

Trastuzumab/Anthracycline Induced Cardiomyopathy

Missed Opportunity For Early Diagnosis and Treatment



Breast Cancer Case Study

Patient CS, 71F, Retired TAB owner, fit and active, supportive family, husband and 4 children

May 2017 - Self-detected left breast lump

- Core biopsy L breast mass and axillary node: G3 IDC, ER neg, PR1-2+ in 20%, HER2 ISH
- positive, infiltrating ductal carcinoma, Stage 4 CT CAP: Multiple (about 7) lung mets, largest 20mm in RUL
- WBBS: No bony mets

ECOG 0

Treatment Plan AC -THP

(Doxorubicin +cyclophosphamide [AC] Q3W x 4 cycles then Paclitaxel D1,8,15 + trastuzumab and pertuzumab [THP] Q3W)

17 May 17 **Baseline ECHO**

	ECHO FINDINGS Sinus rhythm. Technically diffic Normal right and left ventricular	size, wa	Il thickness and s	ystolic function. Normal rig	ht and r	mild left	Mitral valve E velocity	0.7	(0.8-1.3m/sec)	Mitral valve PHT		(ms)
	atrial enlargement. Left ventricu	ılar diast	olic function is imp	paired.			Mitral valve A velocity	1.0	(m/sec)	MV area	>3	(>3
	Normal trileaflet aortic valve. N with trivial regurgitation. Norma						cm ²) MV deceleration time (70-100 ms)	186	(ms)	IVRT		
	fluid. No intracardiac masses.						MV A duration		(ms)	E/A ratio	0.7	
	MEASUREMENTS LV diastolic diameter	44	(35-56 mm)	Aortic root	29	(20-37	LVOT peak m/sec)	0.9	(< 1.2 m/sec)	RVOT peak velocity	0.9	(< 1.2
	mm) LV systolic diameter mm)	30	(mm)	Left atrium	40	(19-40	Ao root peak ms)	1.2	(< 1.8 m/sec)	PA acceleration time		(> 120
	LV septal thickness	8	(7-11 mm)	LA area	25	cm ²	Mn Ao valve gradient m/sec)	< 5	(< 5 mmHg)	TR Velocity	2.6	(< 2.5
	LV post wall thickness Fractional shortening	8	(7-11 mm) %	RA area Asc ao	19	cm ² (mm)	Pk Ao valve gradient 30mmHg)		(mmHg)	Systolic PAP	31	(<
\rightarrow	LV ejection fraction Biplane EF	59	%	RVIDd Tapse	29	(mm) (mm)	AV area (mm/Hq)		cm ²	RAP	3	
	Pulmonary vein S wave (m/sec)		(m/sec)	TVI E'	0.06		(iiiii)			IVC collapse	Norma	al .
	Pulmonary vein D wave		(m/sec)	E/E'	11	(< 10)	CONCLUSION					
	Pulm. vein A reversal (m/sec)		(m/sec)	RV 'S	0.13		 Good right and left ventricu Mild left atrial enlargement Left atrial enlargement 		lic function.			
	Pulm. vein A rev.duration		(ms)				Lett atrial enlargement					

19 May 2017 Commenced C1 AC at Macquarie University Hospital (MUH)

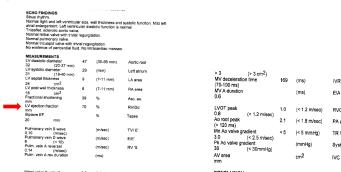
July 2017 Completed 4 cycles AC as planned

1 Aug 17 Restaging CT: Excellent response in breast mass and pulmonary nodules,

but incidental finding of diverticulitis with microperforation on CT

21 Aug 2017 Transfer to another hospital and commenced THP

26 Aug 17



31 Aug 2017 Multiple PEs on CTPA; commenced warfarin

Sept 2017 Noted to be lethargic, unsteady at Day Oncology Unit

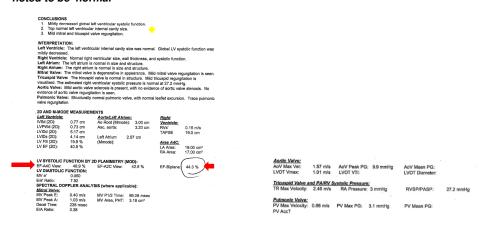
Oct 2017 Noted to be generally unwell; slightly breathless, had a fall at home

paclitaxel ceased, traztusumab and pertuzumab continued.

9 Oct 17



noted to be 'normal



TWO more doses of traztusumab and pertuzumab received.

Nov 2017 Increasing frailty, spastic gait, areflexic (absent reflexes). LFTs rising. Admitted MUH 23 Nov 17 to exclude spinal cord compression

20 Nov 17 CT CAP (CT - Chest Abdomen Pelvis): Ongoing good partial response.



Other Investigations

- MRI brain nothing abnormal detected. Ultrasound abdomen: Mild hepatomegaly, diffuse alteration in echo architecture suggestive of steatosis (fatty change) but no focal lesion seen

27 Nov 17 ECHO

Patient: Referred by: Sonographer: Indication: On		Date of birth: 25/06/1945 Date of study: 27/11/2017 Rhythm: Sinus rhythm. CC Doctor: Image Quality: Fair.	Height (cm): 165 Weight (kg): 73 BSA (m2): 1.80 BMI (kg/m2): 27 Resting BP: /					
Measurement		Dimensions	Normal Adult Range					
	meter 2D (cm):	5.8	M<5.9, F<5.3					
LV Systolic Dia		4.8	M<1.1, F<1.0					
Septal thicknes		0.6						
	nickness 2D (cm):	0.9	M<1.1, F<1.0					
RWT:		0.32	< 0.42					
Indexed LV Ma		97	M<103, F<89					
	olume (cm2 / ml/m2):	34 / 55	<20 cm2 / <32mL/m2					
RA Area (cm2):		22	<18cm2					
thickness. Sev		ated left ventricle (LVEDDV - 7 vere global systolic dysfunction hHg. Visual EF ~ 25-30%.						
			on. RV S' = 7.0 cm/s. TAPSE					
Right Atrium: Mildly dilated								
IAS:		Intra-atrial septum appears intact.						
Valves	Findings							
Mitral valve:		mitral leaflets visulised, with re	educed leaflet excursion.					
Aortic valve:		Tricuspid, mildly sclerotic - no significant gradient. Trivial regurgitation. Normal size aortic root.						
Tricuspid valve	e: Incompleted of	Incompleted coaptation of the tricuspid leaflets with severe, free						
		RVSP = 21 mmHg, with early	peaking Doppler trace.					
	 e: Structurally no 	Structurally normal with trivial regurgitation.						
Pulmonic valv		There is a small posteriorly located pericardial effusion.						

27 Nov 17

Seen by Cardiology: For dobutamine, frusemide infusion, ivabradine, cease Traztuzumab and Pertuzumab. Transferred to CCU.

29-31 Nov 17

Worsening LFTs, confusion, drowsiness. Asterixis noted (flapping tremor or liver flap - tremor of the hand when the wrist is extended-sign of CHF or

1 Dec 17

Code for low BP and rapid AF – transferred to ICU, given metaraminol and commenced noradrenaline. Minimal improvement despite escalation of noradrenaline. Lactate >9. Worsening GCS (Glasgow Coma Scale). Discussion with family – for palliative management. RIP 1730 from Cardiac

Issues on Investigation

Missed opportunities for early diagnosis and treatment of LV dysfunction,



LVEF 59% (May 2017) → 70% (July 2017) → ~40% (October 2017)

From EVIQ



- A significant change after first ECHO (59% \rightarrow 70%) should of triggered a cardiac review, need to compare ECHO results not just look at last results.
- Misinterpretation of echo report 9 Oct 17 "conclusion misleading", need to look at % not

Did not reflect the absolute decrease in the LVEF from 70% to 40+% over a short period of

Change in way of reporting can be confusing for non-cardiologists

Oncologist was unclear what the 'true' LVEF was (ranged from 42.6% to 48.9%)



Highlights the importance of close scrutiny of echo reports and comparison against previous results, and open communication with Cardiology team if in any doubt

Change in Practice for Pharmacy

- Observation from oncologist that pharmacy "did not alert them of changes in ECHO results", whilst not our pharmacy at this point in the patient's treatment we also did not routinely check ECHO results.
- Practice change is that now ECHO reports are checked by pharmacist on initiation of therapy and every 3 months
- Results recorded in patient dispensing history LVEF = X%, looking for significant changes up or down as well as anything below 45% as per EVIQ guidelines
- Like many hospitals we manage the scripts for the oncologists so the trigger for checking ECHO results is when submitting new scripts to medicare, which for Herceptin is every 3 months.
- Since implementation have noted several occasions where ECHO reports are not completed in the designated timeframe and have prompted the process with the