Hyper IgE recurrent infection syndrome in South Asia: is there a different outcome?

Rajiva de Silva1*, Dhanushka Dasanayake1, Manouri Senanayake2, Ramya Ediriweera2, Savithri Dias3, Chandima Karunatileke1, Karen Brocas4, Fariba Tahami4 and Suranjith Seneviratne4

Abstract

Background: Hyper IgE recurrent infection syndrome (HIES) is a rare immune deficiency, characterized by recurrent staphylococcal skin and lung abscesses, pneumonia and increased IgE levels. The majority of autosomal dominant HIES (AD HIGE) is due to hypomorphic mutations in the signal transducer and the activator of transcription 3 (STAT3) gene.

Case presentation: Five patients were diagnosed with HIES, based on the clinical criteria and scoring system developed at the National Institutes of Health (NIH), USA. The STAT3 gene was sequenced and previously described mutations were identified in all five patients. We compare the clinical features of our patients with those from Asia, Europe and the US.

Conclusion: Even though the number of patients is limited, there are some clinical differences in patients from South Asia compared to European and even East Asian patients. However, the mutations detected are located at hot spots seen in western and Asian patients with AD HIGE.

Keywords: Hyper IgE syndrome, Job’s syndrome, Autosomal dominant hyper IgE, STAT3 mutation, Primary immunodeficiency

Background

Hyper IgE recurrent infection syndrome (HIES) is a rare immune deficiency, characterized by recurrent staphylococcal skin and lung abscesses, pneumonia and increased IgE levels [1]. The majority of autosomal dominant HIES (AD HIGE) is due to hypomorphic mutations in the signal transducer and the activator of transcription 3 (STAT3) gene [2], resulting in defects in signal transduction for multiple cytokines (IL 6, IL 23) and impaired function of IL 17 [3]. The mutation leads to infectious complications as well as skeletal, dental, facial and connective tissue abnormalities [4]. Defects in tyrosine kinase 2 (TYK2) [5] and homozygous mutations of dedicator of cytokinesis gene (DOCK8) [6] are responsible for autosomal recessive HIGS (AR HIGE). While there are large studies/case series of HIES from the West [1, 7], data from Asia is scarce [8–14] and the prevalence rate unknown. We hypothesized that there may be a different clinical phenotype or evolution in our region, and that we may have different mutations in the STAT3 gene. We report 5 cases of AD HIGE from Sri Lanka that were identified using clinical criteria and the scoring system developed at the National Institutes of Health, USA [15]. All 23 exons and exon/intron boundaries of STAT3 were amplified by PCR and the purified PCR products were sequenced as previously described [16]; all had mutations in the STAT3 gene.

Case presentation (Tables 1, 2)

Patient 1

A 15 year boy (Fig. 1a) presented with recurrent infections from infancy. He had lower respiratory tract infection (LRTI) with pyopneumothorax at the age of 3 months. He had recurrent (LRTI), scalp and oral abscesses, bilateral otitis media and oral thrush. He developed a generalized rash in the neonatal period and seborrhoeic dermatitis at the age of 5 months. He...
suffered fractures of the radius and ulna of both arms with minor trauma at 7, 10 and 13 years. He retained one primary tooth. X ray and CT scans of the chest at 15 years revealed a bulky lesion in the right lung (Fig. 2a, b). His serum IgE was elevated (> 2000 IU/ml). His serum IgA was reduced (40 mg/dl, normal range = 70–229). His eosinophil count (250/µl, normal = 450), serum IgG, and IgM, isohemagglutinin titre, anti typhoid Vi antibody titre, lymphocyte subsets and nitro blue tetrazolium (NBT) assay were normal. The National Institutes of Health (NIH) score was 70 (Table 3).

A heterozygous mutation with a nucleotide exchange of 1145 G to A in exon 13 leading to an amino acid change R382Q in the DNA binding domain identified in the STAT3 gene.

Patient 2
A 5 years old girl (Fig. 1b, c) (sister of case 1) presented with recurrent infections, including 2 episodes of meningitis at 11 months and 2 years, several episodes of eczema herpeticum and oral thrush. She also had recurrent episodes of upper respiratory tract infections and otitis media. She developed a generalized skin rash at 2 months of age. Her serum IgE was elevated (> 2000 IU/ml) and she had eosinophilia (1000/µl, normal = 450/µl). Her serum immunoglobulins, isohemagglutinin titre, lymphocyte subsets and NBT assay were normal. The anti typhoid Vi vaccine was not done. The National Institutes of Health (NIH) score was 29 (Table 3).

A heterozygous mutation with a nucleotide exchange of 1909 G to A in exon 21 leading to an amino acid change V637M in the SH2 domain identified in the STAT3 gene.

Patient 3
A 9 year old girl presented with recurrent infections from infancy. This included umbilical sepsis and a generalized skin rash during the neonatal period, recurrent skin abscesses since 6 months of age and recurrent episodes of otitis media. She has retained 2 primary teeth. Chest X ray revealed of a right upper lobe pneumatocele. She was diagnosed with the β thalassaemia trait. Her serum IgE was elevated (> 2000 IU/ml), while her eosinophil count was mildly increased (500/µl, normal = 450/µl). Her serum immunoglobulins, isohemagglutinin titre, anti typhoid Vi antibody titre, lymphocyte subsets and NBT assay were normal. The National Institutes of Health (NIH) score was 37 (Table 3).

A heterozygous mutation with a nucleotide exchange of 1909 G to A in exon 21 leading to an amino acid change V637M in the SH2 domain identified in the STAT3 gene.

Patient 4
A 7 year old girl presented with recurrent infections from the neonatal period, including septicemia on day 9 after birth with _S. aureus_ isolated from blood, recurrent skin abscesses which were drained on 5 occasions, 3 episodes of pneumonia, several episodes of otitis media and chickenpox which was complicated

---

**Table 1 Clinical features**

|                      | Patient 1            | Patient 2            | Patient 3            | Patient 4            | Patient 5            |
|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|
| Age at diagnosis and sex | 15 years, male       | 5 years, female      | 9 years, female      | 7 years, female      | 11 years, male       |
| Age at onset         | Neonatal period      | 2 months             | Neonatal period      | Neonatal period      | 4 months             |
| Neonatal skin rash   | Yes                  | No                   | Yes                  | Yes                  | No                   |
| Dermatitis           | Yes                  | Yes                  | Yes                  | Yes                  | Yes                  |
| Candidiasis          | Oral                 | Oral                 | No                   | No                   | No                   |
| Respiratory infections | Recurrent LRTI, pyo- | Recurrent URTI, OM   | Recurrent OM         | Recurrent OM         | Pneumothorax         |
|                      | pneumothorax at 3    |                      |                      |                      |                      |
|                      | months               |                      |                      |                      |                      |
|                      | Recurrent OM         |                      |                      |                      |                      |
| Pneumatocoeles       | Yes                  | No                   | Yes                  | Multiple             | No                   |
| Abscesses            | Skin                 | No                   | Skin                 | Skin, peri-pancreatic | Skin, dento-alveolar, lung |
| Meningitis           | No                   | Yes, recurrent       | No                   | No                   | No                   |
|                      | (11 months, 2 years) |                      |                      |                      |                      |
| Other infections      | No                   | No                   | No                   | Pericardial effusion | No                   |
| Retained teeth       | Yes                  | No                   | No                   | Yes                  | No                   |
| Fractures            | Bilateral radius and ulna | No               | No                   | No                   | Right ulna           |

LRTI lower respiratory infections, URTI upper respiratory infections, OM otitis media
### Table 2 Laboratory Investigations

|                   | Patient 1 | Patient 2 | Patient 3 | Patient 4 | Patient 5 |
|-------------------|-----------|-----------|-----------|-----------|-----------|
| Eosinophil count  | 250       | 1000      | 500       | 8650      | 0         |
| (normal < 450/µl) |           |           |           |           |           |
| Serum IgE level   | > 2000    | > 2000    | > 2000    | > 2000    | > 2000    |
| IU/ml (normal 2–629) |        | (normal 2–307) | (normal 2–696) | (normal 2–403) | (normal 2–696) |
| Serum immunoglobulins (mg/dl) | | | | | |
| IgG (range)       | > 1120    | 1120      | 1098      | 1212      | 985       |
| (726–1085)        | (569–1597)| (559–1492)| (559–1492)| (779–1456)|           |
| IgA (range)       | 40 (70–229)| 57 (55–152)| 153 (54–221)| 161 (54–221)| 44 (2–208)|
| IgM (range)       | > 94.8 (35–72) | > 94.8 (22–100) | 264 (27–118) | 42 (27–118) | > 94.8 (35–132) |
| Isohemagglutinin titre | Normal | Normal | Normal | Normal | Normal |
| (normal > 1:10 dilution) | | | | | |
| Typhoid Vi IgG EU/MI (Gero- | Not done | 503 | Not done | 312 |
| positive ≥ 150 EU/ml) | | | | |
| Lymphocyte subsets (/µl) | | | | | |
| CD3 (normal range) | 42% = 1290 (400–2100) | 32% = 1760 (800–2000) | 34% = 1478 (9300–2000) | 4718 (1500–5000) | 36% = 971 (400–2100) |
| (normal range)    |           |           |           |           |           |
| CD4 (normal range) | 35% = 1075 (200–1200) | 36% = 1980 (800–1800) | 31% = 1341 (399–1200) | 7461 (500–1600) | 27% = 749 (200–1200) |
| CD8 (normal range) | 13% = 399 (200–600) | 20% = 1100 (200–1600) | 23% = 995 (200–1600) | 4125 (600–3000) | 13% = 361 (200–600) |
| CD19 (normal range) |           |           |           |           |           |
| Mutation analysis of STAT3 gene | A heterozygous mutation in 1145 G to A in exon 13 leading to an amino acid change R382Q in the DNA binding domain | A heterozygous mutation in 1145 G to A in exon 13 leading to an amino acid change R382Q in the DNA binding domain | A heterozygous mutation in 1909 G to A in exon 21 leading to an amino acid change V637M in the SH2 domain | A heterozygous mutation in 1144 C to T in exon 13 leading to an amino acid change V637M in the SH2 domain | A heterozygous mutation in 1909 G to A in exon 21 leading to an amino acid change V637M in the SH2 domain |
by post varicella pneumonia at 7 years of age. She also
developed a rash on the scalp and face in the neonatal
period. Her chest X ray showed multiple pneumatoceles.
She has had a pericardial effusion, and a peripancreatic
abscess diagnosed by ultra sound. Both were aspirated.
She had retained 2 primary teeth. She died at 7 years
5 months following a brief respiratory tract infection.
Her serum IgE was elevated (> 2000 IU/ml), while her
eosinophil count was increased (8650/µl), normal = 450/
µl. Her serum immunoglobulins, isohemagglutinin titre,
lymphocyte subsets and NBT assay were normal. The
National Institutes of Health (NIH) score was 59
(Table 3).

A heterozygous mutation with a nucleotide exchange of
1144 C to T in exon 13 leading to an amino acid change
R382W in the DNA binding domain was identified in the
STAT3 gene.

Patient 5
An 11 year old boy presented with recurrent abscesses
since 4 months of age, including skin, dento-alveolar and
lung abscesses. He developed a pyo-pneumothorax at
3½ years, and the aspirated pus grew *P. aeruginosa*. He
had also developed a skin rash at the age of 6 months. He
had a greenstick fracture of the right ulna at 6 years. His
serum IgE was elevated (>2000 IU/ml). His eosinophil
count, serum immunoglobulins, isohemagglutinin
titre, anti typhoid Vi antibody titre, lymphocyte subsets
and NBT assay were normal. The National Institutes of
Health (NIH) score was 28 (Table 3).

A heterozygous mutation with a nucleotide exchange of
1909 G to A in exon 21 leading to an amino acid change
V637M in the SH2 domain identified in the STAT3 gene.

The laboratory investigations and STAT3 mutations
detected in our patients are presented in Table 2. STAT3
mutations are presented in figure. Table 4 shows a
comparison of our patients, with those from the west
India [8], ethnic Chinese from China [9–13], and Japanese patients [13].

**Discussion**

All our patients were from the majority Sinhalese community (who form 74% of the country’s population). A previous case report of AD HIGE from Sri Lanka was also from this community [17]. Eighty percent of our patients had recurrent skin abscesses, and this was similar to the European [7, 16], Chinese [9–13] and Japanese cohorts [14]. On the other hand, only 50% of four reported Indian patients with AD HIGE had recurrent abscesses [8]. One of our patients developed a peripancreatic abscess, while another developed a lung abscess, and both were successfully drained. We could not find other reports of a peripancreatic abscess in AD HIGE. Mucocutaneous candidiasis was seen in 40% of our patients, compared to ≥70% of French [7] and >50% of Chinese [9–13] and Japanese patients [14]. Patients from the US with STAT3 mutations had figures similar to ours [15]. Recurrent pneumonia was seen in ≤50% of Sri Lankan and Indian [8] patients, whereas these were noted in >75% of ethnic Chinese [9–13], and Japanese patients [14] and in the US [16]. One of our patients (case 4) developed pneumonia following varicella. Severe viral infections are typically seen in the AR HIGE [18], and chicken pox pneumonia has rarely been reported in AD-HIGE [7]. One of our patients (case 2) had two episodes of bacterial meningitis. Although meningitis has been reported in AD HIGE [7, 19] recurrent episodes are very rare, with one patient previously reported from India [20]. However, mutation analysis was not performed in that patient. Interestingly, our patient also had several episodes of eczema herpeticum, which is usually seen in patients with the AR HIGE [18]. Vascular malformations and neurological abnormalities are common in AD HIGE patients from the west [21], but were not seen in our patients and in other Asian cohorts [8–14]; however the lack of active detection may be a possible reason for this. High IgE levels are seen in ≥95% of European [7] and Asian patients [8, 14]. Eosinophilia was seen in 60% of our patients; the figures have been higher in other cohorts. Eosinophil counts may fluctuate in time, and the lower value in our cohort may not be a true representation. One patient had partial IgA deficiency, but seroconverted following typhoid Vi vaccination, and had isohemagglutinins. IgA and IgG deficiency has been rarely reported in AD HIGE [22]. Impaired specific antibody responses may occur in some AD HIGE patients [23]. All our patients had isohemagglutinins and all three patients immunized with the typhoid Vi polysaccharide vaccine made good antibody responses.

The mortality rate seems to be higher in South Asia. The son of one of the patients with AD HIGE from India who had typical features but was not included in the study [8], as well as one of our patients expired following infections, a mortality rate of 20% in both instances. The mortality rate was 5% in the French study (another patient had died following an accident) [7]. None of the ethnic Chinese or Japanese patients with STAT3 mutations had died [9–14]. However, 3 of 4 patients with phenotypic AD-HIGE with wild type STAT3 from Taiwan died following a myocardial infarction due to coronary aneurisms, complications from a lymphoma and sepsis [12]. More advanced health care facilities in South East Asia and Europe may be responsible for the better outcomes in these regions.

The mutations in our patients have been recognized previously (Fig. 3, [7]) and were found to be involved with the DNA binding and SH2 domains of the STAT3 gene. There are several hot spots identified in previous studies, including Arginine (R) at position 382 of the DNA binding domain and Valine (V) at position 637 in

| Feature                                | Score | Case 1 | Case 2 | Case 3 | Case 4 | Case 5 |
|----------------------------------------|-------|--------|--------|--------|--------|--------|
| Highest serum IgE level                | 10    | 10     | 10     | 10     | 10     |        |
| Skin abscess                           | 8     | 0      | 8      | 8      | 8      |        |
| Pneumonia                              | 8     | 0      | 0      | 6      | 0      |        |
| Parenchymal lung abnormalities          | 8     | 0      | 8      | 8      | 6      |        |
| Retained primary teeth                  | 1     | 0      | 2      | 2      | 0      |        |
| Scoliosis                               | 0     | 0      | 0      | 0      | 0      |        |
| Fractures with minor trauma             | 8     | 0      | 0      | 0      | 4      |        |
| Highest eosinophil count               | 6     | 6      | 0      | 6      | 0      |        |
| Characteristic face                     | 5     | 2      | 0      | 5      | 0      |        |
| Midline anomaly                        | 0     | 0      | 0      | 0      | 0      |        |
| Newborn rash                           | 4     | 0      | 4      | 4      | 0      |        |
| Eczema                                 | 4     | 2      | 1      | 0      | 0      |        |
| URTI/year                              | 4     | 4      | 0      | 0      | 0      |        |
| Candidiasia                            | 1     | 1      | 0      | 0      | 0      |        |
| Other serious infections               | 0     | 4      | 0      | 4      | 0      |        |
| Fatal infections                       | 0     | 0      | 0      | 0      | 4      |        |
| Hyperextensibility                     | 0     | 0      | 4      | 0      | 0      |        |
| Lymphoma                               | 0     | 0      | 0      | 0      | 0      |        |
| Increased nasal width                  | 1     | 0      | 0      | 0      | 0      |        |
| High palate                            | 2     | 0      | 0      | 2      | 0      |        |
| Young age correction                   |       |        |        |        |        |        |
| Total                                  | 70    | 29     | 37     | 59     | 28     |        |
| STAT3 mutation                         | Yes   | Yes    | Yes    | Yes    | Yes    | Yes    |

Table 3 NIH Score based on [14]
Table 4  Comparison of US, European and Asian patients with STAT3 mutations positive AD-HIGE

| Clinical feature                                      | US (n = 64) [16] | French (n = 60) [7] | Indian (n = 04) [8] | Ethnic Chinese (n = 12) [9–13] | Japanese (n = 08) [14] | Sri Lankan (n = 05) |
|-------------------------------------------------------|-----------------|---------------------|---------------------|--------------------------------|------------------------|-------------------|
| Age range % 1 month–46 years 4 months–35 years 1.7–26 years 6–21 years 5–15 years % (n) % (n) % (n) % (n) % (n) |
| Findings related to infections and immune system       |                 |                     |                     |                                |                        |                   |
| Moderate to severe eczema                             | 90.6 nm         | 95 nm               | 50                  | 75 (9/12)                     | 87.5 (7/8)             | 80                |
| Serum IgE > 2000 IU/ml                                | nm 96           | 100                 | 75 (9/12)           | 100 (8/8)                     | 100                    |                   |
| Eosinophilia (> 2 SD above normal mean)               | 70.7 80         | 75                  | 91.6 (11/12)        | 75 (6/8)                      | 60                     |                   |
| Recurrent pneumonia, X-ray proven                      | 95              | nm                  | 50                  | 75 (9/12)                     | 87.5 (7/8)             | 40                |
| Recurrent skin abscesses                              | 90.6 nm         | 50                  | 100 (12/12)         | 75 (6/8, 2 = 1–2 abscesses)   | 80                     |                   |
| Recurrent (> 3/year) upper respiratory infections      | 45.8 nm         | 71.4 (7/14)         | 37.5 (3/8)          |                                |                        |                   |
| Mucocutaneous candidiasis                             | 43.1 85         | nm                  | 58.3 (7/12)         | 67.5 (5/8)                     | 40                     |                   |
| Pneumatoceles                                         | 74.6 52         | 25                  | 66.6 (8/12)         | 67.5 (5/8)                     | 60                     |                   |
| Newborn rash                                          | 64.9 48         | 50                  | 66.6 (8/12)         | 100 (8/8)                     | 60                     |                   |
| Other serious infections                               | nm 43           | 0                   | 66.6 (8/12)         | 25 (2/8)                      | 40                     |                   |
| Lymphoma, other cancer                                | 03              | 7                   | 0                   | 0                              | 0                      |                   |
| Findings related to bones, teeth, and connective tissue|                 |                     |                     |                                |                        |                   |
| Characteristic face                                    | 90.6 95         | 75                  | 91.6 (11/12)        | 100 (8/8)                     | 60                     |                   |
| Retained primary teeth                                 | 80              | 65 nm               | 100 (5/5)           | 37.5 (3/8)                     | 60                     |                   |
| Hyperextensibility of joints                          | 52.7 50         | nm                  | 58.3 (7/12)         | 50 (4/8)                      | 20                     |                   |
| Increased nasal width (interalar distance > 1 SD above normal value for age, race) | 51.9 85 | nm | 80 (4/5) | 12.5 (1/8) | 20 | |
| Scoliosis > 10°                                       | 26              | 38 nm               | 0                   | 25 (2/8)                      | 60                     |                   |
| Recurrent fractures following minor trauma             | 45.8 42         | nm                  | 8.3 (1/12)          | 25 (2/8)                      | 40                     |                   |
| High-arched palate                                    | 54.7 53         | nm                  | 33.3 (3/12)         | 25 (2/8)                      | 40                     |                   |
| Congenital skeletal anomalies                          | nm 10           | nm                  | nm                  | nm                             | 0                      |                   |
| Focal hyperintensities on brain MRI                   | nm < 1          | nm                  | nm                  | nm                             | ne                     |                   |
| Chiari type I malformation                             | nm              | nm                  | nm                  | nm                             | ne                     |                   |
| Coronary vasculature abnormalities                     | nm              | nm                  | nm                  | nm                             | ne                     |                   |

*nm not mentioned, ne not evaluated*
the SH2 domain [2]. Three of our patients had mutations at position 637 and the other two at position 382. The 1144 C-T, R382W transition has been identified in black, Hispanic and white individuals in the US [2] and in Japanese patients [14]. It was seen in almost half the patients in one study [2]. The 1145 G–A, R382Q transition has been identified in Indian [8], Chinese [9], Japanese [14], black and white patients in the US [2] and the 1909 G–A, V637M transition in Chinese [9] as well as white individuals [2]. The DNA binding region hot spot at arginine 382 may be associated with a higher mortality, as 5 of 7 patients who died due to infection related causes in one study had this mutation, even though it was not statistically significant [24]. The patient who died in our study (no: 4) carried the same mutation. Further studies may be needed in this regard.

**Conclusion**

The mortality rate seems to be higher in South Asia compared to East Asia and the West and recurrent pneumonia is less common in the sub-continent. However, the mutations detected are located at the same hot spots seen in Western and East Asian AD HIGE patients. Less advanced health care facilities in South Asia may be responsible for the worse outcomes in this regions.

**Authors’ contributions**

RDS: Diagnosis, writing manuscript. DD: Diagnosis, writing manuscript. MS: Patient referral. RE: Patient referral. SD: Patient referral. CK: Diagnosis. KB: Sequencing gene. FT: Sequencing gene. SS: Sequencing gene, writing manuscript. All authors read and approved the final manuscript.
Acknowledgements
We thank all patients and their parents for permission to include them in the paper. We acknowledge Binding Site, Birmingham for the ELISA kits for the typhoid Vi antibody assay.

Competing interests
The authors declare that they have no competing interests.

Availability of data and materials
Available.

Consent to participate
Informed, signed consent was obtained from all participants, and signed consent was obtained from the mother of the 2 children (patients 1 and 2) for inclusion of the photographs.

Ethics approval and consent to participate
Ethics approval was obtained from the Ethics committee of the Medical Research Institute, Colombo, Sri Lanka.

Funding
There was no funding.

Publisher’s Note
Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Received: 7 April 2017 Accepted: 10 August 2018
Published online: 02 November 2018

References

1. Grimbalder B, Holland SM, Gallin JI, et al. Hyper IgE syndrome with recurrent infections-autosomal dominant multisystem disorder. N Engl J Med. 1999;340:692–702.
2. Holland SM, DeLeo FR, Elloumi HZ, Hsu AP, Uzel G, Brodsky N, Freeman AF, Demidowich AS, Davis J, Turner ML, Anderson VL, Darnell DN, Welsh PA, Kuhns DB, Malech HL, Gallin JI, Kobayashi SD, Whitney AR, Voyich JM, Musser JM, Woellner C, Schaffer AA, Puck JM, Grimbalder B. STAT3 mutations in the hyper-IgE syndrome. N Engl J Med. 2007;357:1608–19.
3. Minegishi Y, Saito M. Molecular mechanisms of the immunological abnormalities in hyper-IgE syndrome. Ann N Y Acad Sci. 2001;942:34–40.
4. Szczawinska-Poplawsk A, Kycier Z, Pietrucha B, Heropolitska-Pliszka E, Breborowicz A, Gerreth K. The hyperimmunoglobulin E syndrome—clinical manifestation diversity in primary immune deficiency. Orphanet J Rare Dis. 2016;11:76.
5. Woellner C, Schaffer AA, Puck JM, et al. The hyper-IgE syndrome and mutations in TYK2. Immunology. 2007;125:635.
6. Zhang Q, Davis JC, Lamborn IT, et al. Clinical features, STAT3 gene mutations and Th17 Cell analysis in nine children with hyper-IgE syndrome in Mainland China. Scand J Immunol. 2013;78:258–65.
7. Xie L, Hu X, Li Y, Zhang W, Chen L. Hyper-IgE syndrome with STAT3 mutation: a case report in Mainland China. Clin Dev Immunol. 2010. https://doi.org/10.1155/2010/289873.
8. Tang IMS, Lee TL, Chan KW, Ho MHK, Lee PPW, Leung TNH, Lau YL. Signal transducer and activator of transcription 3 (STAT3) gene mutations in two patients with hyperimmunoglobulin E syndrome. HK J Paediatr. 2009;14:10–4.
9. Le W-H, Huang J-L, Lin S-J, Yeh K-W, Chen L-C, Hsieh M-Y, Huang Y-C, Kuo H-C, Yang KD, Yu H-R, Jang T-H, Yang C-H. Clinical aspects and genetic analysis of Taiwanese patients with the phenotype of hyper-immunoglobulin E recurrent infection syndromes (HIES). J Clin Immunol. 2011;31:272–80.
10. Liu J-Y, Li Q, Chen T-T, Guo X, Ge J, Yuan L-X. Destructive pulmonary staphylococcal infection in a boy with hyper-IgE syndrome: a novel mutation in the signal transducer and activator of transcription 3 (STAT3) gene (p. Y657S). Eur J Pediatr. 2011;170:661–6.
11. Minegishi Y, Saito M, Tsujiya S, Tsuge I, Takada H, Hara T, et al. Dominant-negative mutations in the DNA-binding domain of STAT3 cause hyper-IgE syndrome. Nature. 2007;448:1058–62.
12. Grimbalder B, Schaeffer AA, Holland SM, Davis J, et al. Genetic linkage of hyper IgE syndrome to chromosome 4. Am J Hum Genet. 1996;65:735–44.
13. Woellner C, Gertz EM, Schaffer AA, Lagos M, Perro M, Gleckner EO, Pietrogrande MC, Possu F, Franco J, Atamorinos N, Pietruca B, Heropolitska-Pliszka E, Yeganen M, Moin M, Ehsarlou, Snennery AR, Abinun M, Breborowicz A, Niehues T, Kilic SS, Junker A, Turvey SE, Plebani A, Sánchez B, Garty BZ, Pignata C, Cancrini C, Litzman J, Sanal O, Baumann U, Bacchetta R, Hsu AP, Davis JN, Hammarström L, Davies EG, Eren E, Arkwright PD, Moilane JS, Viemmann D, Khan S, Maróli D, Cant AJ, Freeman AF, Puck JM, Holland SM, Grimbalder B. Mutations in STAT3 and diagnostic guidelines for hyper-IgE syndrome. J Allergy Clin Immunol. 2010;125(2):424–32.
14. De Alwis ACD, de Silva R, Gunawardena S, Weerasuriya DC, Jayaweera AHM. A case of hyper IgE syndrome. CMJ. 2006;51(4):149–51.
15. Zhang Q, Davis JC, Lamborn IT, Freeman AF, Jing H, Favreau AJ, Matthews HF, Davis J, Turner ML, Uzel G, Holland SM, Su HC. Combined immunodeficiency associated with DOCK8 mutations. N Engl J Med. 2009;361:2016–55.
16. Beckzke M, Enzinger C, Windpassinger C, Pfeifer D, Fazekas F, Woellner C, Grimbalder B, Kroisel PM. Community acquired Staphylococcus aureus meningitis and cerebral abscesses in a patient with a hyper-IgE and a Dubowitz-like syndrome. J Neurol Sci. 2011;309(1–2):12–5.
17. Katypapa M, Kommalar M, Jayaram S, Javappara P, Ambazhagan A. Recurrent meningitis in hyper IgE syndrome. Indian J Pediatr. 2010;77(4):385–8.
18. Chandesris M-O, Azarine A, Ong K-T, Taleb S, Boutouyrie P, Mousseaux E. Recurrent meningitis and cerebral abscesses in a patient with a hyper-IgE and a Dubowitz-like syndrome. J Neurol Sci. 2011;309(1–2):12–5.
19. Chandesris M-O, Azarine A, Ong K-T, Taleb S, Boutouyrie P, Mousseaux E. Recurrent meningitis in hyper IgE syndrome. Indian J Pediatr. 2010;77(4):385–8.
20. Chandesris M-O, Azarine A, Ong K-T, Taleb S, Boutouyrie P, Mousseaux E. Recurrent meningitis in hyper IgE syndrome. Indian J Pediatr. 2010;77(4):385–8.
21. Chandesris M-O, Azarine A, Ong K-T, Taleb S, Boutouyrie P, Mousseaux E. Recurrent meningitis in hyper IgE syndrome. Indian J Pediatr. 2010;77(4):385–8.
22. Chandesris M-O, Azarine A, Ong K-T, Taleb S, Boutouyrie P, Mousseaux E. Recurrent meningitis in hyper IgE syndrome. Indian J Pediatr. 2010;77(4):385–8.
23. Chandesris M-O, Azarine A, Ong K-T, Taleb S, Boutouyrie P, Mousseaux E. Recurrent meningitis in hyper IgE syndrome. Indian J Pediatr. 2010;77(4):385–8.
24. Chandesris M-O, Azarine A, Ong K-T, Taleb S, Boutouyrie P, Mousseaux E. Recurrent meningitis in hyper IgE syndrome. Indian J Pediatr. 2010;77(4):385–8.
25. Chandesris M-O, Azarine A, Ong K-T, Taleb S, Boutouyrie P, Mousseaux E. Recurrent meningitis in hyper IgE syndrome. Indian J Pediatr. 2010;77(4):385–8.
26. Chandesris M-O, Azarine A, Ong K-T, Taleb S, Boutouyrie P, Mousseaux E. Recurrent meningitis in hyper IgE syndrome. Indian J Pediatr. 2010;77(4):385–8.
27. Chandesris M-O, Azarine A, Ong K-T, Taleb S, Boutouyrie P, Mousseaux E. Recurrent meningitis in hyper IgE syndrome. Indian J Pediatr. 2010;77(4):385–8.
28. Chandesris M-O, Azarine A, Ong K-T, Taleb S, Boutouyrie P, Mousseaux E. Recurrent meningitis in hyper IgE syndrome. Indian J Pediatr. 2010;77(4):385–8.