Colour Doppler echocardiography in children with group A streptococcal infection related tic disorders

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Background & objectives: A possible relationship has been suggested between tic disorders and streptococcal infections. To understand the complex relationship between streptococcal infections and neuropsychiatric disorders in children the present study was done on colour Doppler echocardiography of patients with possible post-streptococcal tic disorders.

Methods: The patients were 23 children (22 males, 1 female) affected by tic disorders, who at the time of the observation presented (or had presented in the past) signs of streptococcal infections temporally related to the onset or recrudescence of tic disorders. Echocardiographic examination and laboratory tests were performed on these children.

Results: In 4 cases a mild mitral insufficiency and in 8 cases a minimal mitral insufficiency was seen, all haemodynamically not significant. Follow up studies (up to 1 yr) showed the consistency and persistence of these findings. Of the 12 patients with echocardiographic abnormalities, 10 displayed very high anti streptolysin O (ASO) titres, 5 showed positive cultures for GAS and 9 had abnormal ESR, even if no significant differences were found in respect to patients with tics and normal echocardiography.

Interpretation & conclusion: With the caution due to the design of study and to low number of patients, our data seem to indicate that the pathophysiology of GAS-infection related tic disorders is similar to that SC, at least in some cases.

Key words Children - echocardiography - GAS infection - tic disorder

In recent years many research groups have stressed a possible relationship between obsessive-compulsive disorder, tic disorders and streptococcal infections. In particular, a post-streptococcal autoimmunity, similar to that of Sydenham's Chorea (SC) has been postulated as a possible pathophysiologic mechanism in a subset of paediatric patients (paediatric autoimmune neuropsychiatric disorders associated with streptococcal infections-PANDAS)1. In these reports the main difference between SC and PANDAS patients was the absence of signs of arthritis or carditis in the latter ones, since the presence of carditis was an exclusion criterion2. The absence of carditis in these patients has been one of the main criticisms to the concept of PANDAS and to its putative pathogenetic mechanism3,4.

Here we report preliminary results of an open study on color doppler echocardiography of patients with possible post-streptococcal tic disorder. This method of investigation has been chosen because it may detect mitral regurgitation even when there is no murmur (silent mitral regurgitation), as happens in some cases of rheumatic carditis5.
Material & Methods

A total of 23 children (22 boys and 1 girl) affected by tic disorders were included from those followed at the outpatients division of Developmental Neuropsychiatric Department of University La Sapienza of Rome.

Inclusion criteria in the study were: to have a tic disorder, age under 18 yr, and onset or recrudescence of tic disorder temporally related to signs of streptococcal infections (raise in ASO titre with or without GAS positive throat swab) at the time of study or in the past. All patients underwent a complete physical and neurological assessment.

The clinical diagnosis of tic disorder was made on the basis of the criteria stated by the Tourette Syndrome Classification Study Group. The actual severity of tic disorder was assessed by the Yale Global Tic Severity Scale (YGTSS). On the basis of a global evaluation of the tic disorder, the patients were classified as "mild tics", "moderate tics" and "severe tics".

Echocardiographic examination and the laboratory tests including complete blood count and erytrocyte sedimentation rate (ESR) were performed the same day.

Specific tests for intercurrent (culture of throat swab specimen) or antecedent (measurement of ASO titre) GAS infections were also carried out.

ASO titres higher than 407 IU were considered abnormal, since in a previous study this value was found to be 2 SD higher than the mean value obtained in a normal control group seen at the time of the study6.

Colour Doppler echocardiography: The echocardiographic data collection was performed with an Acuson Aspen ultrasound scanner with 2.5-5 mHz transducers incorporating colour flow, continuous and pulsed wave Doppler. Standard views (parasternal long axis and short axis, apical four and five chambers) for mitral and aortic valve imaging were obtained. To assess valvular incompetence colour-Doppler technique was carried out, as it reveals a systolic regurgitant jet across atrio-ventricular valves and a diastolic one across semilunar valves. Basically, the regurgitant jets have high velocity as well as a variable degree of turbulence; therefore they usually show aliasing inside the cardiac chamber receiving the blood flow. Pathologic mitral regurgitation was defined as meeting the following four criteria: (i) length of colour jet > 1 cm; (ii) colour jet identified in at least two planes; (iii) mosaic colour jet; and (iv) persistence of the jet throughout systole. Jet orientation was also noted.

By means of direct observation of the regurgitant jet mistakes in diagnosis of valvular incompetence are unlikely to occur. Further such technique allows a semiquantitative assessment of regurgitation amount. The latter evaluation is related to the left atrial backflow magnitude in case of mitral incompetence; the left ventricular outflow tract backflow magnitude in case of incompetence of aortic valve; and the regurgitant jet maximal area - chamber receiving retrograde blood flow area ratio.

All echocardiographic examinations were separately reviewed by two cardiologists blinded for the clinical diagnosis.

Results

The patients had a mean age of 9.6±2.4 yr (range 4 yr 11 months-13 yr); the mean age of onset of tic disorder was 6.1±2.3 yr (range 2-12 yr); the duration of the disorder ranged between 0.2 and 7.1 yr (mean 3.4 yr). Among 23 patients, 13 had a family history positive for tics, 17 were classified as Tourette syndrome, 5 as multiple chronic tics and 1 as transitory tics. The mean YGTSS score was 23.6 (range 3-52); on the basis of their overall tic history, 10 patients were classified as mild tics, 9 as moderate tics and 4 as severe tics. In one patient an "innocent" cardiac murmur had been reported in the past during a routine paediatric follow-up.

Eighteen patients had a recent onset or recrudescence of tics temporally related with signs of streptococcal infections and 5 reported this temporal association for the past, though not in the twelve months before the study. None of the patients had a diagnosis of rheumatic fever in the past.
With the exception of one patient diagnosed for innocent cardiac murmur, all patients had a normal physical and neurological evaluation.

Laboratory test showed that 17 of the 23 patients had ASO titres > 407 IU, 16 had ESR > 16 and 9 had throat swabs positive for GAS. Of the 9 patients positive for GAS, 8 had ASO titre >407 IU and ESR >16. In 12 of 23 patients (52%) color Doppler echocardiography showed abnormalities: a mild mitral insufficiency in 4 cases (Figs 1-2) and a minimal mitral insufficiency in 8 cases (Fig. 3), all haemodynamically not significant.

![Fig. 1. Parasternal long axis view: mild regurgitation of the mitral valve.](image1)

![Fig. 2. Apical four chamber view: confirmed mild regurgitation of the mitral valve.](image2)

All echocardiography positive patients were retested between 6 to 12 months after the first examination. No significant variation of cardiac abnormalities were detected in any of these cases. Of the 12 patients with echocardiographic abnormalities, 10 showed ASO titre > 407 IU, five had a GAS positive swab and 9 had ESR >16 (Table).

![Fig. 3. Parasternal long axis view: minimal regurgitation of the mitral valve.](image3)

<table>
<thead>
<tr>
<th></th>
<th>With echo abnormality</th>
<th>Without echo abnormality</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>12</td>
<td>11</td>
<td>23</td>
</tr>
<tr>
<td>Mean ASO titre $\pm$SD (IU)</td>
<td>912.59 ± 598</td>
<td>617 ± 414</td>
<td>729 ± 543</td>
</tr>
<tr>
<td>ASO titre &gt; 407 (IU)</td>
<td>10</td>
<td>7</td>
<td>17</td>
</tr>
<tr>
<td>ESR &gt;16</td>
<td>9</td>
<td>7</td>
<td>16</td>
</tr>
<tr>
<td>Throat swab positive for GAS</td>
<td>5</td>
<td>4</td>
<td>9</td>
</tr>
</tbody>
</table>

All but one of these patients (the echo-positive children) had a recent onset or recrudescence of tics temporally related to streptococcal infection signs.

No difference in mean age, age at onset of tics, duration of symptoms, familiarity or results of the laboratory tests between patients with or without echocardiographic abnormalities were found (Table).
Discussion

The population studied consisted of children affected by tic disorders of different types and severity but all temporally related to streptococcal infections. In more than half of the children, there was evidence of consistent and persistent echocardiographic abnormalities, in particular mitral regurgitation but haemodynamically not significant. All these echo-positive patients had a negative history for rheumatic fever and all but one had a silent physical examination at the entry in the study.

The rate of echo-abnormalities found in our population (52%) was higher than that reported in the literature in normal children. In one study⁷ mitral regurgitation was shown in 1.83 per cent of 329 normal children and adolescents (but never before the age of 7 yr) and in another study⁸ in 2.4 per cent of 461 children with structurally normal hearts.

On the contrary a high incidence of valvular incompetences, in particular mitral regurgitation, has been described in patients affected by rheumatic fever, also in those without a clinically evident carditis⁹. Similar rates of echocardiographic abnormalities have been reported in children with isolated rheumatic chorea¹⁰.

It was suggested that a subclinical valvitis, echocardiographically distinguishable from "innocent" regurgitations⁹, should be accepted as evidence of carditis in the diagnosis of rheumatic fever¹¹. If this opinion is correct, we can assume that at least some of our patients were suffering by a tic disorder plus an actual or recent streptococcal infection plus a minimal carditis. Could the diagnosis of "rheumatic tic disorder" be appropriate for these children? And, in this case, which type of treatment should be used? With these cardiac abnormalities long standing should these patients receive anti-inflammatory drugs and antibiotic prophylaxis? Or as suggested by Murphy and Pichichero for children with PANDAS¹², is it sufficient to treat the incoming streptococcal infection? Our echo-positive patients were not distinguishable from the negative ones, either for the clinical characteristics of tic disorders or for their relationship with streptococcal infections. Should these two groups of patients considered different or, if not, which treatment should be suggested?

This is the first report on echocardiographic examination of patients affected by tic disorder or by PANDAS. In a previous study² the authors specifically excluded patients with cardiac abnormalities, and the method used to assess them was not reported.

In summary, with the caution due to the low number of cases studied, our data provide new insights on the complex relationship between streptococcal infections and neuropsychiatric disorders in children.

References


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