นิพนธ์ต้นฉบับ

Eleven years of heart transplantation at King Chulalongkorn Memorial Hospital

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Objective : *To review and study the underlying heart diseases, survival period complications and causes of death in heart transplant patients.*

Design : *Retrospective study.*

Setting : *Departments of Pathology, Medicine, Surgery of the Faculty of Medicine, Chulalongkorn University.*

Subjects : *40 heart transplant patients.*

Methods : *Biopsy, necropsy and autopsy materials as well as clinical findings were studied and reviwed.*

Results : *Dilated cardiomyopathy was the most common underlying heart disease Calling for heart transplantation. The first heart transplant patient was still alive and well when this study was done. Bacterial infection, especially pneumonia, was the most common cause of death in the early period, and onset was usually within a few months after operation. Rejection was a less common cause of death in transplant patients in the early period. Most patients died of acute rejection after a 6 month period following operation. Chronic rejection was detected as early at 4 months after transplantation.*

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Conclusions : *Dilated cardiomyopathy is the most common underlying heart disease in transplant patients. Infection is the most common cause of death after heart transplant. After 6 months of operation, acute rejection is the major cause of death.*

Key words : *Heart transplantation, Dilated cardiomyopathy, Infection, Acute rejection.*

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วัตถุประสงค์ : *เพื่อทบทวนและศึกษาโรคหัวใจที่เป็นอยู่ก่อนผ่าตัด ภาวะแทรกซ้อน และสาเหตุตายในผู้ป่วยผ่าตัดเปลี่ยนหัวใจ*

รูปแบบการวิจัย : *การศึกษาแบบย้อนหลัง*

สถาบันการศึกษา : *ภาควิชาพยาธิวิทยา, ภาควิชาอายุรศาสตร์ และภาควิชาศัลยศาสตร์ คณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย*

ผู้เข้าร่วมการรศึกษา : *ผู้ป่วยผ่าตัดเปลี่ยนหัวใจจำนวน 40 รายและผู้ป่วยที่เสียชีวิตจำนวน 26 ราย*

ผลการวิจัย : *โรคกล้ามเนื้อหัวใจพิการชนิดขยายเป็นพยาธิสภาพของผู้ป่วยที่พบบ่อยที่สุด การติดเชื้อจากแบคทีเรียโดยเฉพาะที่ปอดเป็นสาเหตุที่พบบ่อยในระยะแรกภายหลังการผ่าตัด การติดเชื้อจากเชื้อราและไวรัสพบบางรายเท่านั้นภายหลัง 6 เดือนไปแล้ว การสลัดกราฟท์ชนิดเฉียบพลันเป็นสาเหตุตายมากกว่า*

วิเคราะห์และสรุป : *การติดเชื้อจากแบคทีเรีย เชื้อราและไวรัสเป็นสาเหตุตายในระยะ 6 เดือนแรก ภายหลังจากนี้ การสลัดกราฟท์ (rejection) เป็นสาเหตุตายที่พบได้บ่อยกว่า*

The first heart transplantation in Thailand and in an ASEAN country was successfully performed on December 18, 1987 at King Chulalongkorn Memorial Hospital.[1] By December 31, 1998, 40 heart transplantations have been done at this institution. Two major complications and causes of death after transplantation are infection and rejection.[2,3] This study looks at the underlying heart diseases and the occurrence of infection and rejection among the transplant patients at King Chulalongkorn Memorial Hospital.

Meterial and Methods

Materials

Forty heart transplant patients at King Chulalongkorn Memorial Hospital from December 18, 1987 to December 31, 1998 were included in this study. Endomyocardial biopsy was routinely used for monitoring rejection and infection.[4]

Methods

Clinical findings, microbiologic laboratory results, imaging reports, cytology, biopsy, necropsy and autopsy materials were reviewed and studied.

Routine as well as special histochemistry stainings were used for pathologic studies. Immunohistochemistry for T cell, B cell, histiocytes and cytomegalovirus was done.[5,6] Special stains for bacteria, nocardia, acid-fast bacili and fungi were also used.

Etiologic diagnosis of pneumonia was based on histopathology, stainings and /or cultures.

The survival period after transplantation was classified as early and late, witin 6 months and after.

Results

Forty patients with ages ranging from 12 to 63 had heart transplants. The underlying heart diseases are shown in Table 1. Dilated cardiomyopathy was the most common disease and occurred in 21 patients. Ischemic heart disease was the second most common disease and occurred in 9 patients. Twenty-six of the 40 patients had complications and died. Infection was the major cause of death in 14 patients, as shown in Table 2. Eight patients died in the first month after transplantation (Table 2 pt. No. 3, 6, 7, 8, 9,12,13,14) (Fig. 1) Bacterial pneumonia was seen in 6 patients (Fig. 2)(Table 2, pt. \ No. 6,8,9,12,13,14). Pulmonary aspergillosis was seen in 1 patient (Table 2, pt. No. 8). The other 6 patients died at 4 months, 5 months, 1 year 2 months, 2 years 10 months and 6 years after transplantation (Fig.3) (Table 2, pt. No. 1,2,4,5,10,11). Nocardia brain abscess was seen in 1 patient who survived to 4 months after transplantation (Table 2. pt. No. 2). Bacterial pneumonia with myocarditis was seen in 1 patient (pt. No 10). One patient (Table 2. pt. No. 11) had herpes encephalitis and pulmonary T.B.

Table 1. Underlying diseases in 40 heart transplant patients

Diseases	No. of patients
Dilated cardiomyopathy	21
Ischemic heart disease	9
Valvular heart disease	6
Giant cell myocarditis, idiopathic	2
Congenital heart disease	2
Total	40

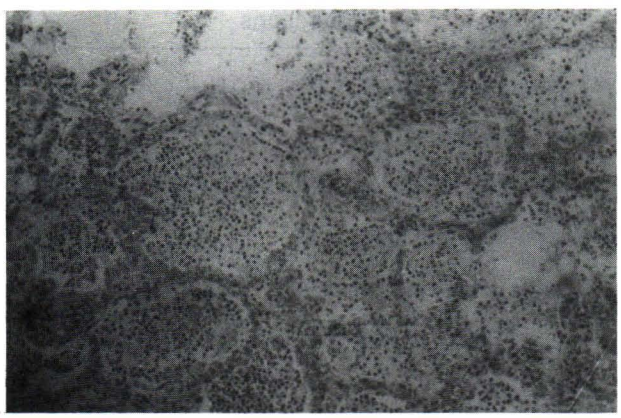

Figure 1. Bacterial bronchopneumonia. H & E x 400

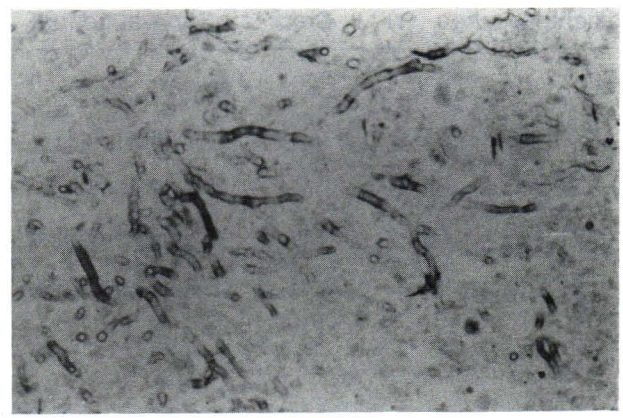

Figure 2. Pulmonary aspergillosis. GMS x 400

Figure 3. Nocardia asteroides brain abscesses.

Three patients (Table 2. pt. No. 1,4,5) who survived more than 1 year after transplantation also died of severe infection. Two patients had sepsis associated with acute renal failure (Table 2,pt.No. 4,5) and 1 patient who survived 6 years died of bacterial pneumonia with aspergillosis (Table 2. pt. No. 1).

Twelve patients died of rejection, as shown in Table 3. Acute cellular rejectionwas seen in 8 patients (Table 3, pt. No.1,2,4,7,8,9,10,12) Three of 8 patients had severe acute cullular rejection (Fig. 4) (Table 3. pt. No. 9, 10, 12). Acute cellular rejection was seen in this patients in 3 months 9 months and 11 months after transplantation. Chronic rejection with accelerated coronary atherosclerosis was the cause of death in 4 patients (Fig. 5)(Table 3, pt. No. 3,5,6,11) who survived more than 1 year after transplantation.

Table 2. Infections as cause of death in 14 patients.

Patient No.	Age (yr)	Sex	Survival period	Infections
1	43	F	6 years	Severe bacterial pneumona and aspergillosis
2	21	M	4 months	Nocardia brain abscess
3	52	M	2 months	Acute aortitis with abscess and dissecting hematoma
4	55	M	2 year 10 months	Acute renal failure with sepsis
5	60	M	1 year 10 months	Acute renal failure with sepsis
6	55	M	2 months	Bilateral tension pneumothorax with pneumonia and enterocolitis
7	35	M	12 days	Postoperative bleeding with infected surgical wound
8	50	F	2 months	Bacterial pneumona with aspergillosis
9	47	F	1 month 12 days	Bacterial pneumonia
10	42	M	4 months	Myocarditis with pneumonia
11	53	M	5 months	Herpes encephalitis, pulmonary T.B.
12	45	M	11 days	Bacterial pneumonia
13	50	M	1 month	Bacterial pneumonia
14	63	M	16 days	Bacterial pneumonia

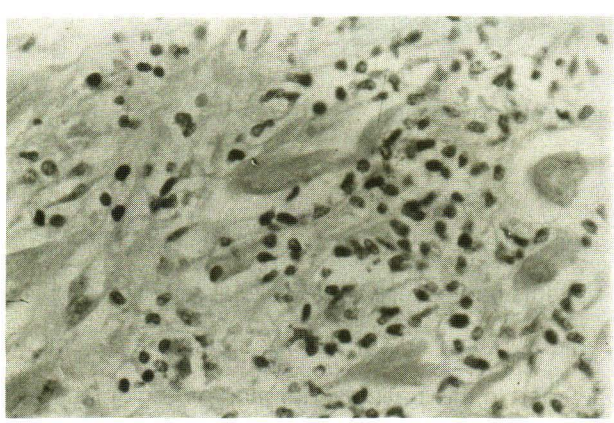

Figure 4. Severe acute cellular rejection, heart H & E x 400

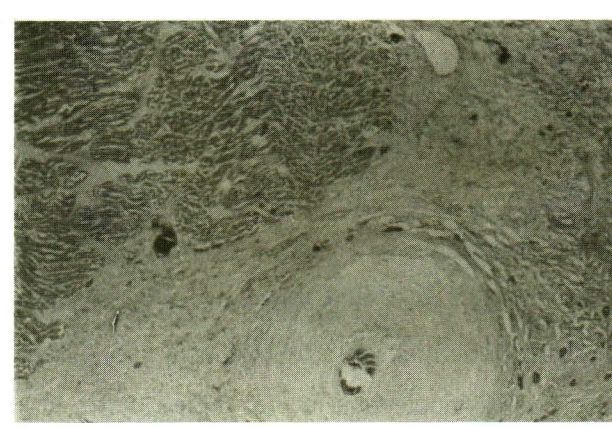

Figure 5. Accelerated coronary atherosclerosclerosis showing concentric intimal thickening with marked narrowing of lumen. H & E x 400

Table 3. Acute and chronic rejection as cause of death in 12 patients.

Patient No.	Age (yr.)	Sex	Survival period	Rejection
1	52	F	11 months	Moderate, acute, heart failure
2	12	M	4 months	Moderate, acute, heart failure
3	31	M	1 year, 8 months	Chronic, heart failure
4	39	M	6 months	Moderate, acute
5	58	M	2 years	Sudden death
6	30	F	2 years 2 months	Sudden death
7	47	M	1 month	Sudden death
8	60	M	11 months	Moderate, acute, heart failure
9	41	M	3 months	Severe acute cellular rejection
10	37	M	9 months	Severe acute cellular rejection
11	40	M	9 years 2 months	Chronic, heart failure
12	22	M	11 months	Severe acute cellular rejection

Discussion

Early infections are usually caused by bacteria that colonize in surgical wounds or anastomotic sites, [7] as seen in our series (Table 2, pts. No. 3,6,7) After 2 months, risk of infection is from by higher organisms such as fungi, nocardia and herpes due to suppression of cell mediated immunity as seen in our patients (Table 2, pts. No. 1,2,8,10,11). Aspergillosis is commonly seen after 1 month of heart-lung transplantation. Fungal infection remains one of the most challenging opportunistic infections after organ transplant.[8] Treatment is still unsatisfactory, probably due to inappropriate antifungal treatments. Cytomegalovirus infection was not seen in our series, and may be due to the high prevalence of serum antibodies in most Thai patients, or may be because of the small number of patients in our series.

Severe acute cellular rejection is still the major cause of death within one year after transplantation as seen is our patients (Table 3, pts No. 9, 10, 12). Chronic rejection with accelerated coronary athrosclerosis was seen in one of our patients who survived more than one year after transplant.

Conclusions

The first Thai heart transplant patient was still alive and well 11 years after his surgery. Infection was the most common cause of death regardless of survival time. The causative agents were mostly bacteria. Higher bacteria and fungi were seen in few cases. Rejection was the most common cause of death after the first 6 months.

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