation pulse with the cardiac rhythm. Therefore, careful monitoring of patients is required when treating lesions located near the heart with IRE ablation. In addition, a full preoperative assessment of the risks of IRE is necessary prior to using this treatment for patients with tumor metastases.

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