Characteristics of Hearts at Necropsy in Patients Treated Chronically With Prednisone (The Corticosteroid Heart)

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It is known that long-term corticosteroid therapy increases fatty deposits in several human tissues. To quantify the quantity of fatty deposits in the heart in patients on prednisone, we examined the heart at necropsy in 37 patients who had received long-term corticosteroid therapy (prednisone in 34) and compared certain findings in them to those in 194 (steroid-naïve) patients also studied at necropsy at Baylor University Medical Center, Dallas, in a 3-year period (2013, 2014, and 2015). Significant differences between the 2 groups were found in age, gender, and frequency of coronary artery disease but not in body mass index, frequency of massive cardiac adiposity, heart weight, or frequency of systemic hypertension or diabetes mellitus. Furthermore, no significant differences were observed in the patients taking ≤20 mg versus those taking >20 mg daily of prednisone. In conclusion, this study observed no significant differences in body mass index, frequency of cardiac adiposity (floating heart), heart weight, or frequencies of systemic hypertension or diabetes mellitus in the patients receiving or not receiving prednisone for a long term, but the prednisone-treated patients were younger, more often women, and had a lower frequency of severe narrowing of ≥1 major coronary arteries. **(Am J Cardiol 2016;118:1935−1940)**

Corticosteroid medicines including prednisone and its equivalents are splendid drugs for multiple different conditions, but unfortunately, they have some detrimental effects on many body organs including the heart.[1−6] The latter include an increase in blood pressure and therefore frequent left ventricular hypertrophy, an increased frequency of atrial fibrillation, and an increase in cardiac adiposity, among others. In 2015, Kitterer et al.[7] described by cardiac magnetic resonance imaging an increase in cardiac fatty deposits in corticosteroid-treated patients with rheumatic diseases compared to controls. This report describes the heart at necropsy in a group of patients treated for a long term with prednisone and compares findings in them to a control necropsy group not treated with corticosteroids.

Methods

During 3 full years (2013, 2014, and 2015), a total of 266 autopsies were performed in adults (all aged >20 years) at Baylor University Medical Center by Dr. Guileyardo: in 15 patients, the autopsy permit did not allow examination of the heart; in 11 cases, Dr. Roberts did not examine the heart, and in 9 cases, the autopsy was in subjects who previously had undergone cardiac transplantation, that is, donor heart only to examine. These 35 cases were eliminated from this study. The remaining 231 cases form the study population. Of them, 37 (16%) had received prednisone for a long term. The cardiac findings in them were compared with the other 194 autopsy cases (84%) in whom no corticosteroid drug had been administered.

Before weighing the heart, the parietal pericardium was entirely removed from the heart, the pulmonary trunk was incised about 2 cm cephalad to the level of the pulmonary valve, the ascending aorta was incised about 2 cm cephalad to the sinotubular junction, and the heart was opened in one of the following manners: The hearts were opened in both left and right parasagittal cuts (Figure 1); the ventricles were cut in "bread-loaf" fashion parallel to the posterior atrioventricular sulcus, each about 1 cm in thickness (Figure 2); or the hearts were opened in a 4-chamber cut exposing all 4 chambers in 1 view. Before weighing the heart after these cuts, each surface was gently patted with paper towels to remove any extraneous formaldehyde or water. Each of the 227 hearts was weighed by Dr. Roberts on 1 of 2 scales (Ohaus Scout Pro Scale accurate to 0.1 g or Acculab Vicon Digital Scale accurate to 1.0 g). The heart weighing was done within a week of the autopsy after fixation of the heart in formaldehyde. After describing and weighing the heart, the medical records were reviewed in each of the 231 cases.

The underlying condition prompting the prednisone therapy was lung disease in 22 patients (63%), kidney disease in 4 (11%), liver disease in 3 (9%), arthritis in 3 (9%), arteritis in 2, myasthenia gravis in 1 (3%), bone

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Figure 1. Heart (515 g) in a 46-year-old man (body mass index 35 kg/m^2) who had idiopathic pulmonary fibrosis and received prednisone 40 mg/day over several years. *(Upper left)* The front of the heart and adipose tissue covers most of the surface of the ventricles. *(Upper right)* The back of the heart. *(Lower left)* After a left parasagittal cut. *(Lower right)* After a right parasagittal cut. The quantity of subepicardial adipose tissue is massive, and the heart floated in a container of formaldehyde.

marrow transplant in 1 (3%), and stem-cell transplant in 1 patient (3%).

Analyses were done using STATA 14.1. Categorical variables were presented as proportions, and continuous variables were presented as mean (SD) or median (range) as applicable. We used Chi-square or Fisher's exact test to compare proportions and Student *t* test or Wilcoxon rank-sum test to compare continuous variables as appropriate. Patients treated with prednisone were gender matched with those patients not on prednisone in a ratio of 1:2. The differences in the baseline characteristics were evaluated individually by a conditional logistic regression analysis. The analysis was repeated including only the patients treated with prednisone categorizing them based on the median dose of prednisone.

The study was approved by the Baylor University Medical Center Institutional Review Board.

Results

Findings in the 37 patients and in the 194 controls are summarized in Table 1. There were significant differences in the 2 groups in gender, age, and frequency of $\geq$1 epicardial coronary arteries being narrowed $>$75% in cross-sectional area (Table 1) but not in frequency of massive cardiac adiposity (Figure 3), body mass index (BMI, Figure 4), heart weight, or frequencies of systemic hypertension or diabetes mellitus. By gender-matched analysis, we found no differences in patients with and without prednisone use (Table 2). Patients receiving $\leq$20 mg/day of prednisone (22 patients) compared to those receiving $>$20 mg/day of prednisone (15 patients) or its equivalent (3 of 37 patients) are summarized in Table 3. Findings in each of the 37 prednisone patients are detailed in Table 4.

The highest prednisone dose varied from 5 to 150 mg (mean 34 mg, median 20). The exact period the patients