



Trastuzumab induced cardiomyopathy with cerebellar stroke: Double Trouble

Sourav Chaturvedi¹✉, Amrutha Garikapati¹, Iftikar Ansari¹, Charan Bagga¹, Sunil Kumar²

¹Post graduate Resident, Department of medicine, Jawahar Lal Nehru Medical College, Datta Meghe Institute of Medical Sciences (Deemed to be University), Wardha, Maharashtra, India

²Professor, Department of medicine, Jawahar Lal Nehru Medical College, Datta Meghe Institute of Medical Sciences (Deemed to be University), Wardha, Maharashtra, India

✉Corresponding author

Post graduate Resident, Department of medicine, Jawahar Lal Nehru Medical College, Datta Meghe Institute of Medical Sciences (Deemed to be University), Wardha, Maharashtra, India

Email: sunilkumarmed@gmail.com / Souravchaturvedi39@gmail.com

Article History

Received: 11 May 2020

Reviewed: 12/May/2020 to 15/June/2020

Accepted: 15 June 2020

E-publication: 20 June 2020

P-Publication: July - August 2020

Citation

Sourav Chaturvedi, Amrutha Garikapati, Iftikar Ansari, Charan Bagga, Sunil Kumar. Trastuzumab induced cardiomyopathy with cerebellar stroke: Double Trouble. *Medical Science*, 2020, 24(104), 2424-2427

Publication License



This work is licensed under a Creative Commons Attribution 4.0 International License.

General Note



Article is recommended to print as color digital version in recycled paper.

ABSTRACT

Trastuzumab is routinely used monoclonal antibody in the treatment of several cancers with high effectiveness, but its use is associated with cardiac toxicity which usually responds to cessation of the drug therapy. We present an unusual case in 40 year old

female being treated for breast carcinoma with trastuzumab developed acute cardiac toxicity in form of cardiomyopathy without atrial fibrillation, who developed stroke.

Keywords: Trastuzumab, Toxicity, Cardiomyopathy, Cerebellar stroke

1. INTRODUCTION

Trastuzumab is a monoclonal antibody used for both early and advanced breast cancer in individuals whose tumours overexpress the human epidermal growth factor receptor 2 (HER2) proteins (Slamon et al., 2011). It significantly improves both disease-free survival and overall survival among such patients (Keefe, 2002). According to Analysis of the Surveillance, Epidemiology, and End Results (SEER) Medicare-linked database, cardiotoxicity as heart failure and cardiomyopathy has been reported to occur with trastuzumab. When administered alone it was 4% and in combination with antineoplastic agents, particularly anthracyclines, it was 27% (Chen et al., 2012; Sylvana et al., 2013).

No case has been reported in literature regarding cardiomyopathy and cerebellar stroke in combination with trastuzumab. We report a case of trastuzumab induced cardiomyopathy, which was also associated with cerebellar stroke in a 40 -years-old female with HER-2 positive cancer of the Left Breast.

2. CASE REPORT

A 40-year-old female presented to medicine department of this hospital with severe headache, slurring of speech, and weakness of left half of the body. She also had history of breathlessness since last one week. She denied any history of cardiac illness or any ischemic heart disease in the past. She was diagnosed as case of left breast carcinoma positive for HER2, and taking treatment as Trastuzumab (Herceptin) every three weeks. After her third trastuzumab infusion, she developed sudden onset of weakness in left half of body, giddiness, severe headache and vomiting. She had been operated for her left breast as total mastectomy 2 month back. On examination, patient was conscious & oriented, power in all four limbs was normal; reflexes in left upper & lower limb were more than normal with left plantar extensor. Her cerebellar examination was positive for nystagmus, knee heel test & dysdia dochokinesia. She was normotensive and nondiabetic. On laboratory investigation, her hemoglobin was 9.6 mg% and total leukocyte count of 7000/cm with 70% polymorphs, other parameters were normal. Her enzyme-linked immunosorbent assay for human immunodeficiency virus was negative. Her random blood sugar was 120 mg/dl, with blood pressure at the time of admission of 150/90 millimeter of mercury in right upper limb supine position. Her thyroid profile was normal.

In view of neurological manifestation, she underwent Magnetic resonance imaging of brain which revealed acute infarct in left cerebellar hemisphere (figure 1). On evaluation of the cerebellar stroke, she underwent cardiac evaluation in the form of electrocardiography which showed T inversion in all precordial leads. Her 2 D Echocardiography revealed cardiomyopathy with ejection fraction of 45% (figure 2).

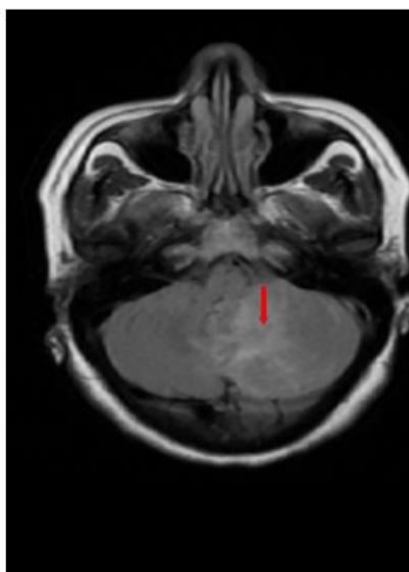


Figure 1 Magnetic resonance imaging of brain revealed acute infarct in left cerebellar hemisphere (Red arrow)

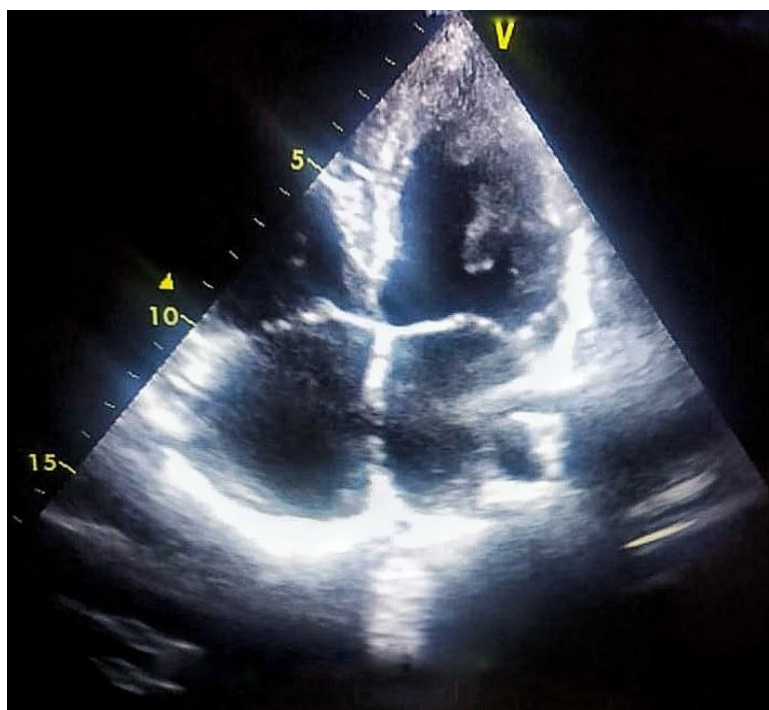


Figure 2 Two-dimensional echocardiographic view showing left and right atrial as well as right ventricle enlargement suggestive of cardiomyopathy (apical 4-chamber view).

Her antinuclear antibody, antidouble-stranded DNA and antiphospholipid antibody were absent. She was put on anticoagulant treatment with warfarin 4 mg per day and trastuzumab treatments were stopped. Patient was kept on regular follow up with an interval of 4 weeks with regular international normalised ration between 1.5-2. Her follow up 2D echocardiography after one month showed left ventricular dysfunction still persisted gradually.

3. DISCUSSION

Trastuzumab, a monoclonal antibody has revolutionised the medico-oncological treatment of breast cancer (both early and advanced). This drug is useful in patients whose tumours overexpress the human epidermal growth factor receptor 2 (HER2) proteins (Slamon et al., 2011). Although its overexpression has poor prognosis, it significantly improves both disease-free survival and overall survival among patients with breast cancer. Most common side effect reported for this drug is cardiotoxicity in the form of cardiomyopathy and heart failure, still its pathogenesis is not clear (Sylvana et al., 2013). More likely mechanism may be due to blocked proto-oncogene ErbB2 signalling pathways, which encodes a receptor tyrosine kinase leading to cardiac injury. Studies have shown decreased expression of ErbB receptors in patients with heart failure, favouring altered ErbB signalling in its pathogenesis (Chen et al., 2012; Sylvana Hidalgo et al., 2013).

Our patient developed cardiomyopathy as left atrial enlargement which later presented as acute cerebellar stroke; even she had no atrial fibrillation or any cardiac illness previously. It is possible that an asymptomatic paroxysmal episode of atrial fibrillation had occurred in this patients leading to stroke and systemic embolic events. In such patients clinically diagnosis becomes difficult due to paroxysmal and asymptomatic nature of atrial fibrillation. In patients having atrial fibrillation with or without heart disease, stroke and systemic embolic events showed an incidence of 0.8% per year (Flaker et al., 2005). Few studies had reported dilated left atria as an independent determinant of embolic events (Flaker et al., 2005; Hoit, 2014).

4. CONCLUSION

This case concludes about increasing awareness among physicians regarding trastuzumab associated cardiotoxicity without documented atrial fibrillation which may present only with brain stroke.

Informed Consent

Patients inform consent was taken and signed by Patient before writing case report

Funding: This research received no external funding.

Conflicts of Interest: The authors declare no conflict of interest.

REFERENCE

1. Chen J, J. B. Long, A. Hurria, C. Owusu, R. M. Steingart, and C. P. Gross. Incidence of heart failure or cardiomyopathy after adjuvant trastuzumab therapy for breast cancer. *American College of Cardiology* 2012; 60 (24) :2504–2512.
2. Flaker GC, Belew K, Beckman K, Vidaillet H, Kron J, Safford R, et al; AFFIRM Investigators. Asymptomatic atrial fibrillation: demographic features and prognostic information from the Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) study. *Am Heart J*. 2005;149:657–663.
3. Hoit BD. Left atrial size and function: role in prognosis. *J Am Coll Cardiol*. 2014;63:493–505.
4. Keefe D. L, Trastuzumab-associated cardiotoxicity. *Cancer* 2002; 95 (7) :1592–1600.
5. Slamon D, W. Eiermann, N. Robert et al., Adjuvant trastuzumab in HER2-positive breast cancer. *New England Journal of Medicine* 2011; 365: 1273–1283.
6. Sylvana Hidalgo, Carol A. Albright, and Gretchen L.Wells. A Case of Trastuzumab-Associated Cardiomyopathy Presenting as an Acute Coronary Syndrome: Acute Trastuzumab Cardiotoxicity. *Case Reports in Cardiology* 2013; Article ID 473979.