

(CASE REPORT)



Description of patient with telangiectasis and palmar erythema without any structural liver changes or changes of liver laboratory parameters due to treatment of Her -2 -positive breast cancer with Ado-Trastuzumab-Emtansine

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Abstract

Ado- Trastuzumab-Emtansine is approved by EMA and FDA for treatment of HER-2-positive metastatic breast cancer. The drug combines the cytotoxic activity of emtansine with trastuzumab [1,2,3]. Here we are describing 50- year old woman with 3-ple positive left breast cancer with metastasis to left axillary lymph nodes treated with the drug. The patient had normal liver and spleen structure on CT of the abdomen with I.V. contrast, along with a normal liver function test. However she did have a mild elevation of her indirect bilirubin after the initiation of the drug. Despite the normal liver and spleen and absence of Cirrhosis the patient developed drug induced spider angiomas on the upper chest, upper back, shoulders along with palmar erythema. The association of the Ado-Trastuzumab-Emtansine with spider angiomas and palmar erythema in those with normal liver and spleen function, with only a mild elevation of indirect bilirubin is discussed in the article [1].

Keywords: Spider angiomas; Palmar erythema; Liver; spleen; Indirect bilirubin; Ado-trastuzumab-emtansine

1. Case report

50- year old female came to our clinic, for scheduling of capsule endoscopy procedure per her oncologist referral. Her other complaint included some reddish type changes on her upper chest, shoulders, upper back along with some redness of her palms that was new. She had past medical history of left invasive breast ductal cancer 0.8cm/0.3 cm with metastasis to the one left axillary lymph node- 0.5 cm. The breast cancer was 3-ple positive- Estrogen and progesterone receptor positive and HER-2- positive, diagnosed in 2020.

In August the same year she underwent bilateral mastectomy and left axillary lymph node dissection. The patient was found to have left invasive ductal cancer (0.8cm/0.3cm) with metastasis to the one left axillary lymph node(0.5 cm) and right breast intraductal benign papilloma. Because of the metastatic nature of her cancer and it being triple positive, her oncologist started treating her with ado-trastuzumab-emtansine every 3- weeks in 8/2020.

Post some treatments the patient noticed the development of small reddish lesions on upper chest, shoulders and upper back and some palm redness.

On our physical examination in the clinic she had multiple blanching spider angiomas on the upper chest, back and shoulders as well as palmar erythema. Dermoscopy image of one of the lesions is shown on figure 1.

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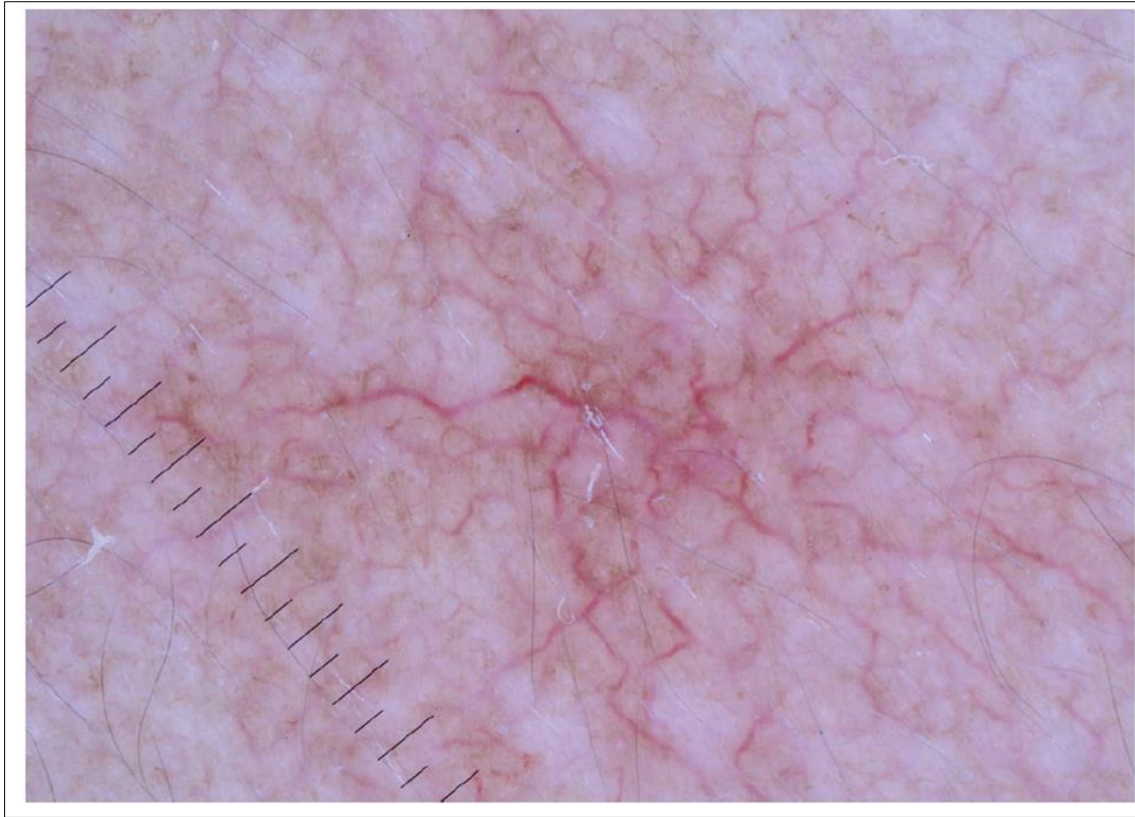


Figure 1 Dermoscopy image of one of spider angiomas lesions

Her abdomen also had some small non blanching cherry angiomas related to her age which she had before starting Chemotherapy. She also had bilateral xanthelasmas on the upper eye lids which she mentioned were present for many years. The remaining of her physical examination was normal besides the scars from the bilateral mastectomy and left axillary lymph node dissection. No splenomegaly or hepatomegaly was appreciated.

The laboratory studies performed 2- months ago in 5/2021 showed normal PT INR- 1.0, normal- basic metabolic panel, AST- 11 IU/L-normal, ALT-30IU/L-normal, albumin -4.1 g/l-normal, Alkaline phosphatase- 89 U/L-normal and total bilirubin was mildly elevated-1.7 mg/dl. The direct bilirubin was normal-0.3 mg/dl with elevated indirect bilirubin. Her total and indirect bilirubin before starting chemotherapy were normal. Her Urinalysis was negative and ECHO of her heart significant for Grade 1 Diastolic dysfunction.

Her CBC showed mild normocytic anemia – Hemoglobin- 11.1 g/dl, Hematocrit-33.6 g/dl WBC were normal- 7.600 cells/mm³ and platelets were normal- 167,000 cells/mm³. She had an EGD done that was suggestive of mild gastritis with H. Pylori being negative.

On her CT of the abdomen- Liver and spleen were completely normal but gallstones were found; she also had some thickening of the urinary bladder mucosa suggestive of cystitis.

Upon our evaluation she sent the patient to lab for a lipid panel, due to the xanthelasmas on the upper eyelid's.

Based on the data we had we made a diagnosis of spider angiomas upper chest and back as well as shoulders and palmar erythema related to Ado-Trastuzumab-Emtansine. We did not find any signs of liver disease – laboratory or imaging to suggest advance liver problem. The mild elevation of the indirect bilirubin might have been related also to chemotherapy although mild Gilbert's disease was also possible. We had only one bilirubin value before the start of chemotherapy. The patient was advised on general skin care on discharge from the clinic.

2. Discussion

Ado-Trastuzumab- Emtansin/T-DM1 is an antibody-drug conjugate that combines the antitumor properties of trastuzumab against HER-2- with the cytotoxic activity of emtansine, a microtubule-inhibitory agent (2,3). Ado-Trastuzumab- Emtansin was first approved by the FDA after results of the EMILIA, a randomized international phase III clinical trial which compared Ado-Trastuzumab- Emtansin monotherapy versus lapatinib and capecitabine in 991 women with HER-2-positive advanced or metastatic Breast Cancer who had been previously treated with trastuzumab and a taxane. T-DM1 showed better progression-free survival as well as better overall survival and safety (3). And most importantly it was better tolerated by the patients. The main adverse effects reported were fatigue, nausea, diarrhea, elevated transaminases, anemia and thrombocytopenia with secondary hemorrhage. Thrombocytopenia and elevated serum concentrations of liver enzymes were the most commonly reported grade 3 or 4 events.

Recently, we have seen accumulation of more reports regarding cutaneous and mucosal telangiectasias. Sibaud *et al* described the first series of mucocutaneous telangiectasia in five women under T-DM1 treatment in 2014[1]. All of them developed grade I transaminitis and three referred history of mild/limited gingival bleeding and/or epistaxis. Thrombocytopenia from grade 1 to 3 was only registered in two patients. Asymptomatic telangiectasias were developed between 2.5 and 14 months after T-DM1 was initiated. Since transaminitis is one of the major side effects of T-DM1 and spider nevi are also seen in other hepatic diseases, they postulate that liver injury may play a role on its development. They also try to relate the mechanism of development of telangiectasia in hereditary hemorrhagic telangiectasia (HHT) to disruption of cytoskeletal microtubules with the cytotoxic activity of emtansine [1,4]. In addition, a case of skin telangiectasias and pulmonary arterial hypertension (PAH) was described by Kwon *et al*. In their article, they propose that some dysfunction in ALK-1 (activin receptor-like kinase) may explain both mucocutaneous telangiectasia and PAH, since ALK-1 mutations have been found to be related to PAH in patients with HHT [5].

Herein, we describe a new case of skin telangiectasia or spider nevi as well as palmar erythema related to T-DM1 treatment. Because of mild normocytic anemia the oncologist referred the patient to us for capsule endoscopy referral [6,7]. The oncologist wanted to make sure that there were no telangiectatic changes throughout the GI tract to explain the anemia although the patient never complained of melena or hematochezia. Her EGD in result did not show any telangiectatic changes in the upper Gastrointestinal tract.

We described this case to alert the physicians that the spider angiomas and palmar erythema can be side effect of the Ado-Trastuzumab- Emtansin unrelated to liver damage. There are reports in which similar skin changes were found in patients due to liver injury related to the drug which was not the case with our patient [8]. The liver function tests and the liver structure were normal in our patient. Also mild elevation of indirect bilirubin was probably also related to the chemotherapeutic drug-T- DM-1.

Conclusion: We described a rare case of telangiectasis and palmar erythema due to Ado- Trastuzumab -Emtansin in patient with Her-2- positive breast cancer. Although the major side effect of the drug is hepatotoxicity in our case the liver test for structure and function were normal. This contributes to the physician knowledge of direct vascular effect of the Ado- Trastuzumab-Emtansin mimicking patients with liver diseases and will benefit the society of physicians knowing about this rare side effect.

Compliance with ethical standards

Acknowledgments

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Disclosure of conflict of interest

The authors have declared no conflicts of interest.

Statement of informed consent

Informed consent was obtained from all participants in the above case report- Description of patient with telangiectasis and palmar erythema without any structural liver changes or changes of liver laboratory parameters due to treatment of Her -2 -positive breast cancer with Ado-Trastuzumab-Emtansine.

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