

A major diagnostic criterion for acute rheumatic fever: Clinical and sub-clinical carditis accompaniment with Sydenham chorea

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ABSTRACT

Objective: Acute rheumatic fever is a prevalent cause of heart disease affecting the whole world. Sydenham chorea, caused by the group A β -hemolytic streptococcus bacteria and characterized by non-rhythmic involuntary movements, is one of the major symptoms of acute rheumatic fever. While Sydenham chorea can be the only symptom in some acute rheumatic fever cases, in others it can also be accompanied by carditis findings. We have conducted this study to examine the co-occurrence of Sydenham chorea with clinical and sub-clinical carditis.

Material and Methods: The records of the cases diagnosed with Sydenham chorea and monitored in our hospital between November 2015 and November 2020 were scanned retrospectively. SPSS 21 was used for data analysis.

Results: The sample consisted of 22 (84.6%) females and 4 (15.4%) males. Chorea was accompanied by arthritis in 6 cases (23%) and by carditis in 22 cases (84.6%), while 4 cases had pure chorea. The severity of the valve involvement was mild in 8, moderate in 10, and severe in 4 cases. During the follow-up of the 22 cases with carditis, valve involvement disappeared in 27.3%, decreased in 36.35%, and remained the same in 36.35%. Valve involvement developed during the follow-up of one case that did not previously have heart involvement (3.8%).

Conclusion: In our study carditis was observed at a significant rate in Sydenham chorea cases. Echocardiography plays an important role in the diagnosis of carditis, hence the diagnosis of acute rheumatic fever, which is a serious problem especially in developing countries.

Keywords: Acute rheumatic fever, carditis, echocardiography, sub-clinical carditis, Sydenham chorea, valve deficiency.

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INTRODUCTION

Acute rheumatic fever (ARF) is a prevalent cause of acquired heart disease affecting the whole world. Although the incidence of ARF has significantly lowered in developed countries, it still remains a major problem in developing countries.^[1] According to the T. Duckett Jones criteria, first established in 1944, then revised several times, the most prevalent major criteria for the diagnosis of ARF are carditis, arthritis, and Sydenham chorea (SC), while some of the less common major criteria are subcutaneous nodules and erythema marginatum.^[1–3] Being one of the major criteria for ARF, SC is seen in 10–30% of the cases.^[4]

SC is a central nervous system disease that affects children, caused by the group A β -hemolytic streptococcus (GAS) bacteria, and characterized by non-rhythmic involuntary movements and behavioral changes.^[5] SC generally emerges 1–8 months after the streptococcus infection, thus no other clinical and laboratory symptoms of rheumatic fever might be present at the time of diagnosis.^[5] Given this, SC itself is a sufficient criterion for the diagnosis of ARF. Such cases, in which there are no other accompanying major or minor criteria, are called “pure chorea”, and constitute 30–50% of all SC cases.^[6] Besides pure chorea cases, there are also ARF cases that manifest themselves with more than one of Jones’ major or minor criteria. Among the most commonly observed concurrent criteria are SC and carditis.

According to the earlier versions of the Jones criteria, carditis diagnosis could only be made in the presence of clinical findings.^[7,8] However, this was proven to be insufficient when it was observed that carditis can also be present without any clinical symptoms as the usage of echocardiography became more prevalent and advanced.^[6,9,10] Hence, sub-clinical carditis, in which no clinical symptoms are present but carditis is observed with echocardiography, was also added as a major diagnostic criterion to the revised version of the Jones criteria in 2015.^[1,5]

In the light of these criteria, we have conducted this study in order to assess the SC cases that are accompanied by clinical and sub-clinical carditis and evaluate the follow-up process of these cases.

MATERIAL AND METHODS

The cases diagnosed with Sydenham chorea with the ICD codes of I02, I02.0, and I02.9 in the five-year period between November 2015 and November 2020 at the pediatrics clinic and pediatric cardiology outward clinic of our hospital were examined retrospectively from the patient records. The cases’ ages, ages at the time of diagnosis, sexes, complaints, physical examination results and laboratory findings at diagnosis or during hospitalization, and the treatments they received were scanned from the hospital records. Approval for the study was obtained from the Hospital Ethics Committee and the Scientific Commission in the Directorate of Health Services (03.03.2021/57).

The findings of the first and most recent echocardiography screenings done at the pediatric cardiology outward clinic were recorded. A Vivid 3 S26 (GE medical) device was used for the echocardiography assessments of the cases. The valve deficiencies were classified as “none, mild, moderate and severe” based on the criteria determined by the American Society of Echocardiography (ASE) according to their echocardiography and Doppler results.^[11]

Table 1: Laboratory findings of cases

	Mean \pm SD	Minimum	Maximum
Leukocyte (mm ³)	7590 \pm 1898	5490	13200
Hemoglobin (g/dl)	11.37 \pm 3.64	9.00	14.00
Hematocrit (%)	34.37 \pm 11.02	29.60	42.30
C-Reactive Protein (mg/dl)	0.77 \pm 1.62	0.00	6.50
Sedimentation (mm/h)	28.76 \pm 27.93	5.00	121.00
Anti Streptolysin-O (U/l)	561.76 \pm 355.88	15.00	1450.00

SD: Standard deviation.

Table 2: Valve involvement and severity in the study group

Severity	n (26)	%
None	4	15.4
Silent	8	30.8
Moderate	10	38.4
Severe	4	15.4

The SPSS 21 statistical software was used for the descriptive analysis of the findings of the cases.

Results

The sample consisted of 22 (84.6%) females and 4 (15.4%) males. The female/male ratio was 5.5. The mean age of the cases at the time of the first diagnosis was 11.22 \pm 2.58 (5.5–14.92) years. 13 cases were hospitalized and monitored at our hospital’s service. The other cases were either hospitalized at other centers or visited the outpatient clinic. The cases were monitored at the pediatric cardiology outpatient clinic. The mean follow-up duration was 37.19 \pm 22.71 (1–75) months.

Complete blood count, acute phase reactants, throat culture growth, anti-streptolysin O values, and other biochemistry and differential tests were conducted. The laboratory findings of the cases are shown in Table 1. As a result of the throat culture (15 cases), no culture growth was observed. The ASO values were under 200 U/L in 3 cases. No pathology was detected in the ECG findings.

Chorea was accompanied by arthritis in 6 cases (23%) and by carditis in 22 cases (84.6%), while 4 cases had pure chorea. Choreic movements were found in 5 cases (19%) in the form of hemichorea (4 right, 1 left). The rest had choreic movements in their entire body. The chorea findings recurred during the follow-up of 3 cases.

The cases with carditis findings had varying degrees of valve deficiency, and 4 cases had left ventricular dilatation. 12 (54.5%) cases had single valve involvement (mitral), whereas 10 (45.5%) had double valve involvement (mitral and aortic). The severity of the valve involvement was mild in 8, moderate in 10, and severe in 4 cases (Table 2). During the follow-up of the 22 cases with carditis findings,

Table 3: Distribution of carditis cases in beginning and the course of valve regurgitation in follow-up

Type of carditis	Sub-clinical	Clinical
Number of patients (22)	8 (36.4%)	14 (63.6%)
Status of valve regurgitation		
New regurgitation	1	0
Same	4	4
Decreased	1	7
Healed	3	3

it was observed that valve involvement disappeared in 27.3%, decreased in 36.35%, and remained the same in 36.35%. Valve involvement developed during the follow-up of one of the four cases that did not previously have heart involvement (3.8%). The clinical and subclinical carditis distributions of the cases and their follow-up status are as in Table 3.

All followed-up cases received benzathine penicillin treatment. 9 cases with high acute-phase levels (35%) also received cortisone and aspirin treatment in addition to chorea treatment.

Cranial MR was taken from 17 cases. There were minimal non-specific changes in the MR reports of 3 of these cases.

For chorea treatment, only haloperidol was administered to 10 of the cases, valproic acid was administered to 4 cases, and both drugs were used together in 11 cases. The drugs that were administered to one of the cases could not be determined from the records.

Discussion

SC is one of the major criteria stated among the Duckett Jones criteria for the diagnosis of ARF. Moreover, presence of SC by itself is sufficient for diagnosis. Considering it is such a significant indicator of ARF, in this study, we have examined and followed up cases with SC. It is stated that SC is observed in 10–20% of ARF cases, frequently between the ages of 5–15,^[1–5] and has a higher incidence rate among females than males.^[12,13] The sex and age distribution of our study group was in line with the literature. SC is known to be caused by group A β -hemolytic streptococcus infections^[4] yet since SC emerges 1–8 months after the infection, no findings of a streptococcus infection might be present at the time of diagnosis.^[1–5] This was observed in our study as there was no reproduction in the collected throat cultures of our cases and the ASO values were under 200U/L in 3 cases. SC manifests itself with non-rhythmic involuntary movements. It usually develops bilaterally but in 20–30% of the cases, it can also be in the form of hemichorea.^[4] In our study, 5 of the cases (19%) had hemichorea. Although SC is generally benign and is known to disappear in 2–6 months,^[1–5] there are also cases in which chorea recurs during the follow-up period. It was stated that the findings might recur within 1–3 years following treatment in 15–20% of SC cases.^[15] Likewise, in our study, we have observed that the chorea findings of 3 cases recurred. The fact that some cases did not properly comply with the benzathine penicillin treatment and that

some had a previous history of rheumatic fever and throat infections might have been some of the factors contributing to this recurrence.

In ARF cases chorea can be observed either along with one or more other symptoms of ARF such as arthritis and carditis or in the form of “pure chorea”, in which there are no other accompanying diseases. Often times pure chorea may be overlooked as it may be incorrectly diagnosed as a mental or psychiatric disease or be mistaken for other diseases that could induce the same clinical picture such as lupus erythematosus, hyperthyroidism, and drug reactions.^[4] On the other hand, cases in which SC is accompanied by other diseases are much easier to diagnose. In our study, we have conducted neurological examinations and laboratory tests on all the cases in order to rule out any possibilities of other diseases. The cases who neither had any findings in their differential diagnosis and their laboratory test results that could suggest another disease nor any noticeable pathologies in their MR test results were evaluated as pure chorea cases. In various studies, it has been reported that the rate of pure chorea is higher, however, in our study group only four cases (15.4%) had pure chorea. The rate of arthritis accompanying SC was reported as 30%, while the rate of carditis accompaniment was reported as 35%.^[4] In our study group, on the other hand, arthritis was observed along with SC in 6 cases (23%) while carditis was observed in 22 cases (84.6%). As the incidence rate of carditis was significantly higher in our sample compared to the previously reported rates, we have focused on the co-occurrence of carditis and SC.

When carditis accompanies SC, it can be seen in the form of clinical or sub-clinical carditis. Although clinical carditis can be easily diagnosed, for the most part, sub-clinical carditis may be overlooked as there are no classic auscultatory findings of valvar dysfunction in these cases but are revealed by echocardiographic measurements.^[1] When the Duckett Jones criteria for ARF were first defined, only clinical carditis was accepted as a criterion, however, in the revised versions, sub-clinical carditis has also been recognized thanks to echocardiography becoming more prevalent. To add to this, in light of these new criteria, Kumar et al.^[16] have reported that sub-clinical carditis is observed in almost all SC cases. A meta-analysis covering 23 studies and 5 continents determined the prevalence of sub-clinical carditis cases among all rheumatic fever cases as 16.8% and it was seen that sub-clinical carditis findings could continue, worsen, disappear, or initially disappear then reappear during the follow-up period.^[17] In the rheumatic fever series of Özdemir et al.,^[12] among 16 SC cases, 5 (31.3%) had clinical carditis, and 8 (50%) had sub-clinical carditis. The researchers determined that valve involvement continued in follow-up in 55% of the sub-clinical carditis cases. In yet another study, it was reported that sub-clinical carditis cases are just as important as clinical carditis cases and that its findings continued during the follow-up of 60% of the cases.^[9] In our study group, 8 (36.4%) of the cases had sub-clinical carditis while 14 (63.6%) had clinical carditis. During the follow-up of these cases, we have observed that valve deficiency continued in 4 cases, decreased in 1 case, and disappeared in 3 cases after treatment. Interestingly, in one of our sub-clinical carditis cases, valve deficiency developed during the follow-up despite initially not having any valvar dysfunctions.

Another point worth mentioning is that although carditis findings are normally not observed in the follow-up of pure chorea cases, Veasy et al.^[10] have found that there were valve disorders in 57%

of pure chorea cases. Similarly, in another study, it was found that mitral stenosis findings develop in 23% of pure chorea cases during their middle ages.^[9] Given that sub-clinical carditis is relatively newly understood, following its acceptance as a Jones' criterion and the increase in diagnosis rates with the advancements in echocardiography, it is possible that what was once classified as pure chorea might have, in fact, been cases of undiagnosed sub-clinical carditis. This is precisely the reason why proper echocardiographic measurements play a crucial role in diagnosing the accompaniment of carditis and SC as leaving such valvar dysfunctions untreated might cause them to become chronic and lead to rheumatic heart disease (RHD). Carapetis et al.^[6] reported that RHD developed in 68% of rheumatic fever cases followed for 15 years. This is especially concerning in developing countries in which acute rheumatic fever is quite prevalent. In order to prevent RHD in these countries, it is crucial to properly diagnose ARF symptoms, including sub-clinical carditis, to administer treatment and follow-up these patients accordingly, and hence echocardiography is of great importance in this process.

Conclusion

In our study we have found that the incidence rate of carditis in SC cases (84.6%) was significantly higher compared to previous studies. While this result is significant in terms of demonstrating how frequently carditis occurs in SC cases and hence showing the importance of echocardiography for this diagnosis, it might be skewed as our study group consisted solely of patients who were under cardiological follow-up and had echocardiography results. Thus, it would be beneficial to conduct multi-centered, larger scale studies on this matter in order to accurately assess acute rheumatic fever, which remains a serious and prevalent issue in developing countries, and its diagnosis criteria such as Sydenham chorea and carditis, and thereby to ensure that ARF patients are diagnosed and treated properly.

Limitations: The study is retrospective and the study group includes a single center and a small number of cases. This has been the difficult part of the study. In addition, the follow-up period covers a short period of time. For more effective results and evaluations, it would be appropriate to conduct multicenter, long-term follow-up and prospective studies with more cases.

Statement

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Ethics Committee Approval: The Zeynep Kamil Maternity and Children's Training and Research Hospital Clinical Research Ethics Committee granted approval for this study (date: 03.03.2021, number: 57).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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