Acromegaly, the Systolic Click Syndrome, and Group D Streptococcal Endocarditis

B. Jugdutt, M.B., Ch.B.;** C. Basualdo, M.D.;†
H. Freeman, M.D.;‡ and P. Crockford, M.D.§

A syndrome consisting of an apical systolic click and late systolic murmur appeared over a period of three months

CASE REPORT

A 48-year-old man presented with acromegaly in June 1973. Classic clinical features were present. The diagnosis was confirmed by finding an expanded sella turcica on skull x-ray films, an intrasellar lesion on fractional pneumoencephalographic examination, and elevated plasma levels of growth hormone (greater than 50 ng/ml) by radioimmunoassay.2,3 unsuppressed by hypoglycemia. Other abnormal findings were glucose intolerance, a low plasma level of testosterone, and elevated urinary levels of hydroxyproline.4 There was neither past nor family history of cardiac disease. In July 1973, the patient underwent a transphenoidal hypophysectomy for an eosinophil adenoma. Plasma levels of growth hormone fell below 50 ng/ml after surgery, and the patient was discharged on a treatment regimen of cortisone and testosterone.

In June 1973, the patient had no cardiac complaints. Examination then revealed a blood pressure of 140/100 mm Hg, no cardiac murmurs, no cardiomegaly on chest radiographs, and atrioventricular conduction delay (PR interval, 0.22 second) on the electrocardiogram. Prior to surgery in July 1973, two additional cardiac findings were present: a grade 2/6 late systolic murmur at the apex, and inverted T waves in leads 2, 3, and aVF on the ECG. In September 1973, a systolic click was an additional auscultatory finding, and this was confirmed by phonocardiographic studies (Fig 1). The click migrated towards the first heart sound with inspiration or following the administration of nitroglycerin. 

The click migrated towards the first heart sound with inspiration or following the administration of nitroglycerin. During the ensuing two months, the patient experienced several episodes of ill-defined pain in the left side of the chest. In December 1973, he was readmitted with a 24-hour history of progressive drowsiness, expressive dysphagia, and fainting (Fig 2).
4/6 crescendo-decrescendo pansystolic murmur which tapered off to a normal second sound. There was no systolic click, but a third heart sound was heard. Crepitations were present over both lungs. Relevant laboratory findings were as follows: hemoglobin level, 9.1 gm/100 ml; white blood cell count, 7,800/cu mm, with 81 percent neutrophils; and an elevated erythrocytic sedimentation rate (50 mm/hr). Group D Streptococcus (S faecalis) was isolated from two consecutive sets of blood cultures. Cerebral angiographic studies revealed a left middle cerebral embolus. Diagnoses of bacterial endocarditis, moderately severe mitral regurgitation (due to ruptured chordae tendineae), pulmonary venous congestion, and a cerebral embolus were made.

Treatment consisted of therapy with digoxin, diuretics, cortisone, and insulin and six weeks of antibiotic therapy. Initially, penicillin (four mega units every four hours) and gentamicin (1 mg/kg every eight hours) were used; three weeks later, ampicillin (2 gm every four hours) was substituted for penicillin on the basis of studies on minimal inhibitory concentrations, bactericidal titers, and synergism. The fever subsided after 24 hours of antibiotic therapy, although conjunctival petechiae appeared eight days later and Roth’s spots 15 days later. By February 1974, the hemogram was normal, and the erythrocytic sedimentation rate was 34 mm/hr.

Cardiac status was reevaluated in March 1974. The phonocardiogram (Fig 2) was unchanged from that of December 1973. Graded exercise testing (bicycle ergometer) did not precipitate angina or arrhythmia. Cardiac catheterization revealed no evidence for an intracardiac shunt; and intracardiac pressures were as follows: right atrium (mean), 5 mm Hg; right ventricle, 20/4 mm Hg; pulmonary artery, 20/10 mm Hg; wedge, a, 12 mm Hg, and v, 15 mm Hg; aorta, 93/68 mm Hg; and left ventricle, 96/13 mm Hg. Left ventricular angiographic studies revealed moderate mitral regurgitation with the typical posterior hump sign at the end of systole caused by prolapse of the posterior leaflet of the mitral valve. Findings from selective coronary angiographic studies were normal. Blood cultures were negative.

On follow-up in December 1974, moderate mitral regurgitation with left ventricular enlargement were present; and the phonocardiogram, as well as the plasma level of growth hormone, remained unchanged.

**DISCUSSION**

In the few reports of systolic murmurs in acromegaly in the literature, neither hemodynamic nor phonocardiographic data are presented. The syndrome of systolic click and late systolic murmur and its progression in our patient were studied by phonocardiography and external recordings and later by cardiac catheterization. The development of the syndrome in this patient who already had some evidence of cardiovascular involvement (mild hypertension and atrioventricular conduction delay) may have been incidental; however, several features consistent with the syndrome were present: vague chest pain with normal coronary arteriograms; endocarditis, which was associated with embolic phenomena and worsening of the mitral regurgitation; and electrocardiographic changes, although the latter were not diagnostic of inferolateral ischemia.

Two questions were prompted by the appearance of the mitral valvular prolapse-click syndrome in this acromegalic patient, but neither could be answered satisfactorily. First, does excessive growth hormone exert a myocardiopathic effect? Goodwin’s description of an acromegalic patient with mitral regurgitation, congestive cardiac failure, and severe myocardial dysfunction may support this contention. Although McGuffin et al found two further cases of acromegalic cardiomyopathy in a prospective study of 57 patients whom they observed over an average of 5% years, they could not correlate concentrations of growth hormone with the presence or absence of cardiac disease.

Secondly, since myxomatous degeneration of the mitral valve usually underlies the mitral valvular prolapse syndrome, was this likely in our patient? No evidence for myxomatous degeneration has been described in acromegaly where pathologic study of the heart has revealed only hypertrophy and fragmentation of the myofibrils with diffuse fibrous-tissue proliferation. On the basis of a patient with a floppy aortic valve, Marfan’s syndrome, and “nodular acidophilic hyperplasia” of the anterior pituitary, Read et al postulated that the floppy valve syndrome could be an expression of pituitary and mucopolysaccharide dysfunction; however, their patient had Marfan’s syndrome, in which myxomatous degeneration of the aortic and mitral valves is common.

**Figure 2.** Phonocardiogram showing pansystolic murmur three months after onset of endocarditis. No click is present. LSB, Left sternal border.
Diffuse Interstitial Fibrosing Pneumonitis and Adenovirus Infection*

Takeshi Kawai, M.D., F.C.C.P.;** Tatsushi Fujisawa,† Yuso Aoyama, M.D.;§ Yoshinari Atsawa, M.D.;** Yoshihiro Yamada, M.D.;** Teruo Aoyagi, M.D., F.C.C.P.;** Atsuo Mikata, M.D.;† and Keizo Kageyama, M.D.†

With electron microscopy, adenovirus particles, which were almost round, variable in density, and 60-80 m.μ in diameter, were observed in the nuclei of type II alveolar epithelial cells, infiltrated plasma cells and alveolar macrophages of a man with chronic interstitial fibrosing pneumonitis. The immunofluorescent technique also suggested adenovirus infection.

The etiology of diffuse interstitial fibrosing pneumonitis is unknown, although Hamman and Rich¹ speculated that an infectious agent, presumably a virus, might be responsible. The existence of inclusion bodies in affected lung specimens has often been reported;²-⁵ however, direct evidence of viral infection has not been confirmed except for one case reported by O'Shea and Yardley⁶ who found Herpes simplex virus or cytomegalovirus-like particles in alveolar lining cells on electron microscopy. In our patient, adenovirus particles were found in the nuclei of biopsied type II alveolar epithelial cells, plasma cells and alveolar macrophages by electron microscopy. Adenoviral infection was also suggested by demonstration of specific fluorescence in the nuclei of alveolar epithelial cells employing anti-type 12 adenovirus serum raised in rabbits.

**CASE REPORT**

A 54-year-old Japanese man noticed a slight productive cough in 1969 which did not interfere with his daily work. In 1971, he underwent a routine general physical examination and the chest roentgenogram disclosed a diffuse bilateral nodular infiltrate. A diagnosis of pneumoccosis was entertained, but he was not treated until 1972 when he was given expectorants and antitussive agents which were not effective. In early March, 1974, he complained of slight dyspnea and was admitted to the Keio University Hospital for evaluation. Family history was noncontributory, but he was affected with syphilis at age 22. On admission, his pulse rate was 88 with respirations of 24 per minute. No cyanosis was noted, but moderate clubbing of the digits was present. On auscultation, crepitant rales (typical Velcro rales) were noted diffusely throughout both lung fields on inspiration and expiration. The liver and spleen were not palpable. No lymphadenopathy or joint involvement was observed. Chest roentgenogram disclosed diffuse reticular shadows which were prominent peripherally and were partly forming honeycombs.

**Laboratory Findings**

Erythrocyte sedimentation rate was 65 mm per hour. Leukocyte count was 13,700 with a differential count of 77.5%.

**Figure 1.** Extensive proliferation of interstitial fibers and muscle bundles, marked mononuclear cell infiltration of the alveolar walls, and remarkable exudation, infiltration and desquamation filling the alveolar spaces, and glandular appearance of proliferated alveolar lining cells were noted. Proliferation of lymphoid follicles was also observed (Hematoxylin and eosin stain; original magnification × 25).

**References**


882 KAWAI ET AL

CHEST, 69: 5, MAY, 1976