Subaortic Stenosis and Autoimmunity

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Abstract

Isolated subaortic stenosis is a disease with unknown etiology. Although familial clusters of the disease suggest a genetic basis, a consistent mode of inheritance was not found. The current treatments are not satisfactory. We interrogated the possibility of an autoimmune basis. As autoimmune disease frequently appear together in a patient or relatives, we studied association between isolated subaortic stenosis and autoimmune disease in a cohort of 14 patients.

History of common autoimmune disease in the patient or relatives, thorough physical examination, and laboratory test (fluorescent antinuclear antibody, antibody against double-strand deoxyribonucleic acid, rheumatoid factor, anti-thyroid peroxidase antibodies, tissue transglutaminase, and anti-endomysial antibody were measured.

We found a patient with vitiligo and subaortic stenosis, and a patient with diabetes mellitus type I among the relatives of the patients. All laboratory test results were normal or borderline.

In conclusion, we found weak evidences for an association between isolated subaortic stenosis and autoimmune disease. Further studies are required to interrogate this hypothesis.

Keywords: Vitiligo, systemic lupus erythematosus, rheumatoid arteritis

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Introduction

Subaortic stenosis (SAS) is a pathology mostly seen with congenital heart diseases like ventricular septal defect, patent ductus arteriosus, aortic valvar stenosis, bicuspid aortic valve, coarctation of aorta, mitral valve anomalies, and interrupted aortic arch (1). It can also be seen after cardiac surgeries. In this situation, abnormal flow was presumed to be responsible for the proliferation of tissue under the aortic valve (rheologic or shear and tear phenomenon). The stenosis can be in different forms: small swelling, membrane, ridge, or long tunnel shape obstruction. SAS can be seen rarely as an isolated form. The etiology of isolated SAS (ISAS) is unknown. It seems that ISAS is not a congenital disease, as it cannot be seen in infancy (2). The high probability of recurrence after surgical removal (up to 33%) is not consistent with a congenital defect as well (1). Genetic basis was assumed; however, no consistent mode of inheritance was found (1).

There are scattered reports of coincidence of ISAS with autoimmune diseases (3). The idea of this study was started when we visited a patient with ISAS and vitiligo in our cardiac clinic. The behavior of the disease and some familial clusters of the disease (1) encouraged us to investigate any association of ISAS with autoimmune diseases, as many autoimmune diseases can occur together in a patient, or the relatives of the patient.

Methods

In a one year period, we enrolled all pediatric or adolescent (0-18 years old) patients with ISAS who accepted to participate in this study. Informed consent was gathered from the patients or their parents. Thorough history was taken especially for the probability of autoimmune diseases in the patients, their family members, or relatives. Complete physical examination was performed and signs of autoimmune diseases, including systemic lupus erythematosus (SLE), rheumatoid arteritis (RA), vitiligo, psoriasis, and other possible occult autoimmune diseases were interrogated. Skin, hairs, mucosa, eyes, thyroid, lungs, and joints are more diligently examined. Blood samples were taken and these parameters were measured: fluorescent antinuclear antibody (FANA, present in SLE), antibody against double-strand deoxyribonucleic acid (anti- dsDNA, present in SLE), rheumatoid factor (RF, present in RA), anti-thyroid peroxidase antibodies (anti-TPO, present in Hashimoto's thyroiditis), tissue transglutaminase IgA (tTG, present in celiac disease), and anti-endomysial antibody (anti-EMA, present in celiac disease). We have used SPSS Statistics for Windows, version 16 (SPSS Inc., Chicago, Ill., USA) for the data analysis. A p value less than 0.05 was considered significant.

Results

We enrolled 14 patients during the study period. There were 4 females (29%) and 10 males (71%). Mean age was 7.57±2.73 years with no difference between the two sexes. Mean age at diagnosis was 4.14±2.85 years in males, and 2.33±2.51 in females (p= 0.76). Mean height and weight of the patients were 1.25±0.22 meters and 30.3±13.1 kilograms, respectively.

In the history taking, there were no report of joint problems, nor prolonged fever (>10 days). In the physical examination, we found café-au-lait maculae in one patient and thyroid enlargement in another one. There was one case of diabetes mellitus type I (DMI) in a cousin of one patient.

FANA titers were negative in 11 and fine speckled 1:80 weakly positive in 3. All tTG levels were normal except a weakly positive result. The remaining laboratory test results were normal in all patients.

Discussion

Our cohort was small, mostly due to the rarity of the disease. ISAS patients generally are evaluated every 6 months at our hospital clinic.

We had no patient resigning to participate. Therefore, we can suppose that we included almost all of our existing patients in this study. The male preference is a characteristic of this disease (2).

In the family history, finding a case of DMI in the relatives of 14 patients is interesting. The incidence of this disease is 15 in 100 thousand people (one in 6.7 thousand). If we suppose that each patient (or the parents) knows the diseases of around hundred relatives, the incidence of DMI among relatives of our patients is around 4.8 times higher than the general population

The patient with vitiligo seen a few years before the start of this study was not among our patients. He was referred to the adult cardiac service after reaching the adult age. If we add him to our cohort, the incidence of vitiligo will be 6.7% (1 in 15), which is more than 3 times the maximum incidence in the normal population (0.5-2%). Although we found some borderline results in the laboratory results, it seems that no evidence for an occult disease was found.

The current treatments against ISAS (surgical excision of the stenotic tissue, sometimes balloon valvoplasty) are not satisfying, due to the high recurrence of the disease and the probability of aortic valve damage and the necessity of valve replacement (2, 4). The autoimmune nature of ISAS may be a hypothesis deserving further and more elaborative studies. If it will be proved, there may be new therapies against the disease with hopefully better long-term results.

Acknowledgment

Professor Aghamohammadi, a brilliant Iranian researcher, unfortunately passed away of COVID-19 in November, 2020. May his soul rest in peace!

Resumo

Izola subaorta stenozo estas malsano kun ne-konata etiologio. Kvankam familiaj kazoj de la malsano sugestas genetikan bazon, neniu konstanta modelo de heredo estas trovita. La nunaj kuracoj ne estas kontentigaj. Ni esploris la eblecon de asocio kun aŭtoimmunaj malsanoj en la pacientaro de 14 homoj.

Historio de oftaj aŭto-immunaj malsanoj en la paciento aŭ liaj/ŝiaj parencoj, kompleta ekzameno, kaj laboratoriaj testoj (fluoreska antinuklea antikorpo), antikorpo kontraŭ duobl-ĉena desoksiribonuklea acido, reumatoida faktoro, anti-tiroid-perksidazaj antikorpoj, hista transglutaminazo, kaj anti-endomizia antikorpo estas analizitaj.

Ni trovis pacienton kun vitiligo kaj subaorta stenozo, kaj pacienton kun diabeto sukera tipo I inter la parencoj. La rezultoj de ĉiuj laboratoriaj testoj estis normalaj aŭ limaj.

Konklude, ni trovis malfortan asocion inter subaorta stenozo kaj aŭtoimmunaj malsanoj. Pliaj esploroj estas bezonataj por enketi tiun hipotezon.

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