Analysis of restenosis following closed mitral valvotomy; healing of wounds

Kapalı mitral valvotomi sonrası restenoz analizi; yara iyileşmesi

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Rheumatic mitral stenosis is a major public health problem in developing countries. Closed mitral valvotomy (CMV) was previously utilized to treat patients who had mitral stenosis with successful outcome and remains an alternative approach in developing countries (1). Limited information is available on the healing of wounds and specific cellular changes that occur on the surface of abnormal mitral valve leaflets and commissures, especially in previously operated patients with CMV (2). For this reason, we used light and scanning electron microscopy to investigate the restenosed mitral valves.

All of the valve specimens were obtained from the patients who had re-mitral stenosis and previously treated with CMV. The patients' mean age was 47.6±8.6 years [range: 33-59 years]. Mean time between initial CMV and reoperation was 15.1±3.8 years [range: 10-24 years]. All of the patients had a history of rheumatic fever in childhood. The mean mitral valve gradient and area were calculated as 16.9±5.9 mmHg and 0.9±0.2 cm^2, respectively.

Each valve specimen was divided into 4 sections: anterolateral and posteromedial commissures, anterior and posterior leaflets. The light and scanning electron microscopic examinations were performed in these sections. Cellularity of the different localizations was evaluated semi-quantitatively (Fig. 1). In light microscopy, commissures had the mean cellularity score of 0.89±0.6 and 0.67±0.5, ($p<0.0001$). Leaflets had the score of 1.67±0.5. This difference was found statistically significant and the leaflets had higher cellularity score than the commissures ($p<0.0001$).

Upon examination of the valves with scanning electron microscope, the endothelium forming the valves was found to be altered especially at the commissural localization. The endothelial cells were elongated in shape with some blood elements attached to them. These blood elements were polymorphonuclear leucocytes and platelets (Fig. 2a). There were microvilli and increased surface structures like filiform processes on the endothelial cells (Fig. 2b). There were also erythocytes attached to the endothelial cells and also embedded in the subendothelial fibrin (Fig. 2c).

Closed mitral valvotomy may be the first surgical choice of treatment of mitral stenosis in the developing countries for suitable patients although the best approach (percutaneous or open surgical interventions) is still controversial in developed countries. Some authors showed that open commissurotomy improved hemodynamic values to a greater extent than closed commissurotomy. On the other hand, some others observed no difference between the techniques (3). It was also suggested that indication for CMV is an unusual circumstance where a cardiopulmonary bypass is either not available or contraindicated, such as during pregnancy (3). Turi et al. (4) and Reyes et al. (5) found comparable hemodynamic results and low restenosis rates following both CMV and balloon valvotomy.

Closed mitral valvotomy is a very useful surgical technique to treat the mitral stenosis in the areas where rheumatic valve disease is epidemic and delays the open surgery. However, reoperation may be required during the follow up. Rutledge et al. (6) reported an 18% incidence of reoperations within a period of 9.6 years after CMV. Saleno et al. (7) reported a 32% incidence of reoperations over a period of 25 years. In our previous study freedom from reoperation after CMV was 81.4±1.3% at ten years, and 141.1 months was the median time required for reoperation (1).

In this study, we investigated a subgroup consisted of the patients undergoing mitral valve replacement with previously performed CMV. The main pathological finding was severe mitral valve stenosis with reduced mitral valve area and fusion of the commissures. This may be caused by rheumatic reactivation process. We found that mitral valves following the CMV progressed to restenosis requiring mitral valve replacement in approximately 15 years.

Limited information is available on the healing of wounds in the mitral valve following CMV. It is important to study the pathology of the heart valves excised during heart valve surgery. The healing of mitral valvular wounds is a slow process that requires between eight and 12 weeks for the formation of a dense collagen scar at the edges in a sheep study (8). In order to clarify mechanisms of restenosis following percutaneous transluminal mitral commissurotomy, Tsuji et al. (9) studied 253 patients with a mean follow-up period of 8±3 years. Twelve patients underwent mitral valve replacement due to restenosis. Visual inspection of the valves did not reveal fusion of the

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commissures. All resected mitral valves had evidence of end-stage rheumatic valvular disease, such as severe fibrosis and calcification. Therefore, histological findings suggested that restenosis is based on end-stage valvular disease (9).

A tear may be occurring anywhere in the mitral valve, in leaflets and commissures during the CMV operation. In this area, acute and chronic wound healing took place following the operation. As a result, scar formation was seen. Connective tissue proliferation was usually seen during wound healing. Connective tissue and parenchymal cells cause remodelling that leads to collagenization and wound shrinkage. The scar area was seen to be irregular and shorter than the original areas because of contraction. Scar areas were collagenized, eosinophilic and had decreased cellularity microscopically. Commissural fusion, leaflet thickening and alteration of the subvalvular apparatus are dominant mechanisms causing clinically important mitral stenosis of rheumatic origin (10).

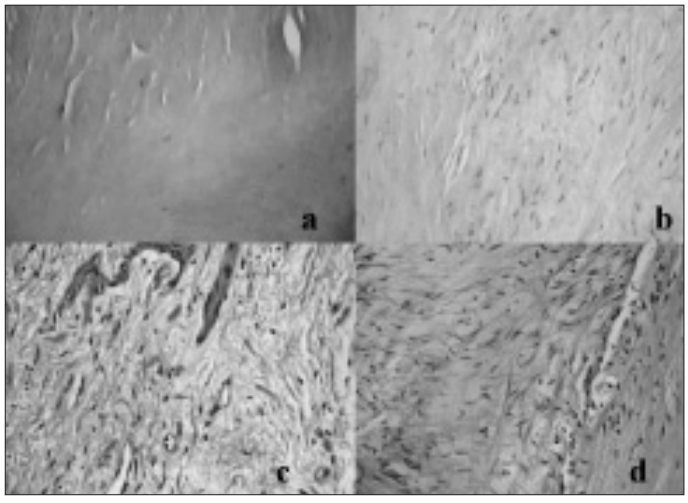

Figure 1. Light microscopic views according to the cellularity classification (hematoxyline and eosin x 20). a - score 0, b - score 1, c - score 2, d - score 3.

In our patients, macroscopically, commissures were observed irregular, and the mean cellularity score was smaller at the commissures when compared with the leaflets.

In conclusion, macroscopic and microscopic findings suggest that splitting and restenosis occurred at the commissures following the CMV.

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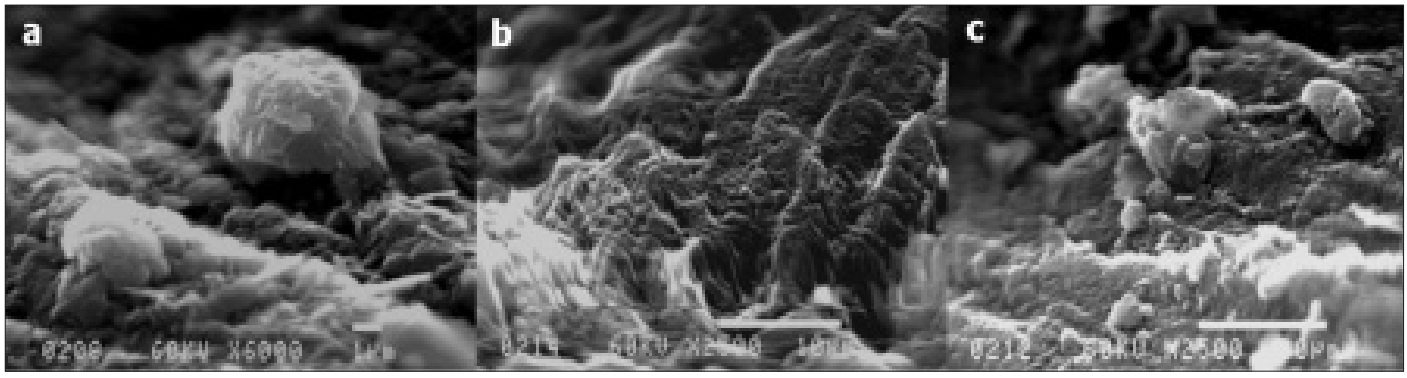

Figure 2. Scanning electron microscopic views a. Blood elements as PMN leucocytes and platelets are attached to endothelium (X6000). b. There are microvilli and increased surface structures like filiform processes on the endothelial cells (X2500). c. There are erythrocytes attached to the endothelial cells and also embedded in the subendothelial fibrin (X2500)