The heart in rheumatic disease

Sir,

I read with interest the review article titled "The heart in rheumatic disease". Regarding acute rheumatic fever the revised Jones criteria have been revised again in 1992. One minor manifestation of the "past history of rheumatic fever or rheumatic heart disease" has been deleted. The other point which I would like to make is regarding the so called triad of fever, polyarthritis and an elevated sedimentation rate, which the author says is the least specific combination meeting the modified Jones criteria. This would be so if one is ignoring the essential criteria. Acute rheumatic fever cannot be diagnosed unless there is evidence of recent Streptococcal infection (raised ASO titre), positive throat culture or recent Scarlet fever), the only exception being rheumatic chorea.

Sarosh A. Khan
Najran General Hospital
Najran
Kingdom of Saudi Arabia

Hepatitis C virus detection and genotyping in liver tissues and sera of Saudi patients using PCR and a line probe assay

Sir,

The recent publication in your Journal by Al-Ahdal et al is most interesting and has added considerably to our knowledge of the epidemiology of Hepatitis C virus (HCV) in the Kingdom. Previous publications have indicated that the predominant HCV genotypes in the Kingdom are types 1 and 4. In the series by Al-Ahdal et al while the predominant genotype was type 1, the predominant type by Al-Faleh et al was type 4. Clearly large series in various parts of the Kingdom is required to determine the epidemiology of HCV genotypes in our area.

We have been performing Polymerase Chain Reaction (PCR) and other nucleic acid amplification techniques (NATs) for the last 2 years for the diagnosis and management of patients with Hepatitis C and recently we instituted the genotyping of HCV using PCR by the commercial kit produced by Sorin Biomedica, Saluggia, Italy. The assay is based on a combination of two well established techniques, the PCR and DNA enzyme immunoassay (DNA EIA). In the first step of this method, a cDNA of about 250 bp corresponding to the HCV core-region is amplified by nested PCR. The target cDNA is then hybridized to type-specific oligonucleotides fixed to a solid phase through an avidin-biotin bridge. The formed hybrids are detected by a standard ELISA using monoclonal antibodies reacting with double-stranded DNA. Typically signal-to-noise (S/N) ratios between 18.2 and 48.6 could be observed when different HCV types/subtypes were analyzed by this method.

We would like to support the publication of Al-Ahdal et al with the preliminary results of our study here in Jeddah, more so that previous studies so far reported have been carried out in institutions located in the Riyadh area.

Serum samples of 10 Saudi patients being investigated in our Hepatology Unit, were examined by Axysm Hepatitis C virus enzyme immunoassay (HIV EIA) and Recombinant immunoblot Assay (RIBA) Table 1. There were 7 males and 3 females with mean age of 47.9 years and ranging from 20 to 66 years. Qualitative PCR by DNA EIA using the Sorin commercial kit was performed to confirm viremia. HCV genotyping was performed using the Sorin kit according the manufacturer's instructions. Our results are shown in Table 1. Six patients had genotype 4, while 2 had genotype 1a, one each with genotype 1b and 5. Two of the

Reply from Author

I thank Dr. Sarosh Ahmed Khan for bringing attention to the fact that the Jones criteria has been revised in 1992. I agree that acute rheumatic fever essentially requires evidence of a recent streptococcal throat infection and humoral-antibody response. Indeed, without the latter, rheumatic fever cannot occur.

Dr. Khan will certainly have much more experience of acute rheumatic fever than I have, since it is now a rarity in North America.

W. Watson Buchanan
Sir William Osler Health Institute
565 Sanatorium Road
Hamilton, Ontario
Canada

References

Table 1 - HCV genotyping on Saudi patients at King Khalid National Guard Hospital, Jeddah

<table>
<thead>
<tr>
<th>No.</th>
<th>Age/Sex</th>
<th>Clinical Details</th>
<th>Serum HCV EIA</th>
<th>HCV RIBA</th>
<th>Qualitative HCV RNA PCR</th>
<th>Genotype</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>46/F</td>
<td>Chronic Active Hepatitis</td>
<td>Detected</td>
<td>ND</td>
<td>Positive</td>
<td>Type 1a</td>
</tr>
<tr>
<td>2</td>
<td>66/M</td>
<td>HCV Antibody Positive with Normal LFT</td>
<td>Detected</td>
<td>ND</td>
<td>Positive</td>
<td>Type 4</td>
</tr>
<tr>
<td>3</td>
<td>23/M</td>
<td>Chronic Active Hepatitis</td>
<td>Detected</td>
<td>ND</td>
<td>Positive</td>
<td>Type 1a</td>
</tr>
<tr>
<td>4</td>
<td>65/F</td>
<td>Liver cirrhosis with Portal Hypertension</td>
<td>Detected</td>
<td>Positive</td>
<td>Positive</td>
<td>Type 4</td>
</tr>
<tr>
<td>5</td>
<td>48/M</td>
<td>Chronic Active Hepatitis</td>
<td>Detected</td>
<td>Positive</td>
<td>Positive</td>
<td>Type 4</td>
</tr>
<tr>
<td>6</td>
<td>35/M</td>
<td>HCV Antibody Positive with Normal LFT</td>
<td>Equivocal</td>
<td>Positive</td>
<td>Positive</td>
<td>Type 4,5</td>
</tr>
<tr>
<td>7</td>
<td>20/M</td>
<td>HCV Antibody Positive with Normal LFT</td>
<td>Equivocal</td>
<td>Positive</td>
<td>Positive</td>
<td>Type 4,5</td>
</tr>
<tr>
<td>8</td>
<td>59/M</td>
<td>Chronic Active Hepatitis</td>
<td>Detected</td>
<td>Positive</td>
<td>Positive</td>
<td>Type 5</td>
</tr>
<tr>
<td>9</td>
<td>66/F</td>
<td>Chronic Active Hepatitis</td>
<td>Detected</td>
<td>ND</td>
<td>Positive</td>
<td>Type 1b</td>
</tr>
<tr>
<td>10</td>
<td>51/M</td>
<td>HCV Antibody Positive with Normal LFT</td>
<td>Detected</td>
<td>ND</td>
<td>Positive</td>
<td>Type 1b</td>
</tr>
</tbody>
</table>

ND = Not done; LFT = Liver Function Tests

patients with genotype 4 had mixed infections with genotype 5 as well. Although our figures are small, it appears that in our area of the Kingdom, genotype 4 may be the predominant genotype. Previous studies have not recorded the presence of genotype 5 in the Kingdom. We were unable to confirm acquisition of the virus outside the Kingdom. None of the patients gave a history of transfusion of blood or blood products. Two patients with equivocal HCV EIA were confirmed positive by the qualitative HCV RNA PCR thus confirming the usefulness of the amplification techniques in the identification of viremia. Our results are in keeping with those of previous reports demonstrated by Okamoto et al and Al-Faleh et al. The main justification of performing the qualitative HCV PCR is that the most sensitive tests for the diagnosis of HCV are those based on molecular hybridization permitting the direct detection of HCV RNA. The usefulness of HCV genotyping has been well established in that it provides epidemiological information, assists in patient treatment with interferon as a predictor for response and is of prognostic value. Recently PCR techniques have been developed which combine the sensitivity of PCR with the simplicity and versatility of conventional immunoassay. Laboratories in the Kingdom performing EIA techniques, especially those of tertiary Institutions, should endeavour to develop these tests so that a large series of data can be made available in order to determine the epidemiology of HCV genotype in the Kingdom and an evidence based strategy for management of HCV liver diseases in the Kingdom.

Ibrahim Mahgoub
Department of Medicine
Abimbola O. Osoba
Mohamed A. Abdelaal
Bakheet Al Shareef
Department of Pathology
King Khalid National Guard Hospital
PO Box 9515
Jeddah 21423
Kingdom of Saudi Arabia

Reply from author

Sir,

The letter entitled “Hepatitis C virus detection and genotyping in liver tissues and sera of Saudi patients using PCR and a line probe assay” by Mahgoub et al, appearing in this issue of the Saudi Medical Journal, is both timely and supportive. We agree that genotyping of hepatitis C virus (HCV) isolates from various regions of the Kingdom is necessary. We have reasons to believe that such a study was

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supported and is being conducted. The work we described in our paper was intended to mainly to investigate the suitability of serum versus liver tissue for the polymerase chain reaction (PCR) determination and genotyping of HCV isolates. We realized and discussed that 15 HCV-positive samples do not suffice a conclusion of genotype predominance. Recently, we published our observation that genotype 4 is the most prevalent by using 119 PCR-positive HCV isolates when the core amplicons of these isolates were sequenced. Therefore, the results obtained from almost all genotyping studies of Saudi isolates indicated the predominance of HCV-4.

Mohammed N. Al-Ahdal
Virology and Infectious Diseases Research Laboratories
King Faisal Specialist Hospital and Research Centre
PO Box 3354
Riyadh 11211
Kingdom of Saudi Arabia

References


Identifying *Helicobacter pylori*: is H and E staining enough?

Sir.

The purpose of this letter is to clarify a misunderstanding in an article printed in the Journal. The first point that every reader may look for is: new sensitivity and specificity of H and E compared with other tests (Urease and Giemsa staining), the values and how they are exactly calculated? Firstly, we must remember that when we are going to calculate the sensitivity and specificity of a test, we must compare the results of the test with gold standard, so that we have true positive, false positive, true negative and false negative. However, in that article, we can not find gold standard, moreover, if we check the author's tables, we can find that H & E staining is the gold standard for other tests. Questions are: (1) What is the gold standard for calculating the sensitivity and specificity of H and E staining and what is true positive and negative? (2) Is H & E staining the gold standard for Giemsa and urease test, that can be seen in the author's tables? If true, how can the title be: Is H & E enough? (3) If we are comparing similar tests, that one operator can perform all of them, it is better that the same operator carries out all the tests with blindness (without knowing about the specimens). If there are several operators, then it is better for every operator to perform the test for every specimen with blindness, and if it is impossible, distribute specimens between operators randomly. In the article, all the Giemsa staining was read by one of the authors, (NM), who may have had different experiences in Giemsa or H & E, and there is bias here: if all of the pathologists have H & E and Giemsa staining sections, can the results be different? Or is the experience of the pathologist in Giemsa an important factor to the true positive results?

Reza O. Samani
No. 1604 Alborz 9 Street
Shahrak Jendarmery
Tehran 14638
Iran

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