Case report

Addressing tuberculosis management in context of default and side effects associated with anti tuberculosis drugs: A case report from Malaysia

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A 22 year hotel waitress with history of productive cough was registered as sputum smear confirmed case of pulmonary tuberculosis. Time delay between onset of symptoms and start of treatment was two months. During the first month of treatment, patient suffered from itchiness and skin rashes associated with anti tuberculosis drugs, which were treated with chlorpheniramine (oral; 4 mg), citrizine (oral; 5 mg) and betamethasone (local application; 0.122% w/w). Patient missed 16 (out of 32) doses of anti TB drugs in continuation phase claiming that she was very busy at work place and forgot to take medication. Although, at the end of treatment, patient’s perception of mental and physical health was improved but ‘social functioning’ and ‘role emotion’ scores were still below Malaysian norms suggesting perceived stigma and lack of tuberculosis knowledge. Patient was classified as cured, though, she did not complete full course of chemotherapy, which is the preliminary requirement for a case to be classified as “cured” or “treatment completed”. Patients working in crowded areas like restaurants, bus stations or market should be isolated from community until they are non-infectious. Use of non sedative anti histamines like fexofenadine, or loratidine should be preferred over first generation anti histamines (chlorpheniramine) in patients with such a lifestyle. Anti tuberculosis treatment should be stopped until rashes are completely resolved. World Health Organization (WHO) has recommended applying “Patient Centered Approach” to cope with the defaulters. There is need for more inclusive efforts of National Tuberculosis Control Programs to improve health related quality of the life of tuberculosis patients.

Key words: Tuberculosis, chlorpheniramine, patients, treatment.

INTRODUCTION

Tuberculosis (TB) is a contagious disease caused by Mycobacterium tuberculosis. It is one of the foremost causes of adult deaths every year with an incidence rate of around 9 million cases per year (Zager and McNerney, 2008). In mid 1990s, directly observed treatment short course (DOTS) strategy was adopted as the basis of tuberculosis control. Isoniazid (H), pyrazinamide (Z), rifampicin (R), ethambutol (E) and streptomycin (S) are recommended as first line treatment (World Health Organization, 2009). Adherence to TB treatment is vital in achieving “cure”. One of the key obstacles to successful treatment outcome is default from TB treatment. World Health Organization (WHO) surveillance data from ten different countries reported emergence of multi drug resistant (MDR) Mycobacterium strains in 32% of the patients returning after default which is quite alarming (World Health Organization, 2009).

Ideally, aim of any treatment program is certainly to retrieve patient’s best state of health and to halt the
transmission of infection (Pozniak et al., 2011). WHO defines “Health” as a state of complete physical, mental and social well-being, and not merely the absence of disease or infirmity (World Health Organization, 1946). Physical, mental and social well-being is a measure of Health Related Quality of Life (HRQoL) (Spilker, 1996; Marra et al., 2008). SF-36 Health Survey is a generic HRQoL assessment questionnaire and consists of 36 items covering 8 dimensions (sub-scales): Physical function (PF), role physical (RP), bodily pain (BP), General health (GH), vitality (VT), social function (SF), role emotional (RE) and mental health (MH). Each dimension scores from 0 to 100 (where 0 being the worst score). SF-36 health survey is reliable and valid tool to access HRQoL both in non-clinical and diseased population (Euteneuer et al., 2006). Physical, mental and social well being is a measure of health related quality of life (HRQoL) (Spilker, 1996; Marra et al., 2008). SF-36 Health Survey is a generic HRQoL assessment questionnaire and consists of 36 items covering 8 dimensions (sub-scales): physical function (PF), role physical (RP), bodily pain (BP), general health (GH), vitality (VT), social function (SF), role emotional (RE) and mental health (MH). Each dimension scores from 0 to 100 (where 0 being the worst score). SF-36 Health Survey is a reliable and valid tool to access HRQoL both in non-clinical and diseased population (Euteneuer et al., 2006).

Outcome of pulmonary tuberculosis (PTB) is reported on the basis of categories developed and recommended by the working group of WHO and International Union against Tuberculosis and Lung disease (IUATLD) (World Health Organization, 2009).

We would like to discuss a case of PTB; during treatment, patient experienced itchiness and skin rashes associated with anti TB drugs. Patient only completed four months of anti TB treatment and was classified as “cured”.

### Table 1. Health related quality of life scores at three different time points of TB treatment.

<table>
<thead>
<tr>
<th>Time point</th>
<th>PF</th>
<th>RP</th>
<th>BP</th>
<th>GH</th>
<th>VT</th>
<th>SF</th>
<th>RE</th>
<th>MH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Start of treatment</td>
<td>30</td>
<td>50</td>
<td>31</td>
<td>30</td>
<td>37.5</td>
<td>50</td>
<td>41.67</td>
<td>40</td>
</tr>
<tr>
<td>After 2 months</td>
<td>70</td>
<td>62.5</td>
<td>62</td>
<td>62</td>
<td>56.25</td>
<td>75</td>
<td>50</td>
<td>70</td>
</tr>
<tr>
<td>End of treatment</td>
<td>85</td>
<td>75</td>
<td>84</td>
<td>72</td>
<td>62.5</td>
<td>75</td>
<td>62.5</td>
<td>75</td>
</tr>
</tbody>
</table>

A 22 year female patient (42 kg) with the history of productive cough for two months, shortness of breath (SOB), night sweats and fever were registered as a new smear positive (S +1, 1 to 9 acid fast bacilli/10 fields) case of PTB at chest clinic, Penang General Hospital. Chest X-ray showed left upper lobe opacity. Erythrocyte sedimentation rate was elevated to 80 mm/h and albumin concentration (33 g/L) was slightly below the normal range. All other biochemical tests were normal. Drugs prescribed for intensive phase (IP) of TB treatment were isoniazid (225 mg), rifampicin (450 mg), pyrazinamide (1200 mg), ethambutol (825 mg) (in fixed dose combination) and vitamin B6 (10 mg) to be administered on daily basis at primary health care unit.

After 10 days, patient reported at chest clinic with the complaints of rashes for which doctor prescribed one tablet of chlorpheniramine (4 mg; at night) and one tablet of citrizine (5 mg; day time) for 20 days. At the same time, she was also prescribed betamethasone (local application: 0.122% w/w) two times in a day. Patient was advised to continue anti TB treatment and report at chest clinic on scheduled appointment (after one month of start of anti TB treatment). At appointment date, patient claimed minimal cough. Sputum smear examination was not done as patient was unable to produce sputum. At this visit, doctor again observed skin rashes (redness, excoriation and hyperkeratinization) on right thigh for which she was prescribed chlorpheniramine (4 mg; oral) three times a day for one week. She was again advised to continue anti TB treatment.

After two months of IP, patient denied cough and other associated symptoms. Patient gained 2 kg weight (44 kg). Chest X-ray showed minimal fibrosis. Acid fast bacilli (AFB) smear was not done as patient was unable to produce sputum. Based on clinical improvement, patient’s therapy was changed to continuation phase (CP). During CP, patient was advised to take isoniazid (700 mg), rifampicin (600 mg) and vitamin B6 (10 mg) biweekly for 4 months at primary health care unit. She was informed to visit chest clinic after two months to evaluate treatment progress. Patient continued her treatment for another two months at primary health care unit and then defaulted from treatment. Several phone calls were made from chest clinic for convincing patient to re-start therapy, although in vain. Patient returned to the chest clinic after three months of defaulting treatment and explained that she was busy at work place. AFB smear examination was not done as patient did not claim any sputum. Based on clinical judgment, her therapy was stopped. Patient missed 16 out of 32 doses in CP and was classified as “cured”.

Table 1 shows HRQoL scores for SF-36v2 Health Survey. Patient was asked to fill a self administered Malay version of SF-36v2 questionnaire at three different time points. Obtained responses were entered in scoring
Persons working in close contact with AFB smear positive TB patients are at higher risk for being infected (Kays, 2005). Transmission of Mycobacterium tuberculosis is positively associated with delay in diagnosis and start of anti TB treatment of infected individual (Sherman et al., 1999). In current case, time difference between onset of symptoms (productive cough) and start of treatment was two months. Patient was a waitress in a hotel making close contact with lot of people rendering them at higher risk of getting TB. Another alarming fact was that patient did not disclose her illness to employer and close friends probably due to stigmatization and fear of losing a job (Liefoooge et al., 1995).

After 10 days of anti TB treatment, patient had experienced itching followed by skin rashes. Skin rashes are major side effect associated with streptomycin, isoniazid, pyrazinamide and rifampicin. In such a case, patient’s anti TB therapy should be immediately stopped and restarted (with or without modification) once side effects are properly resolved (World Health Organization, 2009). Furthermore bearing patient lifestyle in mind, non sedative agents like fexofenadine or loratidine with equivalent anti histamine (Woodward, 1990) efficacy seem to be better contenders.

Another important consideration in current case is the patient’s default from treatment during CP. In current scenario, false perception of being completely cured (Jaiswal et al., 2003), skin rashes (Ramachandran and Prabhakar, 1992) and sedation associated with chlorpheniramine (Nicholson et al., 1991) might be responsible for non adherence. Other causes of default include, lack of patient motivation, economic and transportation problems and socio-psychological factors (Ramachandran and Prabhakar, 1992). It has been further stated that such patients are at higher risk of relapse and drug resistance (Comolet et al., 1998). Convenient clinic hours with minimal waiting time, appointment of close friend or nearby general practitioner as treatment supporter, motivated health care workers with managerial support, provision of incentive packages and proper education of patient about nature and duration of therapy are few op-tions to minimize chances of default in current case.

Not surprisingly, SF-36v2 Health Survey scores at the start of therapy were lower than mean scores reported by Azman and colleagues (Azman et al., 2003) for Malaysian general population. This finding is in line with earlier studies stating that HRQoL is negatively affected in chronic illness like TB (Chamla, 2004). After two months, improvement in HRQoL scores had been observed that might be consequence of improvement in clinical signs and symptoms (Othman et al., 2011). However scores for all eight domains were below Malaysian norms suggesting that patient was still having difficulties in performing her physical and mental functions. At the end of TB treatment, SF-36v2 Health Survey scores showed improvement but SF and RE scores were still below Malaysian norms suggesting perceived stigma and lack of tuberculosis knowledge (Marra et al., 2008; Rajeswari et al., 2002). Ultimately, evidences support the absence of disease but state of “Health” as defined by WHO has not been achieved.

Patient has not completed full course of chemotherapy, which is preliminary requirement for a case to be classified as “cured” or “treatment completed”. However patient defaulted from TB treatment for two consecutive months (last 2 months). Therefore, in spite of classifying her “cured” her therapy should be restarted (World Health Organization, 2009).

CONCLUSION

Treatment delays can be reduced by educating patients about health seeking behavior. Patients working in crowd-ed areas like restaurants, bus stations or market should be isolated from community until they are non-infectious. Memo should be sent to employer about the nature and severity of disease of their affected employee by ensuring that monthly salary is not affected. Alternate but less reliable approach is to counsel infectious patients to wear specially designed masks. Probability of non adherence can be minimized by applying WHO recommended “Patient Centered Approach”. Choice of anti histamines should be based on patient’s lifestyle. This case report also exhibits the need for more inclusive efforts of tuberculosis control programs to improve HRQoL of patients. Besides providing prescribed treatment regimen, DOTS providers and health managers should spot and address emotional, physical and societal impact of tuberculosis. SF 36v2 Health Survey can be used to monitor the progress of treatment from patient’s perspective.

CONFLICTS OF INTEREST

Authors declare that we have no conflicts of interest.

ETHICAL APPROVAL

Ethical approval was taken from Ministry of Health, Malaysia (ref. dim. KKM/NIHSEC/08/08/04P10-69).

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