OUTCOME OF SURGICAL MANAGEMENT OF MULTIDRUG RESISTANT TUBERCULOSIS PESHAWAR EXPERIENCE OF 135 CASES OVER A PERIOD OF 12 YEARS

Aamir Bilal*, Abdul Baseer*, Muhammad Imran*

*Cardiothoracic Surgery Unit, Postgraduate Medical Teaching Institute, Lady Reading Hospital, Peshawar - Pakistan

Address for correspondence:

Abdul Baseer

Cardiothoracic Surgery Unit, Postgraduate Medical Teaching Institute, Lady Reading Hospital, Peshawar - Pakistan

ABSTRACT

Objective: To assess the results of surgery for treatment failure Multidrug-Resistant Tuberculosis.

Methods: Retrospective analysis was done in 135 cases of multidrug-resistant tuberculosis in whom surgical cure was attempted after being declared treatment failure by pulmonologist, at Department of Thoracic surgery, Lady Reading Hospital, Peshawar, Pakistan between the years 2002 to 2014.

Results: There were 81 male and 54 female patients in the age group of 14-54 years. All were sputum positive at the time of surgery. Majority of patients were treated with pulmonary resections (Pneumonectomy [n=31], bilobectomy [n=32] and lobectomy [n=60), while primary thoracoplasty with apicolysis was done in 12 patients. Post operatively 2nd line anti tubercular chemotherapy was prescribed for 24 months.

Mortality was 6/135 (4.44%) and included four early deaths which included respiratory failure in three and myocardial infarction in one and two late death due to bronchopleural fistula with empyema. Morbidity was 14/135 (10.37%) and included seven patients who developed bronchopleural fistula with empyema, apical space in three patients and wound infection in four patients. At a mean follow-up of one year bacteriological cure (-ve Sputum microscopy & Culture) was achieved in 122 out of 129 alive patients (94.56%).

Conclusion: Judiciously performed adjuvant surgery can yield excellent long term bacteriological cure with acceptable mortality and morbidity in treatment failure multidrug-resistant tuberculosis.

Key Words: Multidrug-resistant tuberculosis; treatment failure; Surgery

This article may be cited as: Amer Bilal A, Baseer A, Imran M. Outcome of Surgical Management of Multidrug Resistant Tuberculosis Peshawar Experience of 135 cases over a period of 12 years. Pak J Chest Med 2017; 23(1): 15-9

INTRODUCTION

The role of surgery in tuberculosis has tended to have come the proverbial full circle in the wake of multidrug-resistent tuberculosis (MDR-TB) from starting with collapse therapy to becoming superfluous in the post streptomycin era[1]. The indications for surgery for MDR-TB have remained largely unchanged since they were first described by Iseman et al. in 1990[2].

Multidrug-resistent tuberculosis (MDR-TB) is defined as tuberculosis showing resistance to, at least, isoniazide and rifampacin irrespective of resistance to other drugs is a serious threat to tuberculosis control world-wide[3]. According to the latest WHO statistics, approximately half a million new cases of MDR-TB are diagnosed every year[4] .The world health organization (WHO) estimates that 50 million people world wide are already infected with drug resistant tuberculosis [5,6].Countries and regions are named “hot spots” where MDR-TB makes up more than 3% of the new TB cases. For example, in Estonia nearly 37 percent of the new TB cases were resistant to at least one drug resistant to all four drugs tested was 8.5 percent among new tuberculous patients and the country had the highest level of MDR-TB (14.1%) of any area of the

world among TB patients who had never been treated before .

According to the WHO, levels of MDR-TB will reach an alarming state in South Asia if prompt steps are not taken[5].The incidence of TB increases rapidly in settings where TB control is poor, patients are immunocompromised and also among those with HIV/AIDS or malnutrition [4].Globally, an estimated 20% of patients with TB default, or fail to respond to therapy and develop MDR-TB[5-8].

Pakistan currently ranks fifth amongst countries with highest burden of Tuberculosis alongside the fourth highest burden of Drug Resistant TB globally. In an estimated population of around 180 million with annual incidence of TB being 231/100,000, Pakistan produces about 420,000 new cases annually[9].

Multidrug–resistant tuberculosis is a serious threat to tuberculosis control worldwide with ominous implications in Pakistan context. The medical management of this disease is expensive, toxic and, most unfortunately, far from satisfactory[10,11]. Increasingly, since the last decade in particular, surgical interventions are being employed in the overall management of MDR-TB, with good results[11.12]. In carefully selected cases adjuvant surgery plays very significant role in achieving bacteriological cure[13,14].

Here is our experience with surgical interventions in treatment failure MDR-TB cases, carried out at our tertiary level health centre.

METHODOLOGY

Between the years 2002-2014, 135 patients underwent surgical procedures for treatment failures MDR-TB were retrospectively analyzed.The mean follow-up period was one year. All patients were HIV negative. None of the patient had any gross evidence of bilateral disease.

The medical and surgical chest specialists have comprehensively evaluated the patients and the decision for surgical interventions was jointly taken in all cases. The works up included baseline laboratory investigations, sputum studies, chest radiograph, contrast enhanced computerized tomography (thorax), bronchoscopy and spirometry. All patients were routinely tested for HIV. Pre-anesthetic check ups were done to assess their fitness to withstand the surgical procedure. Their sputum specimens were positive for mycobacterium tuberculosis and sensitivity tests were requested which confirmed their MDR-TB status.

Three to six months of individually tailored second line ATT prescribed in consultation with the referring pulmonologist, except in the emergency state when earlier intervention was necessary. Informed consent included detailed discussion with patients with particular emphasis on the importance of chest physiotherapy periopertively, cessation of smoking where applicable and the necessity of continuation of second line ATT for further 24 months postoperatively. Most of the patients were nutritionally depleted and efforts were made to ensure as much restoration of general health as possible.

Persistence of sputum culture positive MDR-TB after three to six months of planned chemotherapy was the main indication of surgery in either cavitatory or destroyed lung, lesions. Surgical procedures were mainly of a resectional nature, namely pneumonectomy bilobectomy or lobectomy, depending upon the extent of the disease (Table 1).

In 12 emergency cases with hemoptysis where the general condition of the patient was poor for major resection, alternative intervention as primary thoracoplasty with apicolysis was done. Resectional surgeries were carried out by using double lumen endotracheal tube under general anaesthesia through a standard posterolateral thoracotomy.

Pre-emptive measures, such as intercostals flaps, were used with the initial operation to protect the bronchial stumps. Resected specimens were routinely sent for histopathology examination and AFB staining and culture. Postoperatively, second line ATT was continued for 24 months after sputum conversion.

On out patients follow-up visits, chest x-rays were ordered and sputum culture and sensitivity was done for AFB at one, three, six and twelve months and at the completion of chemotherapy. Disease cure was taken with three consecutive reports were negative and failure was defined with sputum positivety, whereas sputum conversion after a documented sputum negative report constituted relapse.

RESULTS

Out of 135 patients, 81 were males and 54 were female patients in the age group of 14-54 years. All were sputum positive at the time of surgery. There were four early postoperative deaths occurring within 30 days of surgery and two late deaths (Table-II), translating into 2.96% early and 1.48% late mortality. Post operative complications (Table –III) included seven patients with bronchopleural fistula (BPF) with empyema, four patients with wound infections and three patients with apical space. Wound infection was managed conservatively while apical space was managed by apical thoracoplasty. Bronchopleural fistula with Empyema

Table 1: Surgical procedures (n=135)

Variable	Frequency	Percentage
Pneumonectomy	31	22.96
Bilobectomy	32	23.70
Lobectomy	60	44.44
Primary Thoracoplasty	12	8.88
TOTAL	**135**	**100**

Table 2: Mortality (n=06)(4.44%)

Variable	Frequency	Percentage
Early death	04	2.96
Respiratory failure	03	2.22
Myocardial infarction	01	0.74
Late death	02	1.48
Bronchopleural fistula with empyema	02	1.48
TOTAL	**06**	**4.44**

Table 3: Morbidity (n=14) (4.44%)

Variable	Frequency	Percentage
Bronchopleural fistula	07	5.185
Apical space	03	2.22
Wound infection	04	2.96
TOTAL	**14**	**10.37**

was treated by open drainage (pleurocutaneous flaps).Initially all alive 129 patients were sputum negative at one, three and six months postoperatively, but later, seven of them changed to positive status after 12 months of follow-up. Hence on the whole, sputum could be made negative in 122/129 alive patients (94.56%), while six patients died.

DISCUSSION

Current treatment guidelines issued by the World Health Organization (WHO) and US Centres for Disease Control and Prevention suggest that surgical interventions may be appropriate as an adjunct to chemotherapy when skilled thoracic surgeons and good postoperative care are available [10,11] .Surgery plays an important role in the overall management of MDR-TB with acceptable mortality and morbidity [12,14,17].Surgical interventions, in carefully cases, along with second line ATT appear as the most favorable option, since, even with the best available medical therapy alone, provides bacteriological cure in the order of 44-77% vis-à-vis more than 90% success rate with adjuvant surgery [12].

Overall mortality is no longer a prohibitive issue, with most series reporting under 3% early mortality[16,17] and we were also able to ensure acceptable operative death despite the poor general health of our patients.

Though operative mortality has decreased, but significant morbidity continues to be nagging problem of surgery in tuberculosis being reported in about 20-25% of cases in many series[12,18,19] and at least claimed as 15% of major complications by others [16,17].such complications have similar spectrum in most reports, BPF with empyema formation being the most distressing manifestation. Prophylactic use of intercostals muscle flap to reinforce bronchial stump reduces the incidence of post operative bronchopleural fistula, as is evident from our series, with 01 BPF out of 25 resections, treated by open drainage (pleurocutaneous flaps)doing fine during follow-up.

Given that poor nutritional status and sputum positively at the time of surgery are found to have been associated with higher rate of complications, we believe the morbidity in the present series is self –explanatory.

Unequivocal consensus is lacking in the literature regarding the application of preoperative chemotherapy. The rationale behind selecting the exact timing of intervention needs to be logical and scientific and whereas it appears logical to use surgery after defined induction phase timings needs to be worked out. Generally accepted timing of surgery is after three months of carefully prescribed second line ATT, achieving optimal bacterial suppression at the time of surgery where bacillary load is not at a perilous high[14,16,20]. Continuation of drugs for 18-24 months postoperatively seems reasonable by most authors[12,14,16,20], and we advise postoperative chemotherapy for 24 months from the time of documented sputum negativity. Given the economics involved, completion of this task is frankly daunting, if not utopian, in our subset of patients. This is an ongoing study; one year follow up has been completed while second year follow-up is in process.

Indications of surgery in MDR –TB remain a contentious issue. However broad consensus is apparent in the context at least in lateralized disease and generally accepted indications include [12,14,16,20]

a) High risk of treatment failure/relapse, including history of two or more relapse or one or more relapse while on therapy, and persistently positive sputum despite 4 to 6 months of treatment

b) Unilateral Cavitating lesion

c) Localized lesion

d) Intolerance to medication 6 and

e) Bilateral disease with cavitory lesions on one side and infiltrative lesions on the other14,21.

In our series non –resolving MDR was the main indication of surgery in both cavitating & destroyed lung lesions. We did not operate on bilateral lung disease.

Bacteriological cure in many series has been fairly impressive, with well over 90% success achieved with adjuvant surgery[2].Most such series are from western world and there is no significant Pakistani data to compare with our cases of failure to convert. Our success rate of 94.5% sputum conversion is very encouraging. Similarly morbidity and mortality figure of 10.37% and 4.44% further advocate the use of surgery for treatment failure MDR TB.

CONCLUSION

MDR-TB is an ever increasing threat in Pakistan. Chemotherapy alone is costly, toxic and prolonged with <50% success rate. Surgery combined with second line ATT, in carefully selected patients, yields a 94.5% success rate with acceptable morbidity and mortality.

REFERRENCES

1. Alexander J. The Collapse Therapy of Tuberculosis Springfield: Charles. C. Thomas 1937.
2. Iseman MD, Madsen L, Goble M, et al. Surgical intervention in the treatment of pulmonary disease caused by drug-resistant Mycobacterium tuberculosis. Am Rev Respir Dis 1990; 141:623-5.
3. WHO. Multidrug and extensively drug-resistant TB (M/XDR-TB). Geneva: WHO, 2009.
4. WHU. Multidrug-resistant tuberculosis (MDR-TB): 2013 Update. Geneva: WHO, 2013.
5. Espinal MA, Simson L, Laszlo A, Boulahbal F, Kim SJ, Renerio A, et al. For the WHO/ International Union against Tuberculosis and Lung Disease Global Working Group on Anti-tuberculosis Drug Resistance Surveillance. Anti-tuberculosis drug resistance in the world. Report no 2. Geneva: world health organization; 2000. Unpublished documentWHO/TB/2000.278. available from URL[www.who.int/gtb/publications/dru].
6. Pablos-Mendez A, Gowda DK, Frieden TR. Controlling multidrug-resistent tuberculosis and access to expensive drugs: A rational framework. Bull World Health Organ. 2002; 80:489-95; discussion 495-500.
7. World Report 2002. Global Tuberculosis Control: Surveillence, planning, financing WHO/CDS/TB/2002.295.
8. World Health Organization. WHO report on the tuberculosis epidemic, 1997 Geneva: WHO 1997.
9. The Stop TB strategy. World Health Organization; 2010 [updated 2010; cited 2010 21st December 2010]; Available from: http://www.who.int/tb/strategy/en/
10. World Health Organization. Guidelines for the programmatic management of drug-resistant tuberculosis, emergency update. 2008 http://apps.who.int/iris/bitstream/10665/43965/1/9789241547581 eng.pdf.Accessed:5 Oct2015.
11. World Health Organization. Guidelines for the programmatic management of drug-resistant tuberculosis, 2011 update. 2011. http://apps.who.int/iris/bitsream/10665/44597/1/978924150

1583 eng.pdf. Accessed: 5 Oct 2015

12. WHO Global DOTS expansion plan, program in the TB control in high burden countries, WHO/CDS/2001.
13. Loddenkemper R, Sugebiel D, Brendel A. Stategies against multidrug resistant tuberculosis. Eur Respir J 2002; 20:66S-77S.
14. MDR-TB Fact sheet, American Lung Association, March 2005.
15. Pomerantz M, Maden L, Goble M, Isemen M. Surgical intervention in the treatment of pulmonary disease caused by drug resistant mycobacterium tuberculosis. Am Rev Respir Dis 1990; 141:623-5.
16. Albino JA, Reihman LB. The treatment of Tuberculosis. Respiration 1998; 65:237-55.
17. Pomrantz BJ, Cleaveland JC, Olson HK, Pomerantz M. Pulmonary resection for MDR-TB. JThoracic Cardiovasc Surg 2001; 121:448-53.
18. Takeda S, Maeda H, Hayakawa M, Sawabata N, Maekura R. Current surgical intervention for multidrug resistant tuberculosis. Ann Thorac Surg 2005;79:959-63.
19. Shirashi Y, Nkajima Y, Katsuragi N, Kurai M, Takahashi N. Resectional surgery combined with chemotherapy remains the treatment of choice for multidrug resistant tuberculosis. J Thorac Cardiovasc Surg 2004; 128:523-8.
20. Leuvan MV, Groot MD, Sheen KP, Von-oppell UO, Willcox PA. Pulmonary resection as an adjunct in the treatment of multidrug resistant tuberculosis.Ann Thorac Surg 1997; 63:1368-72.
21. Parek SK, Lee CM, Heu JP, Song SD. A retrospective study for the outcome of pulmonary resection in 49 patients with multidrug resistant tuberculosis. Int J Tuberc Lung Dis 2002; 6:143-9.