Idiopathic Hypertrophic Subaortic Stenosis: A Case Study

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SUMMARY :

Though the nomenclature and criteria for diagnosis of hypertrophic cardiomyopathy is not entirely satisfactory, the basic pathology is disproportionate hypertrophy of the interventricular septum. An abnormal systolic anterior motion of the mitral valve and dynamic obstruction of the left ventricular out-flow tract over the upper portion of the body of the left ventricle. Though the disease could exist in various subjects which may slightly deviate from the typical picture like presence of asymmetrical septal hypertrophy without abnormal systolic anterior motion of the mitral valve and a concentric hypertrophy of the left ventricular pattern with or without obstruction. The left ventricular cavity is usually small, but at least it is not dilated. Because of the abnormality of relaxation of the left ventricle, the left ventricular end diastolic pressure increases which may lead to enlargement of the left atrium. This abnormality of the left ventricular relaxation and obstruction of the left ventricular out-flow may explain various symptoms, but the severity of the symptoms do not directly correlate with the cardiac catheterization and pathological findings.[16] The left ventricular out-flow obstruction is dynamic in nature which changes from time to time in various maneuvers which effect the left ventricular volume, preload, and afterload. Medical therapy is very rewarding in this disease. Surgical treatment is rarely needed, but is available for selected patients who do not respond to medical therapy. Calcium channel blocker drugs may play an important role in the medical management of this disease.

IDIOPATHIC HYPERTROPHIC SUBAORTIC STENOSIS

Hypertrophic obstructive cardiomyopathy is a complex myocardial disorder usually comprised of a nondilated, hypercontractible left ventricle with or without dynamic obstruction at a subvalavular level. Hypertrophy of the septum in an asymmetrical fashion is an important pathological and echocardiographic finding. Presenting symptoms may be highly variable. A case is presented with hypertrophic obstructive cardiomyopathy and a brief review of the subject is summarized.

Case Report :

This 55 year old male who was admitted to the hospital because of increasing shortness of breath and chest pain. According to the history the patient has been having this chest pain and difficulty breathing since the last 4 or 5 months. These symptoms are gradually getting worse. In the beginning the patient used to have these episodes once or twice a week. For the last few weeks he had been having these symptoms almost everyday. The chest pain is mostly localized to the retrosternal area. The patient feels like something is sitting on his chest and sometimes he feels like a tight band across the chest. Sometimes this chest pain is accompanied with mild difficulty in breathing. In the beginning the patient used to have these symptoms more frequently on heavy exertion, but lately he has been having these symptoms more frequently and started having them on mild exertion like walking a few blocks. His symptoms also get worse on cold days and when he is nervous. The pain does not have any relation with meals or taking deep breaths. Most of the time the pain is relieved by rest for a few minutes. The patient was given Nitroglycerine 1/150 gr prn by his private physician. According to the patient, nitroglycerine

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partially relieved his pain, but sometimes the pain persisted even in spite of taking Nitroglycerine.

The patient is denying any history of paroxysmal nocturnal dyspnea. There is no history of trauma to the chest wall or neck. He is denying having any difficulty in breathing without having chest pain and his shortness of breath is not seasonal in type. There is no history of allergies.

In reviewing the past history, the patient has history of duodenal ulcer 25 years ago. He also had a history of right urethral stone which was removed in 1973. The patient had never had any blood transfusions before. At the present time the patient takes Hygroton 50 gms once a day for mild hypertesnion and Nitroglycerine 1/150 gr prn. The patient smokes occasionally. He chews snuff daily for the last 4 or 5 years. He only drinks on social occasions. On reviewing the family history, his father died at age 74 because of a heart attack. His mother is living and in good health. She is 83 years old. One brother died from a stroke at the age of 50. Another brother is 40 years old and has no medical problems. He has one 50 year old sister who has chronic depression problem, but otherwise healthy.

On physicial examination.the patient appears healthy. He was slightly apprehensive, but no acute distress. The pulse is 104 and regular, Respirations were 14 per minute and regular. Blood pressure was 150/90. He is afebrile. There is no lymphadenopathy. Examination of the ears, eyes, and nose are within normal limits. Examination of the cardiovascular system revealed that there was no evidence of cardiomegaly. S1 and S2 were within normal limits. No S3 or S4. A Grade IV/VI systolic ejection murmur, loudest at the apex with radiation toward the axilla. This murmur is also heard at the lower left sternal border and upper left sternal border. The murmur is not radiating towards the neck. The murmur is separate from S1. No change of murmur while standing or valsalva. The carotid pulse is normal. There was no delay in carotid upstroke. There was no carotid bruit. Peripheral pulses were intact and equal bilaterally. The patient has a lower midline abdominal scar due to previous surgery. Liver and spleen were not palpable. Prostate was normal in size. Extremities were normal without any evidence of cyanosis, clotting, or edema. Examination of the central nervous system did not reveal any localized or laterlized neurological findings.

Laboratory work-up including blood counts and serum electrolytes did not reveal any abnormality. Serum cholesterol was 306. Kidney functions were within normal range. Electrocardiogram showed a regular sinus rhythm, axis + 45 degrees, but there was evidence of left ventricular hypertrophy on EKG. An echocardiogram was done. It was suggestive of idiopathic hypertrophic subaortic stenosis. A cardiac catheterization was done which confirmed the diagnosis of idiopathic hypertrophic subaortic stenosis and coronary artery disease. For detail, please refer to cardiac catheterization data.

The patient was placed on Inderal 40 mgs po q.i.d. and his Hygroton 50 mgs once a day was continued.

The patient had several follow-up visits in the office. His chest pain decreased in intensity and frequency and he showed a marked improvement on present therapy.

Cardiac catehterization report

The cardiac catheterization was performed through the right femoral vein. Hemodynamic data pressure in the right atrium, right ventricle, and pulmonary artery were normal. Pulmonary artery pressure was also normal. The left ventricular end diastolic pressure was normal at rest, but was elevated towards the end of the procedure. There was a moderate subvalvular pressure gradient in the left ventricle. This pressure gradient increased markedly after Amylntrate administration, post PVC, and during valsalva maneuver. Systolic peak pressure gradient was 55 mm of Hg at rest. After Amylnitrate it was increased to 108 mm of Hg. The resting subvalvular left ventricular gradient was unchanged after the administration of 3 mgs of intravenous Inderal. The left ventricular end diastolic pressure rose mildly after administration of Inderal. The subvalvular left ventricular gradient increased approximately 3 times after a PVC associated with an increase left ventricular end diastolic pressure demonstrating a 220 mm gradient. Valsalva maneuver after Inderal administration resulted in a slight increase in the subvalvular gradient. There was no significant gradient across the tricuspid, pulmonic, mitral, or aortic valve. Hydrogen curve was normal ruling out a left to right shunt. AV oxygen difference was normal. The cardiac output was normal. Pulmonary arterial resistance was slightly elevated. Coronary angiogram was also performed. The patient had mild to moderate narrowing of all three vessels.

Conclusion of Cardiac Catheterization Data

1) Asymmetrical hypertrophy with obstruction, severe ;
2) Mild to moderate narrowing of all three vessels.

Discussion :

Hypertrophic cardiomyopathy was first described 26 years ago by Teare.[1] Since then this entity has grown attention of thousands of investigators which has resulted in an improved understanding of this interesting condition. The condition usually manifests as exertional fatigue, dyspnea on exertion, chest pain that could be confused with the pain of angina, and syncopal attacks[2]. The patient could also have palpitations which may be due to atrial or ventricular arrhythmias, though hypertrophic cardiomyopathy is seen in all ages, but is more common in young adults and it may be responsible for a considerable number of sudden deaths.[3]

The cause of hypertrophic cardiomyopathy is still uncertain. There are varous reports in literature which suggest that this disease may be genetically transmitted as an autosomal dominant trait.[4] Hypertrophic obstructive cardiomyopathy can logically be viewed as a disorder of growth which could develop during childhood during the development of the adult left ventricle or this could develop in response to some stimulus that increases the work of the left ventricle. The two most important findings of this condition which is hypertrophy and obstruction could be present simultaneously or one conditon may be present at a particular time without the presence of the other condition.[5]

Though the autopsy findings may not correlate well with clinical findings, the majority of the patients have increase in myocardial mass, secondary hypertrophy of the posterior basilar wall, abnormally arranged myocardial cells in the septum, thickening of the mitral valve is often seen. Pathological examination of the heart also shows abnormality situated and abnormally arranged large muscle bundles over the interventricular septum.[6] About 95% of the patients show a focal myocardial fiber disarray or disorganization.[7] This abnormality involves at least 5% of the ventricular septum. Mostly the upper portion of the interventricular septum. Some patients may have this abnormality over a large portion of the septum as well as left ventricular posterior wall. Individual septal myocardial cells frequently show a Z-band material and nospecific changes of cellular hypertrophy and degeneration. These septal abnormalities are collectively called asymmertrical septal hypertrophy (ASH) which is a very sensitive finding, but unfortunately it is not very specific for this condition and several other conditions could lead to similar kind of changes in the interventricular septum.[8] The thickness of the interventricular septum does not correlate well with the ventricular out-flow tract obstruction at rest.[9] Though a disproportionate thickness of the interventricular septum is an important finding in hypertrophic obstructive cardiomyopathy. A few other conditions like a myocardial infarction of the free wall could lead to thinning of the wall and make a disproportionate thickness of the interventricular septum and could make a false disproportionate thickness of the interventricular septum. Also the right ventricular systolic hypertension leads to thickness of the interventricular septum selectively and could lead to false finding of asymmetrical septal hypertrophy (ASH).[10] The cause of the relatively small size of the ventricular cavities is not clear, but most likely it is due to disproportionate thickened interventricular septum. In contrast the left ventricular cavities, the atrial cavities are usually enlarged and this may be due to decreased left ventricular compliance so the left atrium has to contract with more power to fill up the left ventricle. The majority of the patients with hypertrophic cardiomyopathy have some degree of mitral insufficiency, though the exact etiology of mitral regurgitation is not known. It may be due to excessive tension on the chordae tendineae that prevents closure of the mitral orifice. Though the leaflets are thickened, but thickness of the leaflet alone can not explain the reason for mitral regurgitation. Also the focal scars over the papillary muscles which are usually present also can not explain the presence of mitral regurgitation.

Though the disease has been diagnosed in neonates and older people, the disease is mostly present in young adults (average age of presentation is 26 years). The disease is more difficult to diagnose in the older population because the symptoms could be easily confused with coronary disease. Males and females are involved in equal number.[2] The patient could be totally asymptomatic and the disease could be diagnosed as an incidental finding on an echocardiogram by finding of asymmetrical septal hypertrophy with or without abnormal motion of the anterior mitral

TABLE - I

EFFECT OF VARIOUS INTERVENTIONS ON MURMUR AND GRADIENT IN IHSS

INCREASE IN GRADIENT AND MURMUR	DECREASE IN GRADIENT AND MURMUR
1. Valsalvas maneuver (during strain).	1. Isometric handgrip.
2. Standing	2. Squatting.
3. Post extrasystole.	3. Valsalva maneuver (over shoot phase).
4. Isoproterenol	4. Mueller maneuver
5. Hypovolemia.	5. Beta adrenergic blockade (Propranolol, etc.)
6. Exercise	6. Alpha adrenergic stimulation (pheylephine).
7. Nitroglycerine.	
8. Amylnitrate.	
9. Digitalis.	
10. Tachycardia.	

valve. Another important point to remember is that the patient's symptoms fluctuate markedly because the obstruction of the left ventricular out-flow tract is dynamic in nature and could be intensified by a variety of interventions. The most common symptom is dyspnea which is most likely secondary to impaired left ventricular filling due to a decreased left ventricular compliance and stiffness of the wall which leads to an elevated left ventricular end diastolic pressure and subsequently left atrial and pulmonary venous pressure.[6] Other common symptoms are palpitations which may or may not be related to atrial or ventricular arrhythmias, chest pain suggestive of angina pectoris, exertional fatigue, and syncope mostly at the time of exertion are other common symptoms. Though the coronary arteries are normal, but an imbalance between oxygen supply and demand could occur due to greatly increased myocardial mass. Syncope may be secondary to a low cardiac out-put to meet the body requirement at the time of exertion or may be due to cardiac arrhythmia.[3] Several patients do not have actual syncopal attacks, but they feel like having a syncopal attack (graying out spells). The presence of these symptoms does not correlate directly with the severity of the obstruction.[4]

Physical examination may be totally within normal range. A prominent 4th heart sound is usually present due to decreased left ventricular compliance and a strong left atrial contraction. The precordial impulse is usually forceful and slightly displaced laterally. A prominent late systolic apical impulse is felt. This third impulse may be due to late systolic bulge because of the dynamic obstruction. A systolic thrill may be present at the lower left sternal border. The jugular venous pulse may demonstrate a a-wave due to diminished right ventricular compliance. The carotid pulses are typically normal in the initial portion, but has declined in mid-systole and a secondary pausitive wave. This finding is more readily demonstrated by recording the carotid pulse, but could be well appreciated on physical examination. The 1st heart sound is normal and the 2nd heart sound is also normally split, but in a patient with severe out-flow obstruction a paradoxical splitting may be noted. A 3rd heart sound also present in several patients, but this is not a sign of decompensation. The most important ausculatory finding is a systolic murmur which is crescendo-decrescendo and harsh in quality. It is best heard over the left sternal border area. The murmur does not radiate towards the neck. The intensity of the murmur may fluctuate with the variety of maneuvers. The systolic murmur is due to a combination of out-flow tract obstruction as well as mitral regurgitation.

Sometimes these findings are very difficult to differentiate from typical findings of aortic stenosis.[1,2] An important and useful feature is the upstroke of the carotid pulse. In severe aortic stenosis the upstroke of the carotid pulse is slower and delayed while the initial portion of the carotid pulse in obstructive cardiomyopathy is brisk and normal. Also the location of the murmur of aortic stenosis is more towards the aortic area rather then left sternal border. In the absence of calcification of the aortic valve an ejection sound is usually present in aortic stenosis, but it is absent in hypertrophic cardiomyopathy.[2]

Electrocardiogram usually shows left ventri-

cular hypertrophy with ST-T wave changes.[12] Sometimes the prominent Q-waves are present over inferior and septal leads. These findings may be confused with the findings of myocardial infarction. IHSS is one of the important clinical entities which produces pseudoinfarction electrocardiographic pattern.

X-ray of the chest usually shows left ventricular prominence due to concentric hypertrophy, but the overall heart size is within normal range. The left atrial enlargement may be seen, but this is not a persistent finding on x-ray of the chest.[3,6] X-ray of chest may be totally within normal range in a large number of patients.

A classic echocardiographic finding of hypertrophic cardiomyopathy comprises of increased interventricular septal thickness of 13 mms or greater. The ratio of the interventricular septum to posterior left ventricular wall thickness is usually greater than 1.3 to 1.0. Echocardiography also reveals abnormal motion of the anterior leaflet of the mitral valve towards the interventricular septum in systole.[13] This motion is also called SAM or systolic anterior motion. Echocardiogram of aortic valve may show partial closure of the aortic valve in midsystole. About 10% of the patients may show some of these findings with several congenital or acquired heart diseases. Posterior wall myocardial infarction may lead to thinning of the left ventricular free wall and thickness of the interventricular septum due to pulmonary hypertension and can produce a disproportionate thickening of the interventricular septum and these findings could produce an abnormal ratio of the thickness of the interventricular septum and left ventricular posterior wall.[14] An abnormal systolic systolic anterior motion of the mitral valve has been reported in hypercontractile states during intensive introphic stimulation and volume depletion. A small number of patients with hypertrophic cardiomyopathy may have a diffused hypertrophy which produces a concentric hypertrophy pattern rather than asymmetrical hypertrophy.

Though cardiac catheterization is not necessary in a large number of patients, several patients need this test to confirm the diagnosis.[9,11] The cardiac cathetrization usually shows a diminished diastolic left ventricular compliance and a pressure gradient within the body of the left ventricle. This pressure gradient by careful technique could be demonstrated at the level of the body of the left ventricle and left ventricular out-flow tract. This pressure gradient may be present at rest or sometimes it has to be provoked by infusion of Isoproternol. Also the interventions such as inhalation of Amylnitrate which decreases the end diastolic dimension of the ventricle also provokes or intensifies the pressure gradient. The pressure gradients also increase after a premature ventricular contraction (Brockenbough phenomena).[11] The increase in pressure gradient after a premature ventricular contraction is poorly understood because an increased left ventricular volume after a PVC should have decreased the pressure gradient, but the availability of more calcium at the myocardial sarcomers leads to a more powerful contraction which increases the pressure gradient. The net effect of both of these opposing actions is an increased gradient and an increase in intensity of systolic murmur. Findings at cardiac catheterization poorly correlates with the patient's symptoms. Another important cardiac catheterization finding is elevation of left ventricular end diastolic pressure which is due to abnormal left ventricular compliance which may be due to thickness of the left ventricular wall leading to an abnormal relaxation of the myocardium. Overall left ventricular contractility is within normal limits. In a majority of the patients, an above normal ejection fraction is found.

In patients with hypertrophic obstructive cardiomyopathy, hemodynamic findings can vary from moment to moment. The three basic mechanisms which are involved in the production of dynamic obstruction and physical findings: any increase in contractility of the heart, decreased preload, and a decreased afterload will increase the obstruction in IHSS.[11] In normal people maneuvers which increase the left ventricular contractility intensifies left ventricular outflow tract obstruction while a reduction in contractility (like giving a Beta-blocker) will decrease the pressure gradient in obstruction. A decrease in preload which leads to decreased left ventricular size also increases the obstruction while increase in preload by volume expansion. Increase in preload will decrease the obstruction.[6] An increase in obstruction could also result in a louder and prolonged murmur due to worsening of the obstruction and this also will exaggerate the systolic anterior motion (SAM) on echocardiogram. Because a valsalva maneuver (during strained phase) leads to a decrease in preload and afterload will increase the intensity of murmur and obstruction. Squatting will increase the preload and afterload thus decreasing the intensity of

the murmur. Digitalis glycosides increase the contractility of the heart and could increase the obstruction while Beta-blockers by decreasing the contractility of the heart will diminish the murmur and obstruction. Any condition which leads to a decrease in ventricular volume like hypovolemia are a given Nitroglycerine or Amyl-nitrate and exaggerates the gradient.

In general the treatment is only necessary in patients with symptoms. It is important to follow all the patients closely. The management could be divied into medical and surgical therapy.

Proparanolol is the major therapeutic weapon. This medicine should be started in a small dose like 10 mgs three times a day and should be gradually increased if symptoms persist. A few people may need as much as 200 mgs a day. Propranolol not only decreases the force of the left ventricular contractions and hence decreases the out-flow tract obstruction, but also tends to prevent ventricular arrhythmias. It has been reported that Verapamil may also reduce left ventricular out-flow obstruction and to improve symptoms (this drug has not yet been approved by the FDA for this particular disease).

Surgically treatment is rarely needed for this condition and it is only indicated for those patients who do not respond to an optimal medical therapy. Surgical incision of the muscular thickened portion of the septum is done successfully in a high number of patients with improvement. The surgical mortality is relatively high (8%). Though some patients have severe mitral regurgitaion, but a mitral valve replacement is contra-indicated in these patients because of the worsening of the symptoms after valve replacement.

The long term prognosis of hypertrophic obstructive cardiomyopathy is not yet fully established because the condition has only been widely recognized for about 20 years. It seems likely that the course of this disease is benign in the majority of the patients, but a defnite statement can not be made at the present time. The severity of the symptoms is not closely related to th presence of the severity of obstruction to the left ventricular out-flow. The appearance of atrial fibrillation usually leads to worsening of the symptoms. Pregnancy is usually well tolerated by the majority of the patients with IHHS. Overall there is 3% to 5% annual mortality of this condition, most likely secondary to sudden death. 70% to 80% of the patients may have various kinds of atrial or ventricular arrhythmias diagnosed on 24 hour ambulatory Holter Monitor recording or treadmill exercise testing.[19] It appears like a high dose of Propranolol therapy may show a marked improvement in cardiac arrhythmia and syncopal attack.[17,19] Though at the present time exact nature of the history of cardiac arrhythmia is not known in these patients, but most probably they should be treated aggressively.[17,18,20] Recently it has been shown that Verapamil therapy improved treadmill exercise performance with hypertrophic cardiomyopathy. This improvement is more prominent over a longer period of therapy

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