



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

MEASUREMENTS	Value	Normal Range
LV diastolic diameter (mm)	44 (35-56)	Aortic root 29 (20-37)
LV systolic diameter (mm)	30 (22-37)	Left atrium 40 (19-40)
LV septal thickness (mm)	8 (7-11)	LA area 25 cm ²
LV post wall thickness (mm)	8 (7-11)	RA area 19 cm ²
Fractional shortening (%)	31 %	RAVd 29 (mm)
LV ejection fraction (%)	59 %	TVI E' 0.06
Biplane EF (%)	59 %	E/E' 11 (< 10)
Pulmonary vein S wave (m/sec)	(m/sec)	RV S 0.13
Pulmonary vein D wave (m/sec)	(m/sec)	
Pulm. vein A reversal (m/sec)	(m/sec)	
Pulm. vein A reacceleration (ms)	(ms)	

- 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 ECHO

MEASUREMENTS	Value	Normal Range
LV diastolic diameter (mm)	47 (35-56)	Aortic root 29 (20-37)
LV systolic diameter (mm)	31 (22-37)	Left atrium 40 (19-40)
LV septal thickness (mm)	8 (7-11)	LA area 25 cm ²
LV post wall thickness (mm)	8 (7-11)	RA area 19 cm ²
Fractional shortening (%)	39 %	RAVd 29 (mm)
LV ejection fraction (%)	70 %	TVI E' 0.06
Biplane EF (%)	70 %	E/E' 11 (< 10)
Pulmonary vein S wave (m/sec)	(m/sec)	RV S 0.13
Pulmonary vein D wave (m/sec)	(m/sec)	
Pulm. vein A reversal (m/sec)	(m/sec)	
Pulm. vein A reacceleration (ms)	(ms)	

- 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, trastuzumab and pertuzumab continued.

9 Oct 17 ECHO

noted to be 'normal'

MEASUREMENTS	Value	Normal Range
LV diastolic diameter (mm)	47 (35-56)	Aortic root 29 (20-37)
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- TWO more doses of trastuzumab 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.

Admission Bloods

Test Name	Reference Range	Units	Result
Urea	2.5 - 6.5	mmol/L	5.2
Creatinine	0.5 - 1.2	mmol/L	0.8
Alkaline Phosphatase	30 - 120	U/L	110
Aspartate Aminotransferase	0 - 40	U/L	25
Alanine Aminotransferase	0 - 40	U/L	15
Gamma-GT	0 - 60	U/L	45
Prothrombin Time	11 - 14	sec	12.5
International Normalized Ratio	0.8 - 1.2		1.1
Fibrinogen	2 - 4	g/L	3.5
D-Dimer	< 0.5	mg/L	0.2
Urea	2.5 - 6.5	mmol/L	5.2
Creatinine	0.5 - 1.2	mmol/L	0.8
Alkaline Phosphatase	30 - 120	U/L	110
Aspartate Aminotransferase	0 - 40	U/L	25
Alanine Aminotransferase	0 - 40	U/L	15
Gamma-GT	0 - 60	U/L	45
Prothrombin Time	11 - 14	sec	12.5
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Fibrinogen	2 - 4	g/L	3.5
D-Dimer	< 0.5	mg/L	0.2

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

Measurement	Dimensions	Normal Adult Range
LV Diastolic Diameter 2D (cm)	5.8	M<5.9, F<5.3
LV Systolic Diameter 2D (cm)	4.8	
Septal thickness 2D (cm)	0.6	M<1.1, F<1.0
Posterior wall thickness 2D (cm)	0.9	M<1.1, F<1.0
RWT	0.32	<0.42
Indexed LV Mass (g/m ²)	97	M<103, F<89
LA Area / LA Volume (cm ² / ml/m ²)	34 / 55	<20 cm ² / <32ml/m ²
RA Area (cm ²)	22	<18cm ²

- 27 Nov 17 Seen by Cardiology: For dobutamine, frusemide infusion, ivabradine, cease Trastuzumab 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 liver failure).
- 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 Failure

Issues on Investigation

- Missed opportunities for early diagnosis and treatment of LV dysfunction, indicated by LVEF 59% (May 2017) → 70% (July 2017) → ~40% (October 2017)

Cardiac toxicity	Management
LVEF 40% to 45% AND less than 10% point decline from baseline	Continue treatment and repeat LVEF assessment within 3 weeks
LVEF 40% to 45% AND 10% point or greater decline from baseline	Delay pertuzumab and trastuzumab, repeat LVEF assessment within 3 weeks Discontinue treatment if LVEF has not recovered to within 10% points of baseline
LVEF less than 40%	Delay pertuzumab and trastuzumab, repeat LVEF assessment within 3 weeks Discontinue treatment if LVEF less than 40% is confirmed
Symptomatic Congestive Heart Failure (CHF)	Discontinue pertuzumab and trastuzumab

- A significant change after first ECHO (59%→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 just conclusion.
- 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%)

CONCLUSIONS	Findings
1. Mildly decreased global left ventricular systolic function.	Moderately dilated left ventricle (LVEDDV - 76 ml/m ²), normal wall thickness. Severe global systolic dysfunction, Simpson's EF 23%. LV dP/dt - 699 mmHg. Visual EF - 25-30%.
2. Top normal left ventricular internal cavity size.	Severely dilated. Normal size with reduced longitudinal function. RV S' = 7.0 cm/s. TAPSE = 1.4 cm.
3. Mild mitral and tricuspid valve regurgitation.	Mildly dilated. Intra-atrial septum appears intact.
4. Normal right ventricular size with moderately reduced function.	Tricuspid, mildly sclerotic - no significant gradient. Trivial regurgitation. Incomplete coaptation of the tricuspid leaflets with severe, free regurgitation. RVSP = 21 mmHg, with early peaking Doppler trace. Structurally normal with trivial regurgitation.
5. Severe tricuspid regurgitation due to coaptation defect.	There is a small posteriorly located pericardial effusion.
6. Moderate mitral regurgitation.	

- 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 team.