Evidence of genetic factors in hidradenitis suppurativa

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SUMMARY

Twenty-six probands suffering from hidradenitis suppurativa were identified from Hospital Activity Analysis (H.A.A.) records for the period 1980–83 and by direct referral from hospital specialists over a 6-month period in 1983–84. Investigation of their families eventually confirmed a total of 62 affected individuals from 23 families. In 11 families there was evidence in favour of single gene or Mendelian inheritance; in another three there was familial occurrence; in nine families there was a negative family history at the time of enquiry. The disease appears to be commoner than reports suggest and it is probable that there is an underestimation of affected individuals in our community. Problems of identification including variable age of onset and psycho-social factors were found and may be responsible for false-negative family histories.

Much of the literature of hidradenitis suppurativa has been confined to clinical findings and treatment (Brunsting, 1952; Gordon, 1978; Ching and Stahlgren, 1965). The disease has been classified with acne conglobata and dissecting cellulitis of the scalp as the follicular occlusion triad (Self & Montes, 1979). The authors suggest that following an initial follicular hyperkeratosis, there is obstruction of the pilosebaceous apparatus and associated apocrine glands with subsequent infection. This nevertheless fails to explain why some individuals continue to have recurrent episodes with scarring, abscesses, sinus formation and subcutaneous tunnelling. Other factors would seem to be important. An earlier paper (Knaysi, Cosman & Crikelair, 1968) noted a family history in 3 of 18 patients specifically questioned but there was no further information given. The possibility of genetic factors in this disorder was suggested in a recent report on the first eleven families (A–K) in this paper (Fitzsimmons, Fitzsimmons & Gilbert, 1984). There is a lack of detailed family studies and in view of the ease with which the first three families were identified, further family studies were undertaken.

METHODS

The probands were ascertained from H.A.A. records from a busy general hospital (City Hospital, Hucknall Road, Nottingham) providing specialist plastic surgical services for the East

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Midlands. Affected individuals were also referred from hospital specialties including dermatology and general surgery in the South Trent region. There was an inevitable overlap of patients obtained from these two sources. It was accepted that ascertainment would be incomplete as general practitioners were not contacted and H.A.A. records deal only with in-patients. Out-patients with the disease referred to specialties other than those mentioned were not included.

Hidradenitis suppurativa was diagnosed on the basis of recurrent suppurative cicatrizing lesions of apocrine gland bearing areas of the skin, primarily affecting the axillae and anogenital area. Acne conglobata was diagnosed on the basis of abscesses and scarring affecting predominantly the back, chest and buttocks (Rosner et al., 1982).

Family pedigree information was collected by domiciliary visits or hospital interviews. In 31 of the 62 affected the diagnosis was made by a consultant dermatologist; 17 were examined by the authors; 14 declined to be visited or examined and the diagnosis was presumed on patient and family doctor information.

RESULTS

The total number of patients identified with the disease was 62: 40 female and 22 male. Forty-eight of these were from 11 families; three from three families; and nine from nine families. Two probands did not agree to co-operate with further family investigations (Table 1).

<table>
<thead>
<tr>
<th>TABLE 1. Hidradenitis suppurativa</th>
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<tbody>
<tr>
<td>Total number of affected individuals</td>
</tr>
<tr>
<td>In eleven families A–K</td>
</tr>
<tr>
<td>In three families a–c</td>
</tr>
<tr>
<td>In nine families 1–9</td>
</tr>
<tr>
<td>In two families (uncooperative)</td>
</tr>
<tr>
<td>Total (22 males, 40 females)</td>
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</tbody>
</table>

In the eleven families (A–K, Fig. 1) there were 35 females and 13 males. The disease is transmitted vertically through three generations in five families and through two in six. In family D there is male-to-male transmission and in family B, identical twins II.4 and II.5 were both affected.

In three families (a–c, Fig. 2) there was a history of the disease in a parent of the proband in two families and in a cousin of the proband in the third. In family b, I.1 died from other causes but this family appears to demonstrate a further instance of male-to-male transmission.

In nine families (1–9, Fig. 3) there was no confirmatory evidence of the disease in any other individuals at the time of the investigation. However, this group initially included a further family where it was presumed there was only one affected individual. Subsequent contact with a knowledgeable and co-operative key person confirmed that the proband's mother and sister both suffered from the disease as did their mother in generation I. This is family K.
**FIGURE 1.** Occurrence of hidradenitis suppurativa in eleven families (A–K), indicating possible single gene or Mendelian inheritance (see also next page).

**DISCUSSION**

Familial clustering of disease is well recognized and does not necessarily imply a genetic origin. However, the number of affected individuals in the first eleven families and the mode of transmission through several generations is consistent with single-gene dominant inheritance. The number of first degree affected relatives i.e. parents, sibs and children of the probands is approximately 34% of the total number of first degree relatives of the families A–K (Table 2). This is less than the expected 50%, but is consistent with the proposal that the condition is dominantly transmitted. The male-to-male transmission demonstrated in family D and possibly also in family B would appear to confirm autosomal and not X-linked dominant
inheritance. The disease shows considerable variation in the age of onset and may appear in adolescence or early or even middle adult life. In the families studied there were at least 40 individuals who were first degree relatives of the probands in the group A–K and were under 20 years of age at the time of investigation. They could theoretically develop the disease at some stage in the future. Forty-six of the total 62 affected probands developed the disease in their late teens or early adult life and 16 between the ages of 30 and 40 years. This fact coupled with incomplete ascertainment and variable penetrance may distort the expected proportion of affected individuals and make straightforward segregation analysis difficult. Psycho-social factors were noted to be important and a number of females were reluctant to admit to the disease, particularly vulval disease. In some cases, the presence of the condition was concealed from parents and close relatives. There was significant variation in the severity of the disorder and some patients with minimal axillary lesions had not even attended their family doctor.
Evidence of genetic factors in hidradenitis suppurativa

It is difficult to explain the strikingly different pedigrees in families 1–9. There were at least nine offspring of the probands who were under the age of 20 years at the time of the investigation and could theoretically develop the disease when they are older. These families will require periodic re-examination. It is possible that hidradenitis suppurativa may have several causes, with genetic factors being important in some families but not in others. On occasions, multifactorial inheritance may mimic Mendelism but the number of affected individuals in families A–K considerably exceeds that expected on a multifactorial model. Unfortunately, there is as yet no accurate information on the disease incidence. Figures from one busy dermatological out-patient practice suggest an incidence of approximately 1 in 300 (personal communication, Professor J.A.A. Hunter, Department of Dermatology, Royal Infirmary, Edinburgh). On this basis, if the condition were multifactorial in origin one would expect a frequency of 1 in 50 in first degree relatives of the probands. This is obviously not the case in the families A–K (Fig. 1).

Many dermatologists assume a clear association between hidradenitis and cystic acne.
However, only eight of the affected individuals in this study had acne conglobata and five of these were from one family, family A. This was an unusual pedigree and the acne conglobata which was severe presented in some individuals as early as 6-7 years of age. There was no historical or clinical evidence of an increased incidence of severe acne vulgaris in the remaining patients.
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Detailed investigation of family A did not reveal any biochemical or chromosomal marker in the affected individuals and clinical examination of many patients confirmed only the skin condition. No other associated lesions were detected.

**TABLE 2. Hidradenitis suppurativa. Frequency in first degree relatives of probands**

<table>
<thead>
<tr>
<th>Relationship</th>
<th>Total</th>
<th>No. affected</th>
<th>% Affected</th>
<th>Expected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Siblings</td>
<td>29</td>
<td>10</td>
<td>35%</td>
<td></td>
</tr>
<tr>
<td>Parents</td>
<td>22</td>
<td>8</td>
<td>36%</td>
<td>50%</td>
</tr>
<tr>
<td>Children</td>
<td>19</td>
<td>6</td>
<td>31%</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>70</td>
<td>24</td>
<td>34.3%</td>
<td></td>
</tr>
</tbody>
</table>

**CONCLUSION**

If genetic factors are important in the causation of the disease, it should be possible to confirm this in further family studies. The basic cause of the disease remains obscure but could be related to morphological abnormality of the apocrine glands or abnormalities of relevant tissues such as keratin. There is a need for more detailed clinical information about affected individuals particularly the time of onset, the presence or absence of acneiform lesions and the natural history and incidence of this disease. Most individuals with hidradenitis suppurativa consider the condition to be an extremely burdensome one, although there is an obvious variation in clinical severity. This coupled with the apparent familial implications make it important to enquire and examine relatives of individuals found to be suffering from this disease.
ACKNOWLEDGMENTS

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REFERENCES


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