

## Aleksandra E. Danieluk<sup>1</sup>, Joanna H. Mańdziuk<sup>1</sup>, Marek Z. Wojtukiewicz<sup>2</sup>, Ewa Sierko<sup>2</sup>

<sup>1</sup>Students' Scientific Association affiliated with the Department of Oncology, Medical University of Białystok, Poland

<sup>2</sup>Department of Oncology, Medical University of Białystok, Poland, Comprehensive Cancer Centre in Białystok, Poland

# Heart metastasis in the course of melanoma

### Address for correspondence:

Ewa Sierko, MD, PhD

Klinika Onkologii

Uniwersytet Medyczny w Białymstoku

Białostockie Centrum Onkologii

ul. Ogrodowa 12, 15-027 Białystok

Phone: +48 602 33 70 20

e-mail: ewa.sierko@iq.pl

Oncology in Clinical Practice  
 2016, Vol. 12, No. 3, 97–101  
 Copyright © 2016 Via Medica  
 ISSN 2450–1654

### ABSTRACT

**Introduction.** The majority of melanoma patients develop distant metastases, the most common locations being the liver, the bones, and the brain. Moreover, it is a neoplasm that involves the heart in an unusually high number of cases compared to other neoplasms. However, there is a wide disproportion between metastasis rate to the heart in autopsy studies and antemortem diagnoses.

**Case report.** A 78-year-old female patient presented with a nevus in the lumbar area, diagnosed as malignant melanoma. Six months after the procedure, bilateral metastases in inguinal lymph nodes and recrudescence in the post-procedural scar were surgically removed. Radiotherapy covering the area of affected lymph nodes was carried out. During the next two months, regional recurrence of melanoma and metastases to the lungs and liver were observed. Due to the cancer progression the patient underwent three courses of DTIC chemotherapy; however, new lesions in skin and subcutaneous tissue were discovered, so second-line chemotherapy with ipilimumab was commenced. An echocardiography performed at the time showed no abnormalities. Three months later an ECG showed negative T wave in V2–V4, and CT revealed progression in size of the existing lesions and a new lesion located in the heart, infiltrating the interventricular septum. The patient was referred to hospice care.

**Conclusions.** Since heart metastases are rarely diagnosed antemortem, raising awareness of possible cardiac involvement in the course of melanoma progression among physicians and radiologists is vital. It can lead to more diagnoses of cardiac metastases and therefore provide optimal care for the patients.

**Key words:** melanoma, heart metastasis, rare site of metastasis

Oncol Clin Pract 2016; 12, 3: 97–101

### Introduction

Melanoma, a skin cancer that derives from melanocytes, accounts for 2% of skin cancer cases [1]. Melanoma can be found anywhere on the skin, but it is most likely to appear on the trunk in men and legs in women. It is a highly metastatic cancer, and the majority of the patients develop distant metastases as a result of cancer progression. The most common localisations of the metastases are: the liver, bones, and the brain [2]. Interestingly, it is also a neoplasm which may metastasise to the heart; however, this location of metastatic foci is rarely diagnosed antemortem due to the lack of symptoms in the vast majority of patients. Based on the stage of the disease, therapeutic options include surgery alone (early-staged melano-

mas) or combined with radiotherapy, immunotherapy, chemotherapy, or targeted therapy at advanced stages of the disease.

Below, a case of a patient with systemic dissemination of the melanoma including rare cardiac metastasis is presented.

### Case report

A 78-year-old female patient presented with an irregularly coloured nevus in the lumbar area, which was excised. Pathological examination revealed malignant melanoma with ulceration, sized 1.2 × 1 cm, staged Clark III. The thickness of infiltration was 3 mm, satellite lesions and inflammatory response were absent.

Negative margin was achieved. The lesion was HMB-45 positive and Melan-A negative.

During follow-up, six months after the surgical procedure, bilateral metastases in the inguinal lymph nodes, as well as recurrent disease in the post-surgical scar, were noted.

The metastatic inguinal lymph nodes and the post-surgical scar were surgically removed. Pathological examination revealed two satellite melanoma lesions (8 mm, 4 mm) in post-surgical scar region and metastases in bilateral inguinal lymph nodes (2/6 left, 1/5 right). Electrocardiography (ECG) performed at that time showed left axis deviation and post-ischaemic changes (Fig. 1A).

Four months later, abdomen ultrasonography revealed a hypoechogenic mass sized  $26 \times 14$  mm, in the proximity of the left iliac vessels. Megavoltage 6 MV photon beam IMRT radiotherapy (54 Gy/1.8 Gy/30 fractions) to the bilateral internal and external iliac, inguinal, and obturator lymph nodes was delivered. The dose was increased to the macroscopic tumour bed (by 6 Gy/3 fractions).

During radiotherapy to the lymph nodes, a new red nodule in the post-surgical scar in the lumbar area appeared. The nodule in the lumbar area increased in size over time and was histopathologically proven to be recurrence of melanoma. Other lesions were gradually noted in the same area. Approximately four months after radiotherapy cessation, the post-operative scar in the lumbar area was removed once again, along with the three nodules. Histopathological report indicated malignant melanoma cells in all of them. Adjuvant radiotherapy with photon beam (X6MV) to the dose of 50 Gy/2.5 Gy/20 fractions was commenced to the area of the scar in the lumbar region.

Approximately one month after the radiotherapy to the lumbar scar bed, abdomen ultrasonography and a chest and abdomen CT showed multiple lung and liver metastases, as well as recurrent metastases in the left external iliac/deep inguinal lymph nodes and thickened wall of the sigmoid colon. Colonoscopy revealed adenocarcinoma in the sigmoid and the patient underwent laparoscopic partial rectosigmoid resection. Histopathology report indicated adenocarcinoma G2, pT2N0.

Two months later, chest and abdomen CT revealed an increase in the number and size of the lung and liver metastases, the occurrence of nodules in the thyroid gland, as well as enlargement of the lymph nodes: para-aortic, hepatic hilum, iliac, obturator, left external iliac/deep inguinal, and right inguinal. An ECG performed at that time showed sinus rhythm at 75 bpm with left axis deviation and post-ischaemic changes (Fig. 1B); no abnormalities were seen on echocardiography performed two weeks later.

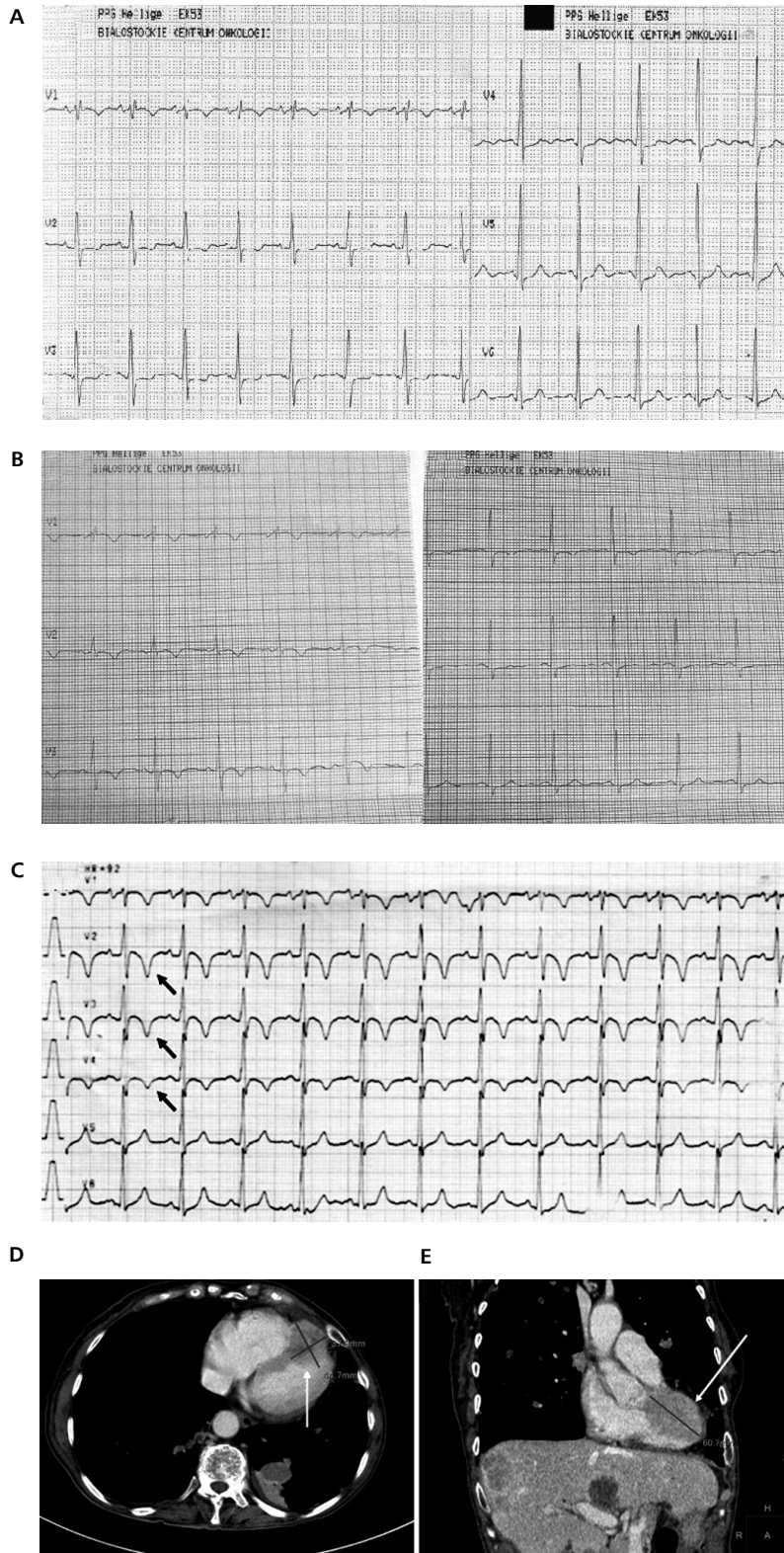
The patient underwent three courses of DTIC chemotherapy (375 mg of DTIC, day 1 to 5), administered

once a month. She did not receive a fourth course because of progression of the disease. After first-line chemotherapy cessation, new lesions in skin and subcutaneous tissue were discovered, while an echocardiography performed at the same time again showed no abnormalities.

A week later, second-line systemic treatment with ipilimumab was started. On admission, apart from the previously existing lesions, the patient showed lymphatic oedema of the left leg and a red nodule on the skin of the abdomen in the anterior axillary line. The patient received four courses of treatment with ipilimumab, once every three weeks. A week after the fourth course, the patient was admitted to the hospital due to malaise, emesis, and constipation. Dyselectrolytaemia was noted and symptomatic treatment was administered; the patient was released after a week. In the following days the patient presented with fever with no other complaints. A month later a CT showed progression in size of the existing lesions and new enlarged axillary left and mediastinal lymph nodes. A nodular mass was found in the uterus and lytic metastases were observed in the third lumbar vertebra. Unexpectedly, there was also a new lesion located in the heart, 43 mm in diameter, infiltrating the interventricular septum (Figs. 1D and 1E). Interestingly, the patient reported no symptoms associated with the cardiovascular system, and on auscultation normal heart sounds with rhythmic heart rate of 76 beats per minute were noted. At the time, blood morphology showed the following results: red blood cell count:  $3.35 \text{ M}/\mu\text{L}$ , haematocrit 30.91, haemoglobin:  $10.45 \text{ g/dL}$ . Laboratory tests revealed normal electrolyte concentration, whereas ECG showed inverted T wave in V2–V4 (Fig. 1C). Although cardiovascular symptoms were absent, the patient's general condition deteriorated in the course of disease progression. In addition, the patient had already been treated with two lines of chemotherapy, the first one being dacarbazine, which has been shown to have the highest survival benefit among cytotoxic therapy [3], and ipilimumab, which is a novel form of molecular targeted therapy and was documented to prolong survival in the group of patients [4]. Other forms of treatment, such as combination chemotherapy, immunotherapy, and biochemotherapy have not been proven to have a survival benefit [3] and given the deterioration of the patient's general state were not considered. For these reasons the patient was referred to hospice care.

## Discussion

Cardiac metastases are rarely present in the population of cancer patients. Interestingly, malignant melanoma is a cancer that involves the heart in an



**Figure 1.** ECG showing post-ischaemic changes (incomplete right bundle branch block) performed at the beginning of the illness (A), during progression of the disease (3 months after radiation therapy to the lumbar scar) (B) and after discovering heart metastasis: reversed T wave in V2–V4 leads (arrows) (C). Chest computed tomography images of a melanoma patient with heart metastasis: a mass infiltrating the interventricular septum was identified (arrows) — axial (D) and frontal (E) images

unusually high number of cases compared to the other neoplasms [5]. However, there is a wide disproportion between metastasis rate to the heart in autopsy studies of melanoma and the number of cases diagnosed during the course of disease progression [6]. Of note, more than half of the patients with systemic dissemination of melanoma have metastases to the heart [6, 7], but since only approximately 10% of these patients present with specific symptoms, less than 1% of them are diagnosed antemortem [6]. Since cardiac metastases usually occur in the late stage of the disseminated disease [5], clinical signs of heart involvement can also be masked by other visceral metastases that give more clear symptoms, resulting in cardiac metastases being overlooked. The non-specific symptoms that should draw clinician's attention to the possibility of occurrence of cardiac metastases are unexplained fatigue, fever, arrhythmia, pericardial effusion, transient ischaemic attack, or heart failure [5, 6]. It is important to remember that cardiac metastases may also cause no evident symptoms, and are rarely the first manifestation of the disseminated disease [6]. Two-dimensional echocardiography is a method of choice to detect cardiac involvement as a noninvasive and inexpensive test. However, transoesophageal echocardiography is preferred to transthoracic echocardiography, especially when lesions in the right atrium are suspected or a surgical intervention is planned [8]. CT and MRI may also provide useful information, and PET ensures high sensitivity and specificity, enabling detection of the metastases at a relatively early stage [7]. A differential diagnosis of possible causes of masses in the heart should be carried out even in the case of a strong suspicion of melanoma metastases. The possibility of cardiac thrombus should be excluded, especially since cancer patients are at a higher than average risk of thrombosis. Diagnostic imaging can differentiate these malignancies, however there are certain difficulties which need to be taken into account. In MRI, melanoma is expected to be hyperintense in T1-weighted images and hypointense in T2-weighted images; unfortunately, many of the images of metastatic melanoma are not typical [9]. Furthermore, the signal intensity of a thrombus can vary depending on its age [10]. The appearance after contrast administration should be helpful in diagnosis, since a thrombus is not likely to enhance, while a metastasis usually does [10]. Early recognition of cardiac metastases is vital for the patient's outcome. The feasibility of the surgical treatment depends on both anatomic location and the extent of invasion of the tumour [7]. Both complete resection and conservative surgery may be beneficial for the patient's wellbeing [6]. Other methods of treatment involve systemic treatment with cytotoxic drugs, biotherapy, radiotherapy, and immunotherapy [7]. In patients with metastatic melanoma, radiotherapy is considered to be a simple

and cost-effective therapeutic option. Its impact varies depending on tumour volume, total dose, and dose per fraction [11].

In the presented case, the patient reported no symptoms specific to cardiac metastases. The only indications that the disease might have spread to the heart were fever and general malaise presented by the patient a month prior to the diagnosis of cardiac metastasis and an inverted T wave in ECG in V2–V4 leads. T-wave inversion is the most common new ECG change in patients with cardiac metastases. New ECG change in cancer patients with no cardiac symptoms suggestive of ischaemia should always draw the clinician's attention to the possibility of heart metastases as patients with normal ECG are unlikely to have them [12]. Thus, ECG may be recommended as a method of choice to monitor heart involvement in the course of disease progression in cancer patients. The method that allowed the diagnosis in this case was CT of the chest. Of note, previous transthoracic echocardiography performed four months earlier showed no abnormalities, and no lesions in the heart were present on a chest CT. Since the patient already presented the late stage of disseminated disease, along with no specific symptoms caused by the heart metastasis, surgical intervention or radiotherapy was infeasible. Apart from that, notwithstanding the detection of cardiac metastases, the patient was treated with ipilimumab, which at that time was considered the first-line treatment for patients with inoperable melanoma cardiac metastases [6].

## Conclusions

Raising awareness of possible cardiac involvement in the course of melanoma progression among physicians, cardiologists, and radiologists is crucial because it can lead to more antemortem diagnoses of cardiac metastases and, therefore, to providing optimal care for the patients.

## References

1. Holm RP. Skin cancer prevention and screening. *S D Med.* 2015; Spec No: 75–77, 79–81.
2. Tas F. Metastatic behavior in melanoma: timing, pattern, survival, and influencing factors. *J Oncol.* 2012; 2012: 647–684.
3. Bhatia S, Tykodi, SS, Thompson JA. Treatment of metastatic melanoma: an overview. *oncology (Williston Park, NY).* 2009; 23: 488–496.
4. Fellner, C. Ipilimumab (Yervoy) Prolongs survival in advanced melanoma: serious side effects and a hefty price tag may limit its use. *Pharmacy and Therapeutics* 2012; 37: 503–530.
5. Geredeli C, Boruban MC, Poyraz N, Artac M, Aribas A, Koral L. Biatrial cardiac metastases in a patient with uterine cervix malignant melanoma. *Case Reports in Cardiology* 2015; 2015: 958756.
6. Lee EY, Choi J-O, Park HN et al. Malignant melanoma of unknown primary origin presenting as cardiac metastasis. *Korean Circulation Journal* 2012; 42: 278–280.

7. Onan B, Onan IS, Polat B. Surgical resection of solitary metastasis of malignant melanoma to the right atrium. *Tex Heart Inst J* 2010; 37: 598–601.
8. Judge JM, Tillou, JD, Slingluff CL, Kern JA, Kron IL, Weiss GR. Surgical management of the patient with metastatic melanoma to the heart. *J Card Surg* 2013; 28: 124–128.
9. Villa A, Eshja E, Dallavalle S, Bassi EM, Turco, A. Cardiac metastases of melanoma as first manifestation of the disease. *Journal of Radiology Case Reports* 2014; 8: 8–15.
10. Chiles C, Woodard PK, Gutierrez FR, Link KM. Metastatic involvement of the heart and pericardium: CT and MR imaging. *Radiographics* 2001; 21: 439–449.
11. Geara FB, Ang KK. Radiation therapy for malignant melanoma. *Surg Clin North Am* 1996; 76: 1383–1398.
12. Cates CU, Virmani, R, Vaughn WK, Robertson RM. Electrocardiographic markers of cardiac metastasis. *American Heart Journal* 1986; 112: 1297–1303.