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Uzay neşteri (CyberKnife®) uygunsuz şok nedeni olabilir

CyberKnife® can cause inappropriate shocks

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Özet– Takılabilir kardiyoverter defibrilatörler (ICD), hayatı tehdit eden ventrikül taşiaritmilerinin tedavisinde giderek artan oranlarda kullanılmaktadırlar. Hayat kurtarıcı özelliği olan bu cihazlar, elektromanyetik enerji kaynaklarına karşı oldukça duyarlıdır. Elektromanyetik etkileşim (elektromanyetik interferans; EMI) sonucu olarak ICD'lerin taşiaritmiyi algılama ve sonlandırma mekanizmalarında bazı sorunlar meydana geldiği bilinmektedir. Yeni nesil ICD'ler ile EMI daha az gözlense de radyoterapi sırasında hala sorun yaşanabilmektedir. Uzay neşteri (CyberKnife®), vücuttaki kötü huylu tümörlerin tedavisi için kullanılan, radyoterapi alanındaki son stereotaktik radyocerrahi teknolojisidir. Özellikle ileri evre tümörlerde veya metastazlarda tercih edilmektedir. Rutin ICD kontrollerinde 5 kez ICD deşarjı olduğu tespit edilen hasta değerlendirmeye alındı.

Summary– Implantable cardioverter-defibrillators (ICD) have been increasingly used to treat life-threatening ventricular tachyarrhythmias. Although they have life-saving capabilities, they are very sensitive to electromagnetic energy sources. It has been reported that many problems associated with the detection of tachyarrhythmias and termination of the mechanism of the ICDs occur due to electromagnetic interference (EMI). In spite of the fact that EMI has been decreasingly observed with the latest generation ICDs, problems may still occur during radiotherapy. The CyberKnife® is the latest stereotactic radiosurgery technology in the field of radiotherapy, and is currently being used for the treatment of malign neoplasms in the body. It is especially preferred for the treatment of advanced stage and/or metastatic tumors. Five ICD shocks were detected in a

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Hastanın rektum adenokarsinomunun akciğer metastazı nedeniyle CyberKnife® ile radyoterapi gördüğü ve şokları bu sırada aldığı öğrenildi. ICD üzerinden alınan intrakardiyak kayıtlar incelendiğinde, şokların EMI nedeniyle meydana gelen aşırı algılamaya bağlı uygunsuz şoklar olduğu saptandı.

patient during routine ICD controls. When the patient was evaluated, it was determined that he had undergone radiotherapy with CyberKnife® technology because of lung metastasis and rectal adenocarcinoma. It was learnt that he had received ICD shocks while he had been on radiotherapy. When the intracardiac electrograms stored in the memory of the ICD were investigated, it was established that the shocks were inappropriate shocks due to oversensing because of exposure to EMI.

Abbreviations:

EMI Electromagnetic interference
ICD Implantable cardioverter-defibrillator
MU monitor unit

Thanks to prolonged life span, likelihood of simultaneous concomitancy of diseases of heart, and other organs increases. If the patient has an implantable cardioverter defibrillator (ICD), modalities used for the diagnosis, and treatment of many other organs should be employed with caution especially in terms electromagnetic interference (EMI). For instance, currently used ICDs are not compatible with magnetic resonance imaging (MRI) . Patients with ICDs can undergo MRI only under certain conditions, and safety measures. Still, diathermy used for the relief of joint pains, lithotripsy utilized for the fragmentation of renal stones, cauteries employed during surgical interventions, electrical cardioversion, and radiofrequency ablation procedures are also sources of EMI, and certain precautions should be taken before application of these procedures against potential risks of EMI. [1,2] Diagnostic radiation has not any important impact on ICDs. However, high-energy radiation used for the treatment of many malignant tumors can create important problems in patients with ICD. CyberKnife® Image-guided Robotic Stereotactic Ablative Radiotherapy System is a stereotactic radiosurgery device which uses linear accelerator. This device is mounted on a robotic system which rotates around the patient under the guidance of CT. It has been suggested that targeted higher doses of focal radiation beams treat especially inoperable or hardly accessible cancerous tissues, while largely sparing normal tissues. Problems associated with ICDs of the patients under radiotherapy dependent on the radiation dose have been reported related to the delay in the detection of

ventricular tachyarrhytmias, and the longer charge time of ICD, decrease in the capacity of ICD generator, inappropriate shocks or inhibition of shocks because of oversensing. [3-6]

Herein, a patient in whom inappropriate shocks were seen secondary to oversensing caused by EMI during application of radiotherapy using CyperKnife® system for pulmonary metastasis of rectal adenocarcinoma is presented, and relevant literature data were overviewed to summarize various approaches indicated for the patient with an ICD who must receive radiotherapy.

CASE PRESENTATION

A 77-year-old male patient whose ICD was reportedly discharged for 5 times with 34 joules during routine pacemaker controls was retrospectively evaluated. The patient who was followed up with the diagnoses of coronary artery disease, and hypertension had undergone a dual-chamber ICD (EnTrust D154ATG; Medtronic, Minneapolis, USA) implantation in 2006 with the indication of ventricular tachycardia. The patient had right hemiparesis because of an attack of cerebral embolism he had suffered in 2009. He had undergone colonoscopic examination in 2010 in another medical center because of complaints of rectal bleeding, and diagnosis of rectal adenocarcinoma was established upon histopathologic examination of the biopsy material which necessitated rectal resection. The same year thoracal tomography of the patient who had complained of nosebleed revealed a mass measuring 22 x 25 mm in the posterior segment of the upper lobe of the right lung. Further PET-CT examination demonstrated cancerous involvement in this focus which was interpreted as a metastatic mass. In consideration of his age, and the presence of other concomitant diseases, for the treatment of pulmonary metastasis, radiotherapy using CyberKnife® system was planned by the department of radiation oncology, and a total dose of 55 Gray (Gy) was applied divided in 5 sessions (11 Gy/session) using 6-18 MV (megavolt) energy delivered by means of a linear accelerator.

During control visits his blood pressure (BP) was 130/85 mm Hg, and pulse rate , 60 bpm. Cardiac, and pulmonary examinations were unremarkable. Electrocardiograms detected heart beats generated by a pacemaker accompanied by atrial fibrillation. On electrocardiogram, left ventricular diastolic, and ventricular diameters were 5.6 cm, and 3.3 cm, respectively. A posterobasal aneurysm was detected on the posterobasal aspect of the left ventricle. Left ventricular ejection fraction was 45 percent. Anteroposterior diameter of the left atrium was 4 cm, and regurgitant flows related to mild mitral, and aortic insufficiency were seen. When intracardiac electrocardiograms stored in

the memory of ICD were analyzed, it was determined that 5 attacks on separate days each lasting for 13-20 secs occurred and ICD defibrillated the heart with a higher-shock energies of 34 joules at each attack. It was also learnt that he was receiving radiotherapy, and felt shivering while these shock waves were delivered. The patient thought that this was due to the radiotherapy therapy he was receiving. Before this therapy he hadn't felt any ICD generated shocks. When all the episodes were analyzed, electromagnetic interferences were detected in atrial, and ventricular channels. It was determined that these vibrations which mimick intracardiac potentials induced oversensing in the form of ventricular fibrillation in the ventricular channel which resulted in the emergence of inappropriate shocks. (Figure 1) During pacemaker controls, any abnormality with the device was not encountered. However, rapid, irregular, and episodic pulses generated from atrial contractions were revealed. Also during the controls, it was observed that he had been suffering from episodes of atrial fibrillation for the last 48 hours. Then he was hospitalized in the clinics, and cardioversion was planned. Anticoagulant therapy was initiated because of the past history of thrombotic stroke. Upon detection of a thrombus in the left atrial appendage on transesophageal echocardiograms, cardioversion was given up, and the patient was discharged while on warfarin therapy.

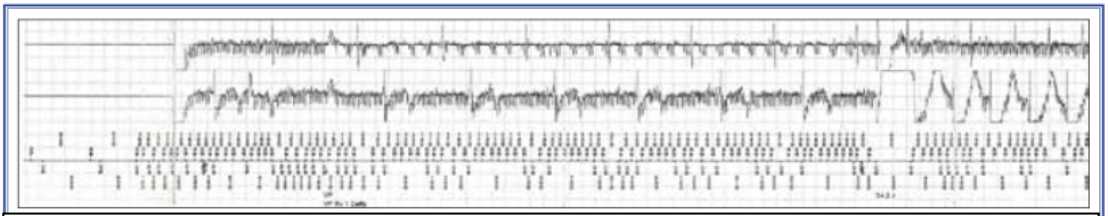

Figure 1. Interferences in both channels during intracardiac recordings are seen. Interferences detected in the ventricular channel are sensed as ventricular fibrillations, and thus ICD delivers defibrillation therapy using 34 joule energy. Upper row: atrial channel; intermediate row: ventricular channel; lower row: reference (index) channel. AR: Heart beats sensed during refractory period in the atrial channel which do not cause generation of any response by ICD; Ab: Atrial beats sensed during the refractory period which do not cause generation of any response by ICD AS: sensing of the atrial beats; VS: sensing of the ventricular beats; FS: sensing of the ventricular fibrillation; CE: completion of the charge time: CD:

DISCUSSION

Despite technological advances, nowadays, ICDs are adversely affected by direct impact of high-energy ionizing radiation, and their resultant electromagnetic interferences (EMI). Generally EMI is a transient phenomenon. Its unfavourable effects on ICD terminate after abolition of EMI. However ionizing radiation causes permanent damage. With the introduction of small, reliable, and

energy-saving CMOS (Complementary Metal Oxide Semiconductor) -which plays an important role especially in memory functions of ICD- into current use, latest generation pacemakers, and linear accelerators have become more sensitive to high-energy gamma waves, electrons, protons, and neutrons emitted by cobalt radiators, linear accelerators, and betatrons. The degree of this sensitivity has been stated to be 5 -10-fold higher for ICDs, when compared with the pacemakers. As a result of exposure to high-energy radiation, negatively charged electrons dissociate from silicon dioxyde layer covering of CMOS circuits. Thus, from many points of the layer with increased positive charge leakage currents are generated. The unfavourable effects of these abnormal electrical currents can induce critical temporary or permanent problems in the detection, and treatment mechanism of ventricular tachyarrhytmias by ICDs.[2-4] These adverse effects of radiotherapy on ICD have been determined in review articles analyzing *in vitro* experimental studies, retrospective clinical investigations involving scarce number of patients, and case reports. Herein, in consideration of our case, we reviewed relevant literature information

In their in vitro experimental investigations, Hurkmans et al,[5] evaluated exogenously delivered shock energies, and battery charge times of 11 ICD devices manufactured by different firms, and also relationship between increasing doses of radiation, and their sensing, and pacing functions using 6MV linear accelerators and radiation doses ranging between 0.5-120 Gy. Four ICDs could attain shock energy values below the programmed shock energy level of 30 joules namely 18-21 joules. In addition to this problem, a decrease in the ventricular sensing threshold of one ICD was recorded. Also two ICDs demonstrated sensing abnormalities, while charge time of one ICD was delayed. In one ICD, all of these problems were encountered. The investigators emphasized that if treatment functions of four ICD devices could have sensed ventricular tachyarrhytmias, then inappropriate shocks would appear. Four devices lost their functions because of complete cessation of stimulant radiation energy output ranging between 0.5, and 1.5 Gy.[5] In another *in vitro* study, Rodriguez et al.[6] applied 6MV energy, and 250 Gy radiation dose on four ICD devices. Prolongation of charge times, and decrease in the capacitance of the ICD batteries were observed with increasing doses of radiation

In vivo experiments related to ICDs have been cited in the literature. Nemec,[7] reported a case with polimorphic ventricular tachycardia caused by asynchronous and rapid ventricular pacing provided by ICD in a patient who had undergone radiotherapy because of lung cancer. A permanent damage in ICD was not reported after this spontaneously resolved episode of

tachyarrhytmia. In this case, very close vicinity of field of radiotherapy to the implantation site of ICD was emphasized.

Gelblum et al .[8] examined 33 patients with ICDs who had undergone radiotherapy including 8 cases with lung cancer. Only in one patient whose ICD gave audible alarm, restoration of factory settings of ICD was determined, and ICD was reprogrammed. Its output energy of 15 MV was reduced to 6 MV, and radiotherapy was maintained. Afterwards any problem related to ICD was not detected. This patient was exposed to total radiation dose of 0.2 Gy. In other patients ICD functioned without any problem. Only 3 of a total of 33 patients ICD was exposed to doses over 2 Gy. Based on these results, unfavourable effects of high-energy radiation on ICD were expressed, and application of lower energy (< 10 MV) was recommended in order to protect ICD from harmful effects of radiation.

Kapa et al.[9] retrospectively examined ICDs of 5 patients who had been on radiotherapy for various types of cancers including one case with pulmonary cancer, and couldn't encounter any evidence of dysfunction. Still, Niehaus et al.[10], and Ferrara et al.[11] examined patients with implanted ICDs for various types of cancers who had undergone radiotherapy (3, and 8 patients, respectively). Sepe et al [12] published a report on a patient with ICD. The investigators could not detect any abnormality in sensing or pacing functions of ICDs exposed to radiation doses below 5 Gy. Sepe et al recommended radiation dose delivery rates of ≤ 300 MU/min for patients with ICD[11]

In addition to aforementioned unfavourable effects of ICD on radiotherapy, prevention of shock therapy, and electrical stimulus generating function of ICD, and problems of surveilance, and programming of ICD have been also reported in the literature.[4,13-15]

CyberKnife® which plays a prominent role especially in the treatment of inoperable non-small cell pulmonary carcinoma, is a stereotactic radiosurgery device which uses a linear accelerator mounted on an image-guided robotic manipulator with a capability of rotating around the patient After precise tracking, and storage of the coordinates of the targeted tumour in the memory of the system, with the aid of markers located inside the tumor, and on the skin surface, radiation beams are focused on the cancerous tissue isosynchronously with respiratory rate of the patient to achieve effective radiotherapy.[16] In our patient even though radiotherapy was focused on the right-sided mass using CyberKnife® system, it created electromagnetic interference with the ICD implanted on the left side. At the time when the radiation beams focused by the rotating robotic arm on the patient pass over the implanted site of ICD battery or electrode, this site is exposed to higher radiation doses. Detection of a single inappropriate shock

wave in every recording of ICD within 13-20 seconds during application of multiple daily radiotherapeutic doses delivered from different angles on separate days in radiotherapy sessions lasting nearly one hour has been associated with electromagnetic interferences generated during this short time period. Artifacts on the ventricular channel because of EMI were sensed as intracardiac potentials. These interferences defined as ventricular fibrillation due to oversensing by ICD, induced inappropriate shocks because of tachyarrhytmia treatment mechanisms of ICD had not been inactivated beforehand.

As seen in the abovementioned studies, radiation tolerance of ICDs manufactured by different firms varies unpredictably. [3] To avoid adverse effects of EMI, and ionizing radiation, before, during, and after termination of radiotherapy, some measures should be taken as for safety of the patient, and the device. The patient should be informed of these measures, and abovementioned potential complications still, in order to evaluate potential unfavourable effects of the therapy on the patient, and ICD, oncologist who will guide the radiotherapy, and cardiologist who monitors the patient, and ICD should be in collaboration. Patients who carry an ICD should refrain from direct application of radiation on the ICD battery, and electrode. If the ICD is directly within the field radiotherapy, the problem can be resolved by changing its site of implantation before, and if not possible, replacement of the ICD should be thought after the procedure. ICD should be at least 3 cm away from the radiation field. The amount of radiation exposure of ICD should be known beforehand. This measurement can be performed using dosimetre or estimated by calculation formulas. [17] Before radiotherapy, safe dose should be determined in collaboration with the firm representatrive in-charge. It has been recommended that radiation dose exposed by ICD should not exceed 1-5 Gy depending on its manufacturer, and model of the device. Radiation dose exposure limit of the ICD of our patient was determined as 5 Gy by the manufacturing firm.[18] Immediately before the procedure, a magnet should be placed over the ICD or ICD should be reprogrammed in order to inactivate ICD's treatment mechanisms of tachyarrhytmias. Thus, ICD will only monitor the patient, and will not activate its treatment mechanism even in case of ventricular tachyarrhytmias. For that reason, during the procedure, patient's heart rhythm should be monitored, and executive representative of the manufacturing firm of the patient's ICD, and the equipment required for cardiopulmonary resuscitation should be readily accessible. If any problem related to ICD arises, a cardiologist should be consulted. ICD should be controlled in detail before, and at weekly intervals during radiotherapy (some authors

suggest after termination of radiotherapy) and at the end of the therapy. These controls should be maintained during the first months after treatment in consideration of cumulative effects of radiation. If functional disorders appear, ICD should be replaced.[3-5,19,20] If all of these safety measures are implemented, then harmful effects of radiation on ICD can be minimized. Besides, development of extremely painful inappropriate shocks will be prevented, and battery life of ICD will be prolonged.

In our community, increasing number of patients with ICD require radiotherapy. Based on our case report, and literature information, we thought that preparation of a guideline will be appropriate which explains the points that should be taken into consideration before (preparatory phase) , during, and following radiotherapy Therefore, prospective clinical studies targeting short-and long-term unfavourable effects of radiotherapy on ICDs should be conducted in colloboration with the department of radiology.

Conflict of interest: None declared

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Key words: Equipment failure; defibrillators, implantable; neoplasm/radiotherapy; radiotherapy dose/standards; stereotactic radiosurgery; practice guideline