Hyper IgE Syndrome with Large Recurrent Head Abscesses Misdiagnosed as Folliculitis

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Hyper IgE syndrome (HIES) is a rare primary immunodeficiency disease. Most cases of HIES occur early in life. Nondescript symptoms tend to either mislead to delay in diagnosis or a delay in diagnosis. We report a case of a child with hyper IgE syndrome who initially presented with recurrent head abscesses and was misdiagnosed as suffering from “folliculitis”.

CASE PRESENTATION
A 5-year-old child was admitted to our hospital with a 4-year history of recurrent head abscesses and aggravation for 1 month. He had been clinically diagnosed with folliculitis and treated with antibiotics, with minimal relief. One month prior to admission, his condition had taken a turn for the worse when several scattered cold abscesses each grew to the size of a fist (Fig. 1a).

Further questioning revealed that the patient had a past medical history of repeated eczema, frequent upper respiratory infections (>10 times/year), and one hospitalization due to supposed septicemia. He had no family history of HIES or any other immunodeficiency disease. There was a characteristic appearance with forehead carina, widely-spaced eyes, and a broad nasal ridge. Other significant physical findings included residual root and tooth defects of the deciduous teeth in the upper and lower jaw, as well as mild lumbar scoliosis (Fig. 1b, c).

Laboratory analysis revealed serum IgE levels >6,000 ng/ml (0–691.4 ng/ml), with an ESR of 29 mm/h (0–15 mm/h) and C-reactive protein of 6.13 mg/l (0–3 mg/l). Routine blood tests showed a white blood cell count of 14.47 × 10⁹/l (5.0–12.0 × 10⁹/l), a neutrophil count of 8.07 × 10⁹/l (1.8–6.3 × 10⁹/l), and an eosinophil ratio of 13.00% (0.5–5.0 × 10⁹/l). Laboratory analysis revealed serum IgE levels >6,000 ng/ml (0–691.4 ng/ml), with an ESR of 29 mm/h (0–15 mm/h) and C-reactive protein of 6.13 mg/l (0–3 mg/l). Routine blood tests showed a white blood cell count of 14.47 × 10⁹/l (5.0–12.0 × 10⁹/l), a neutrophil count of 8.07 × 10⁹/l (1.8–6.3 × 10⁹/l), and an eosinophil ratio of 13.00% (0.5–5.0 × 10⁹/l). *Staphylococcus aureus* was detected in the patient’s abscesses. The lumbar plains showed slight scoliosis and the oral plains suggested a high arched palate. The pathological section showed that mixed inflammatory cells, including eosinophils and neutrophils, had infiltrated into the subcutaneous tissue, with associated abscess formation (hematoxylin–eosin; original magnification: a) × 40; b) × 200).

In 1999, the National Institutes of Health established HIES diagnostic criteria (1) (Table I). In this case, clinical evidence, together with laboratory and histopathological findings, clearly indicated a diagnosis of hyper IgE syndrome (total score: 42 points; see Table I). Significant improvement was noted in the patient following vancomycin and fusidic acid ointment as systemic and topical treatments, respectively.

DISCUSSION
HIES is a rare disease, with an annual incidence ranging from 1 in 500,000 to 1 in 100,000 (2). There are 2 distinct forms of HIES: Type 1, autosomal-dominant HIES (AD-HIES), is negatively correlated with mutations in STAT3, which is the most prevalent mutation described and accounts for the majority of HIES cases; Type 2, autosomal-recessive HIES (AR-HIES), is mainly caused by dysregulation in DOCK8, TYK2, PGM3, and SPINK5 (3). HIES is a multisystem disorder associated with varied clinical manifestations. An eczematoid rash is usually the initial clinical manifestation of HIES, generally starting on the scalp and face (4). Recurrent skin infection with *S. aureus* results in “cold” abscesses lacking the usual features of warmth and erythema, and is a nearly universal feature of HIES. Sinopulmonary infections caused by *S. aureus* are also common in HIES. A total of 97% of patients have serum IgE >2,000 ng/ml, and 83% of HIES patients exhibit typical facial features that include a prominent forehead, facial asmetry, sunken eyes, broad nasal ridge and fleshy nose, prognathism, and craniosynostosis. Approximately 65% of HIES patients have mus-
curskeletal abnormalities, including hyperextensibility of the joints, scoliosis, osteopenia, and pathological frac-
tures (5). The risk of malignancies, especially lymphoma, should 
not be overlooked in patients with HIES (6). Cutis verticis 
gyrata has also been reported in HIES patients (7).

For patients suspected to have hyper IgE syndrome, 
other immunodeficiency diseases such as Omenn syn-
drome (OS) and Wiskott-Aldrich Syndrome (WAS), both 
of which are associated with elevated IgE and eosinophils, 
should first be excluded. OS is typically manifested by 
the triad consisting of eczema, thrombocytopenia, and 
primary immunological screening. Children with WAS 
experience relatively early onset of symptoms including 
trauricular color, thrombocytopenia, and immunodeficiency. 

The therapeutic mainstay during the early stages of hyper 
IgE syndrome is preventing recurrent infections and sub-
sequent lung remodeling. Treatment with prophylactic anti-
microbials effectively eliminates S. aureus and decreases 
the frequency of pneumonia. Appropriate skin care such as 
bleach baths or other antiseptic treatments can be undertaken 
in order to prevent skin infections. HIES patients usually 
do not need to take precautions to prevent potential fungal 
flections (4). The role of bone marrow transplantation in 
HIES remains unclear, although it has been reported that 
the immunological and non-immunological manifestations of 
HIES in 2 patients completely disappeared following bone 
marrow transplantation (8). INF-γ, plasma transfusion, and 
intravenous immunoglobulins may normalize serum hyper 
IgE and increase neutrophil chemotaxis. Monoclonal anti-
IgE treatment has been shown to reduce serum IgE levels, 
although the pros and cons of this approach are still unclear 
(2). In this current case study, abscess incision and drainage 
were required in order to reduce pain and inflammation. In 
addition, although photodynamic therapy (PDT) leads to 
excellent results in the treatment of perforated folliculitis, 
its therapeutic potential in cases of hyper IgE syndrome 
has not been mentioned in any previous research. We are 
curious to see if PDT will eventually become a recognized 
treatment for HIES.

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The authors have no conflicts of interest to declare.

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plantation cures patients with autosomal dominant hyper-IgE 

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**Table I. NIH-HIES scoring system and patient scores**

<table>
<thead>
<tr>
<th>Clinical findings</th>
<th>Clinical findings</th>
<th>POINTS</th>
<th>POINTS</th>
<th>POINTS</th>
<th>POINTS</th>
<th>POINTS</th>
<th>POINTS</th>
<th>Patient's score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Highest serum-IgE level (IU/ml)</td>
<td>&lt;200</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>Skin abscess</td>
<td>None</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>Pneumonia (episodes over lifetime)</td>
<td>None</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>Parenchymal lung anomalies</td>
<td>None</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>Retained primary teeth</td>
<td>None</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>Scolliosis, maximum curvature</td>
<td>&lt;10°</td>
<td>1–2</td>
<td>3</td>
<td>4–6</td>
<td>&gt;6</td>
<td>1–2</td>
<td>3</td>
<td>4–6</td>
</tr>
<tr>
<td>Fractures with minor trauma</td>
<td>None</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>Highest eosinophil count (cells/µl)</td>
<td>&lt;700</td>
<td>1–2</td>
<td>3</td>
<td>4–6</td>
<td>&gt;6</td>
<td>1–2</td>
<td>3</td>
<td>4–6</td>
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<tr>
<td>Characteristic face</td>
<td>Absent</td>
<td>Mildly present</td>
<td>Present</td>
<td>Present</td>
<td>5</td>
<td></td>
<td></td>
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<tr>
<td>Midline anomaly</td>
<td>Absent</td>
<td>Mildly present</td>
<td>Present</td>
<td>Present</td>
<td>5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Newborn rash</td>
<td>Absent</td>
<td>Mildly present</td>
<td>Present</td>
<td>Present</td>
<td>5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eczema (worst stage)</td>
<td>Absent</td>
<td>Mild</td>
<td>Moderate</td>
<td>Severe</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper respiratory infections per year</td>
<td>1–2</td>
<td>3</td>
<td>4–6</td>
<td>&gt;6</td>
<td>1–2</td>
<td>3</td>
<td>4–6</td>
<td>&gt;6</td>
</tr>
<tr>
<td>Candidiasis</td>
<td>None</td>
<td>Oral</td>
<td>Fingernails</td>
<td>Systemic</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other serious infections</td>
<td>None</td>
<td>Oral</td>
<td>Fingernails</td>
<td>Systemic</td>
<td>4</td>
<td></td>
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<tr>
<td>Fatal infection</td>
<td>Absent</td>
<td>Present</td>
<td>Present</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Hyperextensibility</td>
<td>Absent</td>
<td>Present</td>
<td>Present</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Lymphoma</td>
<td>Absent</td>
<td>Present</td>
<td>Present</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increased nasal width</td>
<td>&lt;150/μl</td>
<td>1–2</td>
<td>3</td>
<td>4–6</td>
<td>&gt;6</td>
<td>1–2</td>
<td>3</td>
<td>4–6</td>
</tr>
<tr>
<td>High palate</td>
<td>Absent</td>
<td>Present</td>
<td>Present</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Young-age correction</td>
<td>&gt;5 years</td>
<td>2–5 years</td>
<td>1–2 years</td>
<td>≤1 year</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*The entry in the furthest-right column is assigned the maximum points allowed for each finding. Normal < 130 IU/ml. 700/µl = 1 standard deviation (SD), 800/µl = 2 SD above the mean value for normal individuals. For example, cleft palate, cleft tongue, hemivertebra, other vertebral anomaly, etc. (see Grimbacher et al. [1999]).*