Autoimmune hepatitis in older patients

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Abstract

Aim: autoimmune hepatitis (AIH) is thought to present rarely in old people. The aims of the present study were to (i) review individuals diagnosed clinically as having AIH presenting over or under 65 years of age at Freeman Hospital, Newcastle, from 1979 to 1993 and (ii) compare diagnostic and histological scores, treatment and outcome, and hence provide a useful profile of the disease in older patients.

Methods: 310 individuals with a histological diagnosis of chronic hepatitis were identified, and review of the medical notes of 286 revealed 54 with a diagnosis of AIH. Of these, 12 (22%) were ≥65 years of age at presentation.

Results: at presentation, the mean diagnostic score (according to the diagnostic scoring system devised by an international panel; maximum score, 17) of the whole group was 11.5 (SD 3.5) and the mean score for those ≥65 years was 9 (SD 3). The mean histological grade (intensity of necro-inflammatory activity; maximum, 18) for the elderly group was 6 (SD 2) compared with 4.5 (SD 0.5) for the whole group. Despite this, 42% of the elderly sufferers had received no immunosuppressive therapy (versus 12% of the younger group). At follow-up, 26% in both groups had developed cirrhosis. None of the elderly group (but 7% of the younger group) had died from complications of chronic liver disease.

Conclusion: we present data on 12 patients presenting at 65 years and over with AIH. In elderly individuals diagnosis may be more difficult, and treatment appears often to have been withheld. Despite this, and the more severe initial histological grade, the prognosis appeared no worse than in younger, usually correctly treated, patients.

Keywords: autoimmune hepatitis, elderly patients

Introduction

Autoimmune chronic active hepatitis, now termed autoimmune hepatitis (AIH), is a condition of unknown aetiology, characterized by progressive destruction of liver parenchyma, often leading to hepatic fibrosis and subsequent cirrhosis, and responding to immunosuppressive therapy with steroids with or without azathioprine [1].

The original descriptions of AIH concerned young females with hypergammaglobulinaemia, circulating autoantibodies, abnormal, often hepatitis, liver function tests and a chronic fluctuating course [2]. It has however become clear that AIH is a diverse condition that can affect both sexes and spares no age group.

Presentation of AIH in older subjects is thought to be rare, indeed the largest series of elderly patients to date has described five cases [3]. It is unclear, however, to what extent this 'rarity' is due to under-recognition or to a lack of clear definition of the disease in elderly individuals.

Recently, new parameters for the clinical diagnosis and histological definition of the disease have been suggested: in 1992, at the Biennial Meeting of the International Association for the Study of the Liver, an international panel was convened to review all the features of AIH and to determine a consensus on diagnostic criteria [4]. Minimum required parameters for a diagnostic score, prior to liver biopsy, were developed, centred upon serum aminotransferase, gammaglobulin concentrations and titres of circulating autoantibodies, after exclusion of all other possible aetiological factors.

In addition, in 1995, a previously described histological grading and staging scoring system for chronic hepatitis (Knodell score) was refined and this has subsequently been applied to patients with AIH [5]. Grade refers to the intensity of necro-inflammatory activity, whilst staging is a measure of fibrosis and architectural alteration (i.e. structural progression of the disease), currently believed to be the consequence of the necro-inflammatory process.
Using information from the above diagnostic and histological systems, we decided to examine AIH in subjects aged 65 years and over at presentation and to compare diagnostic and histological scores, treatment and outcome with those found presenting under 65 years of age, in a liver disease centre with additional interest in geriatric medicine.

This allows us to provide the first reliable body of information concerning the presentation, diagnosis and treatment of AIH in older patients.

Methods

Computerized pathology records from 1979 to 1993 at the Freeman Hospital, Newcastle upon Tyne, were examined to find all individuals with a histological descriptive diagnosis of chronic hepatitis.

The medical notes of all subjects identified from the pathology records were then sought and reviewed. Those in whom a clinical diagnosis of AIH had been made and in whom one or more of the following autoantibodies had been found to be positive to a titre of ≥1:40—smooth muscle, antinuclear, liver/kidney/microsomal—were included.

Exclusions included those with evidence of viral hepatitis, i.e. positive hepatitis B or C serology, significant alcohol intake (≥40g/day), the consumption of any medication that might conceivably be associated with chronic hepatitis, those with all negative autoantibodies, those with other autoantibodies (e.g. antimitochondrial antibodies—suggestive of primary biliary cirrhosis), or clinical or radiological data to suggest sclerosing cholangitis.

The diagnostic scoring criteria suggested by the international panel were applied retrospectively to each individual. This system allocates scores to certain parameters, prioritizing those felt to be important to the diagnosis by giving them a higher numerical score and giving a negative score to those parameters felt to make a diagnosis of AIH less likely. The aggregate scores can be calculated before and after treatment. A 'definite' diagnosis of AIH is a score of >15 before treatment and >17 after, whilst a 'probable' diagnosis is 10-15 before and 12-17 after [4].

Liver biopsies of all individuals were reviewed independently by two histopathologists who were unaware of the diagnostic score, and graded and staged according to the internationally recognized histological scoring system [5].

Results

Three hundred and ten individuals with a histological diagnosis of chronic hepatitis were identified from the computerized histology records. The medical records were not available for 24 patients (8%). Review of the medical notes of the remaining 286 revealed 54 with a clinical and histological diagnosis of AIH and circulating autoantibodies to a titre ≥1:40 (19% of total).

Twelve of this group of 54 patients were 65 years of age or older at the time of presentation. Mean follow-up (from presentation to most recent hospital review) was 3.5 years in those aged 65 and over (range 1-8 years) and was not significantly different in those under 65 (see Table 1).

The three scoring systems were applied to both groups. Mean scores revealed that the clinical diagnostic score before treatment was lower in the older group, whilst the histological grade, an indicator of the degree of hepatic inflammation, was higher (Table 1).

The elderly group appeared to present less acutely, with more insidious, non-specific symptoms (Figure 1).

Table 1. Details of patients with a clinical and histological diagnosis of autoimmune hepatitis and circulating autoantibodies to a titre ≥1:40

<table>
<thead>
<tr>
<th>Age at presentation (years)</th>
<th>&lt;65</th>
<th>≥65</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, years (SD)</td>
<td>47.4 (12.4)</td>
<td>68.8 (2.5)</td>
</tr>
<tr>
<td>No. of subjects</td>
<td>42</td>
<td>12</td>
</tr>
<tr>
<td>Sex distribution, % male</td>
<td>19</td>
<td>25</td>
</tr>
<tr>
<td>Mean follow-up, years (range)</td>
<td>6.5 (1-14)</td>
<td>3.5 (1-8)</td>
</tr>
<tr>
<td>Mean diagnostic score before treatment (SD)a</td>
<td>11.5 (3.5)</td>
<td>9 (3)</td>
</tr>
<tr>
<td>Histological findingsb</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean grade (SD)</td>
<td>4.5 (0.5)</td>
<td>6 (2)</td>
</tr>
<tr>
<td>Mean score (SD)</td>
<td>3.6 (2)</td>
<td>3.2 (2.6)</td>
</tr>
</tbody>
</table>

aMaximum score, 17.
bMaximum grade, 18; maximum stage, 6.
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Figure 1. Patients with autoimmune hepatitis: symptoms at presentation in those older and younger than 65 years. 1, major (jaundice, signs of hepatic failure); 2, minor (lethargy, pruritus, pale stools, abdominal pain etc.); 3, asymptomatic.

than the younger group, 42% of whom presented with symptoms indicative of decompensated liver disease.

In terms of treatment, 42% of elderly individuals had received none, whilst most younger sufferers were treated with prednisolone with or without azathioprine (Figure 2). There was no significant difference in the grading score (inflammatory activity) between elderly subjects given immunosuppressive treatment and those untreated. The outcomes for the five elderly untreated subjects were as follows: two died from a disease unrelated to the liver disease within an average 1.5 years of follow-up and three survived (mean follow-up 3 years). Of the three survivors, one subject’s liver function tests returned to normal without treatment after one liver biopsy and the other two were felt to have continued disease but received no immunosuppressive therapy.

Five elderly subjects received treatment with prednisolone alone, one of these died 2 years into follow-up, two developed cirrhosis, whilst the remaining two have a chronic hepatitis. A further two of the elderly patients were treated with prednisolone and azathioprine: one developed cirrhosis, the other chronic hepatitis.

All the elderly AIH sufferers in this study who died did so from a disease unrelated to liver disease, unlike the younger group, of whom 7% died as a result of complications of decompensated liver disease (Figure 3).

Discussion

We have described a group of 12 patients with AIH who presented for the first time aged 65 years or older. Although by no means frequent, AIH in elderly patients may be more common than previously thought. During the 14 years from 1979 to 1993 at Freeman Hospital, Newcastle upon Tyne, those aged 65 and older accounted for 22% of patients with circulating autoantibodies and diagnosed histologically as having AIH. It has been previously noted, as we have also seen in this study, that approximately three-quarters of sufferers are female [6].

AIH in elderly subjects may be subject to underreporting even in the light of this study. In general, liver biopsy is regarded as essential to confirm the diagnosis, assess activity, show the presence or absence of cirrhosis and to follow treatment [2]. In elderly individuals with non-specific symptoms, liver histology may not be obtained, potentially leading to an underestimation of the true incidence of the disease. Since the patients in this study were identified through liver biopsy findings, an unknown additional number of patients may have fallen into this category and the true prevalence of AIH may be greater than seen in this study. Furthermore, it is possible that a small number of individuals whose liver biopsies were not classified as ‘chronic hepatitis’ but as ‘severe active cirrhosis’ may have been omitted from this series as they were not detected on the computer histology search.

Age should not be regarded as a contraindication to liver biopsy: it is a safe procedure in experienced hands. One recent study [7] revealed that 6% of liver biopsies in England and Wales are performed on those over 80 years of age, with an overall mortality of 0.13–0.33% and no increased mortality with increasing age.

Elderly sufferers were assessed as less ‘severe’ using the clinical diagnostic criteria suggested by the international panel, despite worse histological inflammatory
grades. This underlines the importance of liver biopsy as a diagnostic procedure in older individuals presenting with signs and symptoms suggestive of AIH.

Rigorous scoring systems, based largely on evidence from studies involving younger subjects and extrapolated to elderly patients, must be interpreted with caution.

Controlled clinical trials of treatment of AIH have shown that corticosteroid treatment prolongs life [8, 9] and induces remission. Acutely, the response can be so dramatic as to be almost diagnostic of AIH.

The milder symptoms at presentation may be a reason why steroid treatment was not offered to some of these older patients. The lack of liver-related deaths, despite lack of treatment in 42%, over a mean follow-up of over 3 years, suggests that the disease may be clinically less aggressive in older AIH patients. Nevertheless 58% of patients did receive immunosuppres- sant treatment and none died from liver-related disease. We would therefore suggest that immunosuppressive treatment is appropriate in such patients.

Acknowledgements

J.L.N. was funded by the Astra Foundation.

Key points

- Autoimmune hepatitis presents uncommonly in patients over 65 years of age: 12 out of a series of 54 patients presented after 65 years.
- In older patients, despite presentation being more insidious, prognosis was surprisingly good.
- Liver histology at presentation was more 'advanced' in those presenting over 65 years of age.

References


Received 11 December 1996