BEHOLD, it's getting longer

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Introduction

Multidrug-resistant (MDR) tuberculosis (TB) is caused by tubercle bacilli resistant to at least two most potent first-line anti-TB drugs, isoniazid and rifampicin. The treatment of MDR-TB requires the combination of second-line anti-TB drugs which potentially have more side effects. Here, we would like to present to you the clinical histories and management of two MDR-TB patients who developed anti-TB drug-related cardio-toxicities.

Case 1

Our first patient is a 14-year-old boy suffering from type I diabetes mellitus (DM) and was put on insulin since 2015. He was diagnosed to have MDR pulmonary TB in November 2019 with CXR showing bilateral lung infiltrative shadows and Acid-Fast-Bacilli (AFB) were detected in his sputum. Line probe assay detected rpoB gene mutation and katG gene mutation. Baseline electrocardiogram (ECG) showed QTcF (corrected QT interval using Fridericia exponential correction formula) interval 370ms. Anti-TB drugs were started in November 2019 including kanamycin 600mg, ethambutol 600mg, cycloserine 500mg, levofloxacin 600mg and prothionamide 500mg. Clofazimine 100mg was added to the anti-TB drug regimen few days later and cycloserine was withdrawn from the regimen because of mood disturbance. Subsequent drug susceptibility testing showed resistance to isoniazid, rifampicin, ethambutol and pyrazinamide. Ethambutol was then withdrawn from the anti-TB drug regimen and the dosage of anti-TB drugs were adjusted to kanamycin 600mg, levofloxacin 750mg, prothionamide 750mg and clofazimine 100mg. Two months after the start of anti-TB drugs, his ECG showed prolonged QTcF interval up to 523ms (Figure 1). He did not experience any symptoms of arrhythmia. The only other drug taken was insulin. The serum electrolytes and thyroid function test showed normal results. All anti-TB drugs were then withheld. The QTcF interval became 429ms one week later. Kanamycin 600mg, delamanid 200mg and linezolid 600mg were started on 5 February 2020. This is followed by the addition of levofloxacin 600mg and prothionamide 750mg on 14 February 2020. ECG monitoring after resumption of anti-TB drugs showed that the QTcF intervals were less than 500ms. He tolerated the anti-TB medications well and there were progressive radiological and microbiological improvements.

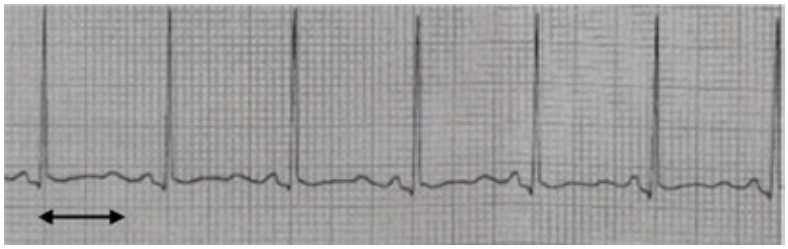


Figure 1. Lead II of ECG showing QTcF=523ms 2 months after start of second-line drugs

Summary of second-line anti-TB drug regimen and QTcF intervals of the first patient:

Treatment Regimen	Period	Remarks	QTcF Interval with Date
Km, E, Cs, Lfx, Pto	21/11/2019 – 24/11/2019	Lfx 600mg	20/11/2019: QTcF=370ms
Km, E, Cs, Lfx, Pto, Cfz	25/11/2019 – 27/11/2019	add Cfz	-
Km, E, Lfx, Pto, Cfz	28/11/2019 – 23/12/2019	off Cs	2/12/2019: QTcF=417ms
Km, Lfx, Pto, Cfz	24/12/2019 – 7/1/2020	off E	-
Km, Lfx, Pto, Cfz	8/1/2020 – 28/1/2020	↑Lfx to 750mg	-
Withheld treatment	29/1/2020 – 4/2/2020	prolonged QTcF	29/1/2020: QTcF=523ms
Km, Dlm, Lzd	5/2/2020 – 13/2/2020	-	5/2/2020: QTcF=429ms
Km, Dlm, Lzd, Lfx, Pto	14/2/2020 – 4/8/2020	↓Lfx to 600mg	3/3/2020: QTcF=476ms
Dlm, Lzd, Lfx, Pto	5/8/2020 onward	-	15/4/2020: QTcF=409ms 28/6/2020: QTcF=404ms 26/8/2020: QTcF=408ms

Km: kanamycin, E: ethambutol, Cs: cycloserine, Lfx: levofloxacin, Pto: prothionamide, Cfz: clofazimine, Dlm: delamanid, Lzd: linezolid

Case 2

Our second patient is a 57-year-old lady who was diagnosed to have left-sided cervical TB lymphadenopathy. Fine needle aspiration of the enlarged lymph node showed granulomatous inflammation and AFB on Ziehl-Neelsen staining. She was started on standard first-line anti-TB drug regimen (isoniazid, rifampicin, ethambutol and pyrazinamide) on 27 May 2019. Although Chest X-ray didn't show any significant lung lesion, computer tomography scan of thorax revealed mild focal bronchiectasis at right upper lobe and small non-specific ground glass nodules in right upper lobe and right lower lobe. Her sputum culture showed mycobacterium tuberculosis which was resistant to both isoniazid and rifampicin. Anti-TB drugs were then changed to second-line regimen including linezolid 600mg, levofloxacin 750mg, clofazimine 100mg, cycloserine 750mg and ethambutol 800mg in July 2019. On 17 July 2019, her ECG showed that the QTcF interval was 427ms. She tolerated the anti-TB drugs well initially and the enlarged cervical lymph node progressively decreased in size. Serial ECGs were performed and showed QTcF intervals below 500ms until 10 August 2020 (i.e. about 13 months after the initiation of second-line treatment). The QTcF interval was found to be 505ms (Figure 2). She didn't receive any other medication and there were no significant serum electrolytes disturbances. Anti-TB drugs were then withheld and repeated ECG four days later showing QTcF interval to be 373ms. Anti-TB drugs were resumed with the same regimen except that clofazimine was withdrawn. However, QTcF interval was found to be prolonged again and became 506ms one week afterwards. By decreasing the dosage of levofloxacin to 500mg daily, the QTcF interval was able to be maintained less than 500ms. The regimen was eventually finalized to include ethambutol 700mg, cycloserine 500mg, linezolid 600mg (thrice per week) and levofloxacin 500mg.

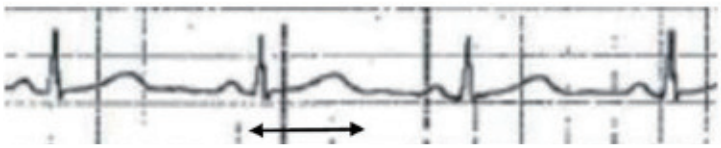


Figure 2. Lead II of ECG showing QTcF=505ms 13 months after start of second-line drugs

Summary of second-line anti-TB drug regimen and QTcF intervals of the second patient:

Treatment Regimen	Period	Remarks	QTcF Interval with Date
E, Lzd, Lfx, Cs, Cfz	17/7/2019 – 9/8/2020	Lfx 750mg	17/7/2019: QTcF=427ms 15/10/2019: QTcF=445ms 14/1/2020: QTcF=436ms 24/3/2020: QTcF=426ms
Withheld treatment	10/8/2020 – 13/8/2020	prolonged QTcF	10/8/2020: QTcF=505ms
E, Lzd, Lfx, Cs	14/8/2020 – 20/8/2020	off Cfz	14/8/2020: QTcF=373ms
Withheld treatment	21/8/2020 – 3/9/2020	prolonged QTcF	21/8/2020: QTcF=506ms 27/8/2020: QTcF=446ms
E, Lzd, Cs	4/9/2020 – 17/9/2020	withheld Lfx	4/9/20020: QTcF=410ms 11/9/2020: QTcF=412ms
E, Lzd, Cs, Lfx	18/9/2020 onward	added back Lfx but↓ to 500mg	18/9/2020: QTcF=414ms 25/9/2020: QTcF=404ms

H: isoniazid, R: rifampicin, E: ethambutol, Z: pyrazinamide, Lzd: linezolid, Lfx: levofloxacin, Cs: cycloserine, Cfz: clofazimine

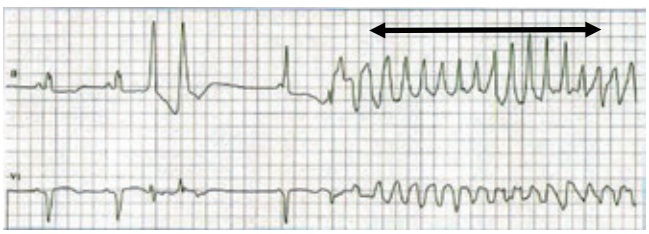
Both patients were suffering from MDR-TB and were put on anti-MDR TB medications including clofazimine and levofloxacin. There were significant prolongations of QTcF intervals during treatment but without any arrhythmia. Clofazimine was withdrawn from the regimen in both patients and levofloxacin dosages were reduced in order to keep QTcF intervals within normal range.

Discussion

A: Significance of QTc interval and Torsades de Pointes

Electrocardiogram (ECG) detects the sum of electrical activities that are taking place within the heart. QT interval on the ECG denotes the starting of ventricular depolarization till the end of ventricular repolarization that leads to ventricular contractions. Significance of QT interval was not appreciated until 1957. Jervell and Lange-Nielsen described a family in which four out of six children had a peculiar heart disease in combination with deafness[1]. All the children did not have any structural heart disease but their ECGs showed prolongation of QT intervals. They presented with repeated fainting attacks and three of the children died suddenly at the age of four, five and nine. The events were later found to be related to a polymorphic ventricular tachycardia named Torsades de Pointes (TdP) (Figure 3) which may degenerate into ventricular fibrillation causing sudden cardiac death. TdP is a distinctive polymorphic ventricular tachycardia in which the QRS amplitudes vary and the QRS complexes appear to twist around the baseline. All TdPs are preceded by prolongation of QT intervals, which may either be congenital or acquired. Thus, QT interval prolongation predicts the occurrence of TdP.

Figure 3. ECG pattern of Torsades de Pointes[2]



QT interval varies with heart rate. For comparison of QT interval at different heart rates, a correction formula is required to derive a corrected QT (QTc) interval which estimates the QT interval at a heart rate of sixty beats per minute. Bazett formula ($QTcB = QT / \sqrt{RR}$)[3] and Fridericia exponential correction formula ($QTcF = QT / \sqrt[3]{RR}$)[4] are the two most commonly used correction formulae. Bazett formula works best between the heart rates of 60

and 100 beats per minute, while it may give erroneous results at both slower and faster heart rates. The Fridericia exponential correction formula has the same limitation at slow heart rates, but is more accurate than Bazett's correction at faster heart rates. For assessing the QTc interval of patients receiving QT prolonging anti-TB medications, Fridericia exponential correction formula is preferred as it was used during the phase II studies of the novel anti-TB medications.

QTc is considered to be prolonged when it is >450ms among male and >470ms among female. There is no threshold of QTc interval prolongation at which TdP will occur. For each 10ms increase in QTc interval, there is 5 – 7% increase in the risk of developing TdP. QTc interval >500ms is associated with a two to three-fold higher risk for developing TdP and is widely considered as the point at which intervention is needed[5].

B: Anti-tuberculosis drugs causing prolongation of QTc interval

Numerous factors including unmodifiable and acquired factors can contribute to QT interval prolongation as listed in Table 1[6]. Their effects on QT interval are additive. Drug is one of the commonest and readily removable factors. Assessing the effect on QT interval is currently one of the safety markers in new drug development[7].

Table 1[6]. Risk factors for QTc prolongation and Torsades de Pointes

Baseline and Unmodified Predisposition	Acquired Risk Factors: Clinical Conditions
• Underlying conduction abnormalities (subclinical long QT syndrome): genetic predisposition, family history of sudden death • Bradycardia • Female sex • Advanced age (linearly increased risk after 60 years)	Electrolyte imbalance • Hypokalemia (for any reason) • Severe hypomagnesaemia • Hypocalcaemia Structural and functional heart problems • Recent conversion from atrial fibrillation • Ischemic and congestive heart disease • Ischemic cardiomyopathy • Dilated or hypertrophic congestive heart disease • Congestive heart failure Frequent conditions of TB patients • HIV infection (due to potential additive clinical risk factors, particularly in advanced disease and multiple medications) • Low BMI: malnutrition, starvation and wasting syndrome • Severe vomiting and diarrhea creating low potassium levels Impaired renal function Impaired hepatic function Hypothyroidism

Among the recommended anti-MDR TB medications by the World Health Organisation (WHO)[8], clofazimine (Cfz), fluoroquinolones (FQs), bedaquiline (Bdq) and delamanid (Dlm) are known to have QT interval prolongation effects.

Clofazimine is a very old drug that did not undergo today's rigorous testing before it was put into market. Shurjeel reported the first case of TdP related to clofazimine[9]. QT interval prolongation was detected when clofazimine was used in combination with bedaquiline[10].

All fluoroquinolones pose the risk of QT interval prolongation as a class effect. However, the pro-arrhythmic potential is not the same for all FQs. Grepafloxacin was removed from the market voluntarily in 1999 due to reports of seven cardiac-related deaths, of which three were reported as TdP. Moxifloxacin is associated with the highest possibility to be associated with the risk of both arrhythmia and cardiovascular mortality as compared to other currently marketed

FQs[11]. Overall risk of TdP was about one per million FQs prescriptions and they were usually associated with other risk factors predisposing to TdP[12].

Delamanid is derived from the nitro-dihydro-imidazooxazole class of compounds. It inhibits mycolic acid synthesis of the bacterial wall and shows potent in vitro and in vivo activities against both drug-susceptible and drug-resistant strains of Mycobacterium tuberculosis. In phase II clinical trial of delamanid development, the effect on QTcF interval was compared among the three groups, (1) backbone drug regimen plus placebo, (2) backbone drug regimen plus delamanid 100mg twice daily and (3) backbone drug regimen plus delamanid 200mg twice daily. Although no clinical event related to QT interval prolongation was observed, QT interval prolongation was reported significantly more frequently in the groups receiving delamanid (3.8% in placebo group, 9.9% in delamanid 100mg twice daily group and 13.1% in delamanid 200mg twice daily group)[13].

Bedaquiline belongs to diarylquinoline group compound. It inhibits mycobacterial ATP synthesis and depletes cellular energy store. It shows bactericidal activity in vitro. In phase IIb clinical trial of bedaquiline development, it was found that bedaquiline group showed a mean increased in QTcF interval of 15.4ms compared to 3.3ms in placebo group. The QTcF interval gradually decreased after stopping Bdq at week 24 and became similar to that of the placebo group by week 60[14].

C: Recommendations for monitoring and management of prolonged QTc interval in patients receiving anti-MDR TB medications

Guidelines and recommendations about monitoring and management of QT interval prolongation in patients on anti-MDR TB medications have been published by different international authorities[15,16,17]. The salient points are summarized as follows:

1. If bedaquiline or delamanid is used alone, ECG monitor at baseline, week 2, 4, 8, 12, 24 after the start of treatment. If two or more QT interval prolonging agents are used concomitantly, monitor QT interval at least monthly[15]
2. Hospitalize patients if symptomatic e.g. palpitations, fainting, syncope or if asymptomatic but QTcF greater than 500ms (confirmed by repeating ECG)
3. Stop the suspected causative drugs
4. Correct any electrolytes imbalance
5. Remove other amendable QT interval prolonging risk factors (Table 1)
6. Periodic monitoring QTcF interval until normalized
7. Consider the following adjustments of the anti-TB drugs regimen in consultation with the case management committee:
   - 7.1. Critical QT prolonging anti-TB drugs can be added back once QTcF become stable, i.e. QTcF <450ms for male, QTcF <470ms for female
   - 7.2. Non-TB drugs that cause QT prolongation or affect heart rhythm should be avoided
   - 7.3. If clofazimine was used, not to resume unless no other drugs choice
   - 7.4. If moxifloxacin was used, consider replacing with levofloxacin
   - 7.5. If the patient was put on bedaquiline (or delamanid) and it is considered critical to the regimen, consider adding the drug back to the patient's regimen while suspending all other QT prolonging drugs[16]
   - 7.6. Do at least weekly ECG and on ad hoc basis until stable
   - 7.7. Stop the culprit agents if the QTcF >500ms

D: Conclusions

Anti-tuberculosis drugs, clofazimine, fluoroquinolones, delamanid and bedaquiline may cause QT interval prolongation which is a surrogate for Torsades de Pointes that may further degenerate to fatal ventricular arrhythmia. Regular monitoring of QTcF interval is needed when they are prescribed and the anti-TB drug regimen has to be adjusted if QTcF interval was found to be greater than 500ms or whenever arrhythmic symptoms occurred. There is no hard and fast rule on which particular drug can be re-introduced successfully. The final regimen depends on the likely efficacy of a particular drug and the tolerability of the patient.

References:

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To treat or not to treat

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Introduction

Despite modern advancement in clinical medicine with various guidelines and evidences, there are times and circumstances when we still puzzle on what are the best options for our patients. We would like to introduce a case which demonstrated our dilemma in treating a patient or not with a common encounter for Respiratory physicians: an abnormal chest radiograph.

Case Presentation

A 70 years old lady, a non-smoker with a past medical history of hypertension and diabetes mellitus, was referred to our medical clinic in 2010 for workup of any underlying hyperparathyroidism with incidental finding of asymptomatic renal stone. Chest radiograph was performed for routine checkup and it showed multiple lung masses of various sizes and irregular border. No internal cavitation or calcification was seen. Bilateral costophrenic angles were sharp (Figure 1).

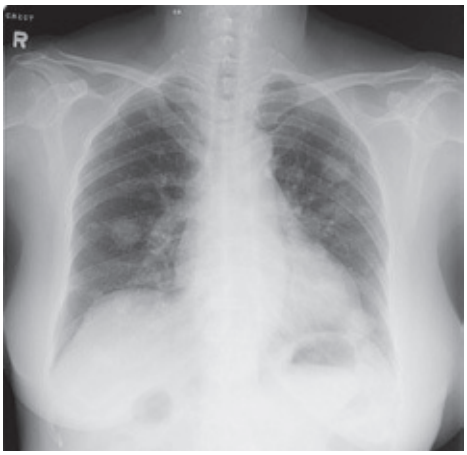

Figure 1. Chest radiograph on presentation 2010

She had no respiratory symptoms including cough, sputum, haemoptysis, shortness of breath, fever, weight loss or loss of appetite. Physical examination was unremarkable with a normal examination for respiratory, cardiovascular and abdominal systems. There was no finger clubbing or palpable lymph nodes.

An old chest radiograph taken at the Accident and Emergency Department (AED) in 2008 was reviewed from her medical records which showed similar lung nodules (Figure 2).

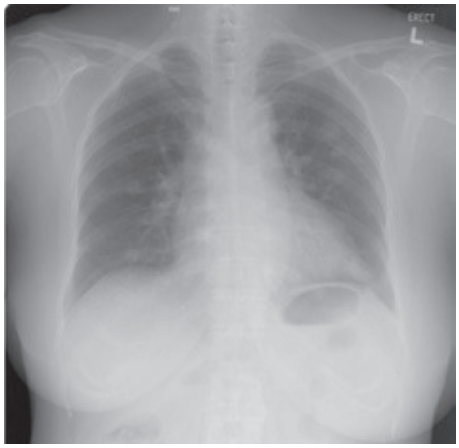

Figure 2. Chest radiograph 2008

Blood tests showed a normal complete blood picture, liver and renal function test, calcium phosphate level, protein and albumin level. Tumor markers including alpha fetal protein and carcinoembryonic antigen were normal. Thyroid stimulating hormone and parathyroid hormone level were also normal. Sputum investigation

was unremarkable with routine culture yielded oral commensals only, no acid-fast bacilli and no malignant cells on cytology.

A contrast computer tomography was arranged for further assessment of the lung masses (Figure 3). Multiple calcified masses with varying sizes and speculated border were noted over bilateral lung fields with normal mediastinum and hila.

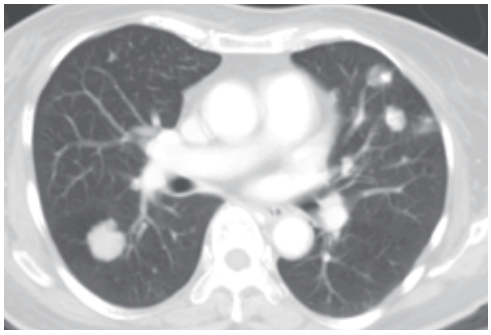

Figure 3. Contrast CT thorax 2010

Bronchoscopy noted no endobronchial lesion. Bronchoalvelolar lavage was unremarkable for bacterial and fungal culture, acid-fast bacilli culture and cytology. Transbronchial biopsy taken at RB6 did not noted any malignant cells.

In view of the negative bronchoscopy, CT guided fine needle aspiration cytology (CT guided FNAC) was performed to one of the left upper lobe masses. The tissue pathology (Figure 4a and 4b) shows multiple fragments of lung tissue with patchy deposition of eosinophilic, amorphous material in the parenchyma and at the walls of blood vessels. Special staining showed no fungal organism or acid-fast bacilli. Congo red and crystal violet showed equivocal staining. Immunohistochemically the eosinophilic materials were variably positive with amyloid P marker. Immunostaining for Kappa and Lamda light chain was inconclusive for any light chain restriction.

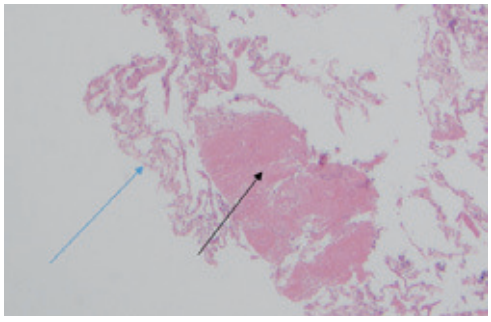

Figure 4a. H&E slide of CT guided FNAC. Alveolar tissue (blue arrow) and amyloid (black arrow), the latter of which appears as eosinophilic amorphous material with cracking artifacts.

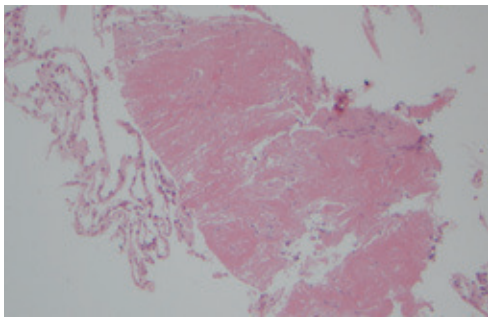

Figure 4b. A magnified version of the tissue depicted by the black arrow in the above slide

Further investigations to look for any underlying diseases and extent of involvement were pursued. IgG level was increased IgG 21.5 g/l (7-16.0 g/l) IgA 3.6 g/l (0.7-4.0 g/l) IgM 1.1 g/l (0.4-2.3 g/l)>. Serum plasma electrophoresis noted diffuse increase in physiological gamma immunoglobulin. 24-hour urine total protein was 0.67 g/l and urine protein electrophoresis noted predominantly features of glomerular proteinuria. Erythrocyte sedimentary rate was elevated 48 mm/hr (<20 mm/hr) while C reactive protein was normal <0.6 mg/l (<0.9 mg/l). Antinuclear antibody showed speckled pattern with titre 1:160. Anti-double strand DNA was 14 IU/ml (</=50 IU/ml). Anti-myeloperoxidase and anti-proteinaese-3 were negative. Anti-extractable nuclear antigen showed weakly positive anti-Ro and Anti-La. Anti-cardiolipin was negative. Echocardiogram was performed with normal findings. She refused renal and rectal biopsy as she was asymptomatic and invasiveness of the procedures involved. The assessment of was rendered inadequate at this stage due to patient's refusal.

A diagnosis of at least localized pulmonary amyloidosis was made. With the patient being asymptomatic, a conservative approach with close expectant observation was adopted. Follow-up clinic visits with review of symptoms and serial chest radiographs in 2011 to 2016 were unremarkable. However, her chest radiograph worsened since 2016 with increasing sizes and extent of lung opacities despite patient remaining asymptomatic (Figure 5, Figure 6 and Figure 7).

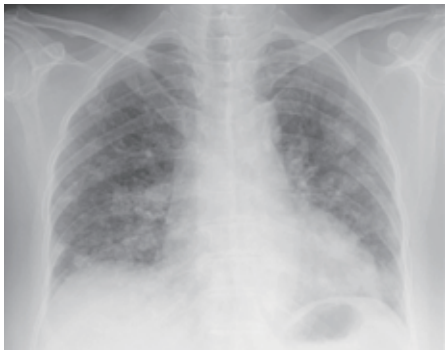

Figure 5. Chest radiograph 2016

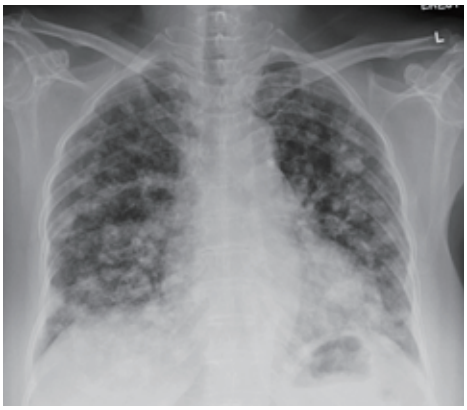

Figure 6. Chest radiograph 2017

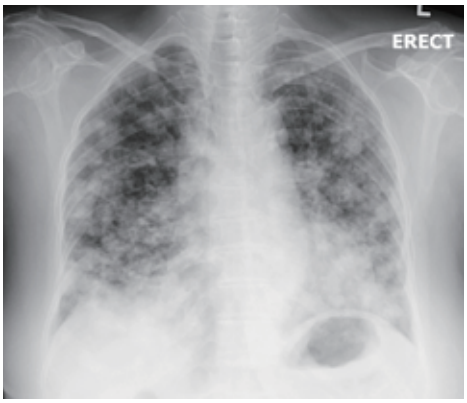

Figure 7. Chest radiograph 2018

She refused further investigation till 2019 when she complained of on and off productive cough with exertional dyspnea. Worsening of proteinuria with 24-hour urine protein 1.07 g/day was also noted. She also presented with left nipple discharge. A biopsy of the left breast tissue was performed (Figure 8, Figure 9 and Figure 10).

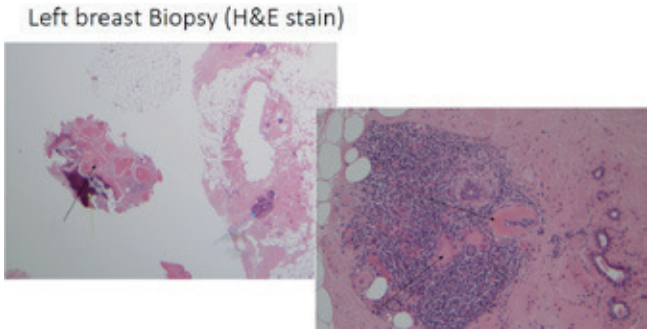

Figure 8. Left breast tissue under H&E stain. Left photo: blue arrow shows normal breast tissue composed of ducts and lobules in a background of fibroadipose tissue. Black arrow shows amyloid deposition; Calcified material is marked by the green arrow; Amyloid deposits are labelled by black arrow on the photon on the right.

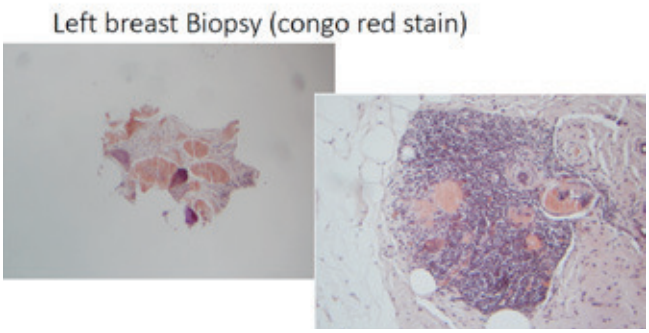

Figure 9. Left breast tissue under Congo Red stain. Characteristic salmon pink colour was noted.

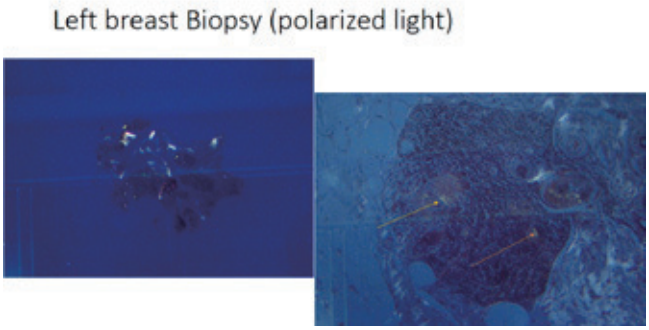

Figure 10. Left breast tissue under polarized light. Characteristic apple green biregringence.

A follow-up computer tomography of the thorax was performed in 2020 which showed marked disease progression compared with that of 2010 (Figure 11).

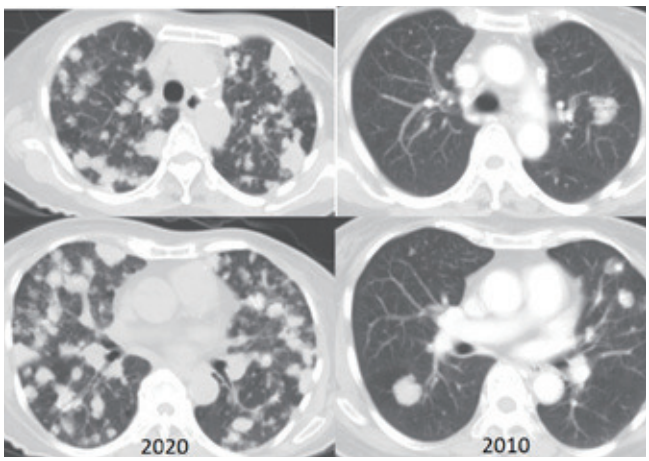

Figure 11. Comparison of CT thorax in 2010 and 2020

In view of symptomatic multiple organ involvement (lungs and breast), she agreed to proceed to further investigation. Serum free light chain was performed with free keppa 434 mg/L (3.3-19.4 mg/L) free lamda 82.8 mg/L (5.7-26.3 mg/L) K/L ratio 5.23 (0.26-1.65). Bone marrow examination was performed which showed normal cellular marrow showing mild plasmacytosis. Immunostaining showed a kappa to lamda ratio of 2:3 and no definite light chain restriction detected. No

amyloid deposition detected. Repeated Echocardiogram in 2020 was again normal. Nephrotic proteinuria was noted with total protein/creatinine ratio 5.02. Amyloid protein typing is not readily available in our locality.

Haematologist opinion was sought and suggested the breast and lung biopsy were not conclusive of light chain amyloidosis and bone marrow with 6% plasma cell only and no light chain restriction. Rheumatologist also reviewed the patient and suggested it was unlikely for amyloidosis to precede the diagnosis of autoimmune disease.

Amyloidosis Review

Amyloidosis is caused by deposition of autologous protein in tissues and organs in the form of fibrils, causing functional damages to the organs involved. It is classified according to the types of underlying abnormal protein produced, namely AL, AA, ATTR and AB2M.

Amyloidosis is a rather uncommon disease entity with the incidence of AL amyloidosis 9.7 to 14.0 cases per million person-years[1]. The gold standard for diagnosis is tissue biopsy and histological examination aiming either at the dysfunctional organ or clinically uninvolved site. Abdominal fat pad biopsy has a reported sensitivity of 57 – 85% and specificity 91 – 100%[2-5]; Rectal biopsy has a reported sensitivity of 84%[6]. Amyloid typing would be important in determining the treatment of choice. Identifying the extent of disease also confers prognosis implications.

For workup of suspected amyloidosis, serum plasma electrophoresis and fixation and serum free light chain should be performed. Tissue biopsy obtained from the affected organ should be sent for Congo red staining and amyloid protein typing if available. Workup of extent of disease would include cardiac echocardiogram, cardiac magnetic resonance imaging for cardiac involvement, 24-hour urine for proteinuria and renal function test for kidney involvement, liver function test for liver involvement screening to screen for systemic involvement.

Pulmonary Amyloidosis

Pulmonary amyloidosis is a rare diagnosis. A report from Mayo clinic reported a total of 76 patients with autopsy proven amyloidosis. Only one among the reported cases was diagnosed ante mortem and the remaining 75 cases were clinically unsuspected. AL type of amyloidosis accounted for 76% of the reported cases[7].

Various types of pulmonary involvement of amyloidosis have been described and namely diffuse alveolar septal, nodular, tracheobronchial, adenopathy and pleural effusion (Table 1).

Classification	Amyloid protein	Pathogenesis	Characteristics
Diffuse alveolar septal	AL, AA, ATTR	Amyloid deposits in the blood vessels and alveolar-septa	Least common, but most severe Systemic amyloidosis
Nodular	AL	One or more nodular deposits in the lung	Localized disease Complication of Sjogren syndrome
Tracheobronchial	AL, rare AA	Nodular deposits in trachea and large bronchi, diffuse submucosal disease	Most common
Adenopathy	AL	Circulating monoclonal immunoglobulin	
Pleural effusion	AL	Direct infiltration of pleura	

Table 1. Types of pulmonary involvement of amyloidosis

The symptoms of pulmonary amyloidosis may vary from cough, dyspnoea which can be due to diffuse alveolar involvement impairing gaseous exchange and tracheobronchial stenosis, haemoptysis as a result of arterial dissection of medium and small sized vessels, to asymptomatic. Tracheobronchial involvement with resultant stenosis is the main symptomatic presentation in organ-limited amyloidosis[8].

Management of pulmonary amyloidosis would depend on the extent of involvement and typing of amyloidosis.

For localized disease, observation could be reasonable for asymptomatic patient. Bronchoscopic treatment includes Nd:YAG Laser therapy, cryotherapy and airway stenting. External beam radiation has been described as effective. Surgical resection was also reported to be effective[9-13].

In systemic amyloidosis, chemotherapy and stem cell or organ transplantation may be appropriate. For AL amyloidosis, chemotherapy (anti-myeloma therapy) targeting underlying clonal B cell dyscrasia with the aim of reducing production of amyloidogenic light chains can be initiated. Autologous stem cell transplantation (ASCT) should be considered for eligible patients. For AA amyloidosis, therapy should be directed at suppressing underlying inflammatory condition. For Hereditary amyloidosis, synthesis of the abnormal protein is predominantly in the liver (like fibrinogen, ApoA1 and TTR), liver transplantation should be considered[14]. Development of other therapeutics is still ongoing.

Discussion

A case of amyloidosis initially presented locally with asymptomatic lung involvement but later noted to be a case of systemic amyloidosis with breast and possible renal involvement in view of significant otherwise unexplained proteinuria. It demostrated in amyloidosis involving the lungs, patients could remain asymptomatic and stable for years even without treatment. Yet, the disease could subsequently deteriorate clinically and radiologically.

Extent of disease involvement need thorough investigation as it confers to prognostic differences. Patients with localized AL amyloidosis had a significantly better disease-specific 10-year survival compared with systemic AL amyloidosis. (96.0 vs. 51.9%)[15].

Expertise in amyloid protein typing would also affect the management of patients suffering from amyloidosis but is not readily available in our locality yet.

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