รายงานผู้ป่วย

The first successful heart transplantation in Thailand and the Asean region.

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Ongcharit C, Sanpradit M, Leungtaviboon K, Bunyatpiyapat S, Waikitipong S, Ongcharit C.N., Meenapinan K, Surawong K, Songpong P, Suwanakul P, Jimakorn P, Charoenwongese P. The first successful heart transplantation in Thailand and the Asean region. Chula Med J 1988 Sep; 32(9): 835-840

Cardiac transplantation is now accepted as a form of therapy for advanced, end-stage cardiac diseases with normal pulmonary vascular resistance. Generally the indications for orthotopic heart transplantation include cardiomyopathy and severe coronary artery disease with myocardium dysfunction or unfavorable anatomy for bypass graft. We have performed the first case of cardiac transplantation in Thailand and the Asean region on December 18, 1987. The recipient was a 19 years old man who suffered from dilated cardiomyopathy. He had multiple episodes of congestive heart failure and ventricular arrhythmia. The donor was a 46 years old woman with intracerebral hemorrhage. She had brain-death and was judged to be appropriate for her cardiac donation. The operation was performed and the donor heart beat well. The perioperative course was uneventful. The immunosuppression included cyclosporin A, Azathioprine and Prednisolone. Now 7 months after the operation the recipient can lead a near normal life. He has no dyspnea or cardiac arrhythmia.

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Received for publication. July 11, 1988.

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ในปัจจุบันนี้เป็นที่ยอมรับกันว่าการผ่าตัดเปลี่ยนหัวใจเป็นการรักษาวิธีหนึ่ง สำหรับโรคหัวใจระยะสุดท้าย ซึ่งมีสภาพของหลอดเลือดภายในปอดเป็นปกติ โดยทั่วไปข้อบ่งชี้ที่จะทำผ่าตัดเปลี่ยนหัวใจโดยวิธีตัดเอาหัวใจเดิมออกและเปลี่ยนเอาหัวใจจากผู้อื่นมาใส่ให้ ที่ทำกันส่วนมาก ได้แก่ โรคกล้ามเนื้อหัวใจพิการ และโรคหลอดเลือดโคโรนารี่ ที่ทำให้กล้ามเนื้อหัวใจหมดสภาพที่จะทำหน้าที่ได้หรือหลอดเลือดโคโรนารี่ที่เป็นโรคนั้นไม่เหมาะสมที่จะทำผ่าตัด วิธีต่อเบี่ยงเส้นเลือด (bypass graft) ให้ได้ เราได้ทำการผ่าตัดเปลี่ยนหัวใจเป็นรายแรกในประเทศไทยและประเทศกลุ่มอาเซียนเมื่อวันที่ 18 เดือนธันวาคม พ.ศ. 2530 ให้กับผู้ป่วยชายอายุ 19 ปี ป่วยด้วยโรคกล้ามเนื้อหัวใจพิการโป่งพอง (Dilated cardiomyopathy) มีประวัติหัวใจวายและการเต้นของหัวใจผิดปกติหลายครั้งในระยะ 10 เดือนที่ผ่านมา การรักษาด้วยยาอย่างเต็มที่ไม่ได้ผล ผู้ป่วยใกล้จะเสียชีวิตคือ เป็นโรคหัวใจระยะสุดท้าย (End-stage heart disease) มีวิธีรักษาที่จะช่วยชีวิตได้วิธีเดียวคือ ต้องทำการผ่าตัดเปลี่ยนหัวใจให้ใหม่ หัวใจที่นำมาผ่าตัดเปลี่ยนให้ นำมาจากผู้บริจาค (donor) เป็นผู้หญิงอายุ 46 ปี เสียชีวิตจากโรคเส้นโลหิตในสมองแตก อยู่ในสภาพสมองตาย (brain death) มีหัวใจอยู่ในสภาพเหมาะสมและเข้ากันได้กับผู้ป่วย (recipient) ภายหลังการผ่าตัดหัวใจที่เปลี่ยนให้ใหม่บีบตัวได้ดี ผู้ป่วยฟื้นจากการผ่าตัดโดยไม่มีภาวะแทรกซ้อนใด ๆ ยากดภูมิต้านทานที่ให้อยู่ ได้แก่ ไซโคลสปอรินเอ (Cyclosporin A) อซาไทโอพรีน (Azathioprine) และเพรดนิโซโลน (Prednisolone) ขณะเขียนรายงานนี้ ได้ทำผ่าตัดมาแล้วเป็นเวลา 7 เดือน ผู้ป่วยสามารถออกกำลังกายและใช้ชีวิตได้อย่างปกติ ทั้งการหายใจและการเต้นของหัวใจเป็นปกติ

CASE HISTORY:

A man, P.B., born in the Surin Provinec of northeastern Thailand was 19 years old ten months ago when he noticed frequent episodes of dyspnea, and could not do his ordinary work. He was admitted to the local hospital and treated for heart failure with small improvement. He took medication daily and had to rest in the hospital for parenteral medication and oxygen several times. Finally he was referred to Chulalongkorn Hospital. His initial physical findings included blood pressure 100/80 mmHg., HR 90/min irregular, RR 20/min. His jugular veins were engorged 3 cm. above the sternal angle. The cardiac point of maximum impulse was on the 6th ICS 2 cm. lateral to the midclavicular line. No cardiac murmurs were detected. He also had hepatomegaly. His initial laboratory tests were within normal limits. The chest roentgenography showed evidence of cardiomegaly, generalized. (fig. 1) The electrocardiogram revealed frequent PVC and occasional APC, LVH with secondary ST-T changes. An echocardiogram was made and revealed evidences of low cardiac output state. No organic lesions of the valves were seen. The calculated cardiac ejection fraction is only 22 per cent. Cardiac catherization was done. He had high left ventricular end diastolic pressure (LVEDP) without evidence of valvular disease. His left ventricle contracted poorly. The calculated pulmonary vascular resistance was only 3 Wood units per square metre.

During the admission, he had to be transferred to the intensive care unit due to congestive heart failure and cardiogenic shock with frequent ventricular ectopic beats, shown by electrocardiogram (fig. 2). After response to medical treatment he had to take digitalis, diuretic, dysopyramide and vasodilators and he was in functional class 4.

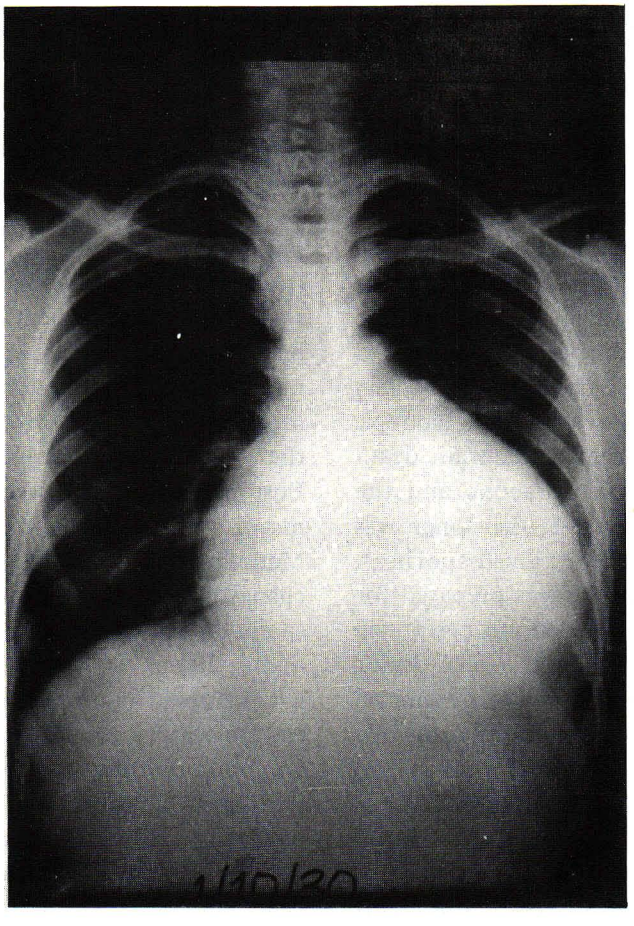

Figure 1. Preoperative chest x-ray of the recipient.

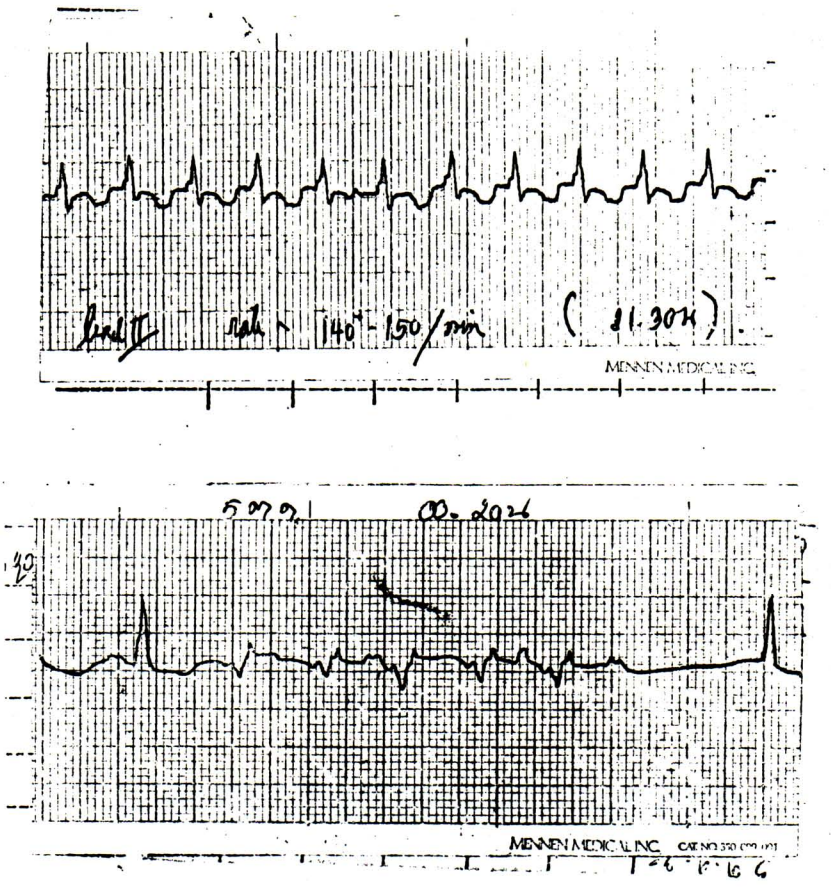

Figure 2. Preoperative electrocardiographic record of the recipient.

On the evening of December 17th, 1987, we were informed by the neurosurgeons that there was a brain-dead patient. She had normal chest x-ray, EKG, and her blood was the same group and matched well with the recipient's. Her heart could maintain normal blood pressure and pulse-rate without inotropic support. After the announcement of brain death by the neurologists and neurosurgeons and the consent was signed by her relative, the donor was moved to the operating room. Cyclosporin A was given to the recipient and he was prepared for open-cardiac surgery. The operation was performed in the two nearby operating rooms. The donor heart was taken from the donor after it was examined and judged to be in good condition. Meanwhile the recipient's chest was opened and venous and arterial cannulations was made to prepare for cardiopulmonary bypass. The recipient's heart was excised near totally, leaving a posterior portion of the left atrium, the interatrial septum and a cuff of right atrium including the SVC and IVC, and the ascending aorta and main trunk of the pulmonary artery. The donor heart was trimmed and anastomoses were made using continuous polypropylene suture with the recipient's left atrium, right atrium, pulmonary artery and finally the aorta. After removal of the aortic cross-clamps, methylprednisolone was given to the recipient intravenously. The donor heart beat forcefully, spontaneously, and could maintain the blood pressure with the aid of low dose inotropic drugs. Isoproterenol was given to maintain the heart rate at about 110 beats per minutes. Postoperative course was rather benign. He was monitored in an isolated intensive care unit. Methylprednisolone was given for three doses and changed to oral prednisolone. Maintenance cyclosporin A was given orally to maintain the blood level above 200 ng/cc. Azathioprine was also given to augment immunosuppression. Transvenous endomyocardial biopsies were performed and showed only mild rejection which turned to normal state in the lastest biopsy. Now the patient lives comfortably and can do daily activities without dyspnea. The chest x-ray showed a smaller and normal new heart compared to the preoperative size. (fig. 3) Only immunosuppressive drugs and diuretics are required for the maintenance medical treatment. Soon he will be expected to leave the hospital and go to work. However, close follow up is required even late in to the postoperative period.

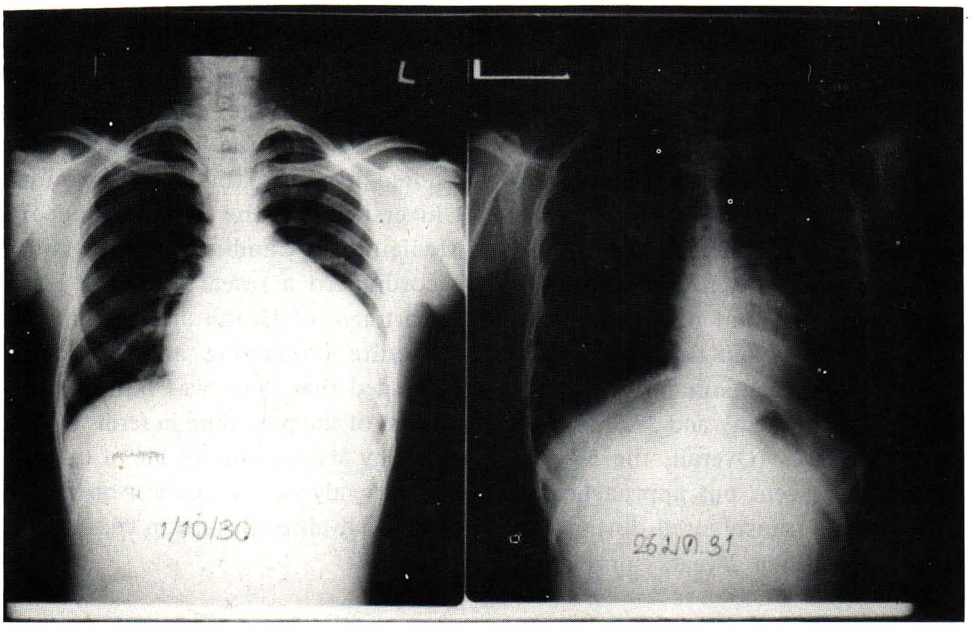

Figure 3. Chest x-ray 5 weeks after the transplantation (right), compared to the preoperative chest x-ray (left).

DISCUSSION:

Dilated cardiomyopathy was previously judged an incurable and fatal disease. Medical treatment can only partially relief the symptoms, and the patients usually die of either heart failure or malignant arrhythmias within months. After the modern era of heart transplantation began in December 1967 when Christiaan Barnard reported a successful transplantation of the human heart at Cape Town, South Africa[1], heart transplantation has proved to be the answer for this disease. Previously the result of heart transplantation was poor, but with the advent of Cyclosporin A in 1979, the result of the operation has improved enormously. Cyclosporin is a cyclic peptide consisting of 11 amino acids. It is effective as an immunosuppressant because of specific reversible inhibition of immunocompetent lymphocytes and seens preferentially to inhibit T-lymphocytes.[2]

Two forms of acute rejection may be seen in the cardiac transplant patient. Hyperacute rejection generally results from ABO incompatiblity or from a positive lymphocytotoxic cross match and occurs within the first few hours after transplantation. The more common type of acute rejection is a cellular phenomenon that is first seen 10 to 14 days following transplantation, with the patient at highest risk over the ensueing 60 days. Signs and symptoms occur late in the course of rejection. The transvenous endomyocardial biopsy is a sensitive method to detect rejection. The biopsy is read using the criteria described by Billingham[3] and rejection is graded into mild, moderate or severe degree. At most transplant centers, mild rejection is not treated, and the biopsy is repeated in 4 days. Moderate rejection is treated with intravenous methylprednisolone. Severe rejection is treated with the same regimen as moderate rejection, but in addition antihuman thymocyte globulin is given each day for 3 to 6 days.[4] Because late acute rejection may occur, patients are maintained on chronic immunosuppression with both prednisolone and cyclosporin in tapering doses.

Major problems in the long-term recipient have included retransplantation, malignancy, and graft atherosclerosis. Indications for retransplantation include refractory ventricular tachyarrhythmias, intractable acute rejection, and the development of severe graft coronary atherosclerosis. Graft atherosclerosis was thought to have resulted from immune injury of the coronary artery intima, causing complement and platelet activation, platelet aggregation, and release of mitogenic factor with eventual myointimal thickening and atherosclerosis. Griepp have demonstrated a significantly lower incidence of graft atherosclerosis in patients treated with warfarin and dipyridamole following transplantation[5] The incidence of graft atherosclerosis is significantly higher in hearts taken from donors 35 years of age or older. A lower incidence has been found both in patients with HLA-A2 antigen matches and in

those with serum triglyceride levels less than 280 mg. per dl.[6] Attention to diet and exercise in the post-transplant period is therefore of major importance.

The world-wide results of cardiac transplantation are very encouraging. The first official report of the International Heart Transplantation Registry[7] contains some pertinent data. The registry represents the results of 21 transplantation centers. Both orthotopic and heterotopic transplant recipients are included. A total of 807 patients were registered between 1968 and December 1983. Overall 53.4 per cent of patients underwent heart transplantation for cardiomyopathy and 37.3 per cent for coronary artery disease. Overall, the 5 years survival is around 35 per cent but approaches 60 per cent in those patients transplanted during and after 1978. Of interest is the 2-years survival of almost 75 per cent in 340 patients treated with cyclosporin compared with a 2-years survival of 43 per cent in 447 patients treated with conventional immunosuppression. The costbenefits of and the quality of life in the heart transplant programmes studied by Department of Economic at Brunel University and the Department of Community Medicine at Cambridge University in England according to a research report from the British Department of Health and Social Security Office[8] are quite interesting and encouraging. It was concluded that there was little doubt of the effectiveness of the procedure in terms of the improvement in quality and quantity of life of transplanted patients. It is currently viewed by most of the world as a valid form of advanced therapy in end-stage heart disease.[9]

References

1. Barnard CN. Human cardiac transplantation: an evaluation of the first two operations performed at the Groote Schuur Hospital, Cape Town. Am J Cardiol 1968 Oct; 22(4): 584-596
2. White DJ, Nagao T, Davies HS. Experimental transplantation in small animals. In: White DJG, ed. Cyclosporin A. New York: Elsevier Biomedical Press, 1982.89
3. Billingham ME. Diagnosis of cardiac rejection by endomyocardial biopsy. Heart Transplant 1981; 1(1): 25-30
4. Levett JM, Karp RB. Heart transplantation. Surg Clin North Am 1985 Jun; 65(3): 613-635
5. Griepp RB, Stinson EB, Bieber CP, Reitz BA, Copeland JG, Oyer PE, Alderman E. Control of graft arterio-sclerosis in human heart transplant recipients. Surgery 1977 Mar; 81(3): 262-269
6. Pennock JL, Oyer PE, Reitz BA, Jamieson SW, Bieber CP, Wallwork J, Stinson EB, Shumway NE. Cardiac transplantation in perspective for the future: Survival Complications, rehabilitation and cost. J Thorac Cardiovasc Surg 1982 Feb; 83(2): 168-177
7. Kaye MP. The International Heart Transplantation Registry: First official report-May 1984. Heart Transplant 1984; 3: 278-279
8. Buxton MT, Acheson R, Caine N, Gibson S, O'Brien B. Costs and Benefits of the Heart Transplant Programmes at Harefield and Papworth Hospitals. Department of Health and Social Security Office of the Chief Scientist. Res Rep 1985; 12: 153-159
9. Schoeder JS, Hunt S. Cardiac transplantation: update 1987. JAMA 1987 Dec 4; 258(21): 3142-3145