

CORRESPONDENCE

Hyper IgE syndrome diagnosed in early infancy by gene analysis of *STAT3* mutation

A baby was delivered at 40 weeks gestation and the birth weight was 3,186 g. There was no family history of Hyper IgE syndrome (HIES). Five days after birth, reddish papules with pustules appeared on the head and trunk, which rapidly worsened (*figure 1A*). Laboratory findings revealed a white blood cell count of 80800/ μ L with a normal differential. The eosinophil count was high, at 24%. The serum IgE level was 5,590 IU/mL (normal range 0-100 IU/mL). Bacteriological cultures from the pustule grew methicillin-resistant *Staphylococcus aureus* (MRSA). Afterwards, he suffered from recurrent eczema and uncontrolled infections, including mucocutaneous candidiasis, omphalitis, otitis media and hordeolum. Eighty days after birth, skin abscesses, which were not accompanied by the usual signs of inflammation, appeared on his scalp (*figure 1B*). These abscesses were so-called cold abscesses. At this point, the National Institutes of Health (NIH) score of this patient was 42. From this observation, HIES was suspected and we performed a genetic analysis. The mutation V637M [1] in the SH2 domain of the *STAT3* protein was detected. The *STAT3* mutation was not detected in his family. He was started on daily trimethoprim-sulfamethoxazole for treatment and prophylaxis. There was partial clearing of his dermatitis



Figure 1. A) Pustules and reddish papules with erosion and yellow crust on the patient's head and trunk. B) Recurrent abscesses without inflammation, so-called cold abscesses.

with the intermittent use of topical corticosteroids. Antibiotics and topical corticosteroids resulted in alleviation of his dermatitis. At the age of 2.5 years, the patient had symptoms of slight eczema and mucocutaneous candidiasis, accompanied by characteristic facial features including a prominent forehead and a broad nasal bridge. There was no recurrence of abscesses. There were no skeletal abnormalities but the patient had a short stature of -3 standard deviations.

HIES is a rare primary immunodeficiency, characterized by eczema associated with extremely high serum IgE levels and eosinophilia, along with recurrent skin abscesses and pneumonia. Recently, the causative genes of HIES were discovered. Type 1 HIES, that is, sporadic inheritance, is mainly due to mutations in the Janus-activated kinase/signal transducer and activator of transcription (JAK-STAT)-mediated cytokine signals [2]. A null mutation in tyrosine kinase 2 (*TYK2*) was identified in a patient with type 2 HIES, which is autosomally recessively inherited [3]. *STAT3* and *TYK2* mutations lead to impaired Th17 cell function. Engelhardt reported that patients with severe combined immunodeficiency detected to a homozygous dedicator of cytokinesis 8 protein (*DOCK8*) fulfilled the criteria of HIES, and this was autosomally recessively inherited [4]. Grimbacher *et al.* reported the incidence of various features of HIES: the occurrence of eczema was 100%, a peak IgE $> 2,000$ IU/mL was present in 97% of cases, eosinophilia was 93%, cold abscess was 87%, mucocutaneous candidiasis was 83%, and characteristic facial features were present in 83% of cases. These features were also present in our case. Pneumonia, lung cyst and bone fractures also had comparatively high incidences; these features were absent in our case. It is necessary to observe the clinical course and detect the characteristic facial features and skeletal abnormalities to reach a definitive diagnosis. However, with the identification of *STAT3* mutations and the development of molecular diagnostic techniques, a definite diagnosis can be made earlier. The early diagnosis of type 1 HIES by genetic analysis of *STAT3* mutations has seldom been reported [5]. Recently, a PCR-based high-resolution DNA-melting assay to scan selected exons of the *STAT3* gene for mutations responsible for HIES has been reported [6], and may prove to be a useful diagnostic test in the future. However, molecular tests are not widely available at present. As the early manifestation of HIES is mainly a cutaneous eruption, the diagnosis has to be made carefully, with an index of suspicion if there are features of immunodeficiency. ■

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¹ Departments of Dermatology,
Japan
² Pediatrics, Kitasato University
School of Medicine, 1-15-1
Kitasato, Sagami-hara, Minamiku,
Kanagawa, 252-0374 Japan
³ Department of Immune
Regulation, Tokyo Medical and
Dental University, Tokyo,
Japan
<watarai@med.kitasato-u.ac.jp>

Akira WATARAI¹
Shiro NIYAMA¹
Miho MORITA¹
Yuki BANDO²
Yoshiyuki MINEGISHI³
Kensei KATSUOKA¹

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Meningothelial hamartoma of the scalp in a 78-year-old man

Meningothelial hamartoma (MH) was first described by Suster and Rosai [1] as a hamartoma of the scalp showing a mixture of fat, blood vessels, nerves and ectopic meningeothelial cells. Similar cases have probably been described as rudimentary meningocele, sequestered meningocele or cutaneous meningioma [2, 3]. MH is congenital and it is believed to be a result of a developmental defect related to displaced ectopic meningeothelial remnants at this site [1]. It has also been postulated that it represents a form of meningocele with an obliterated intracranial communication [4]. MH typically presents as a nodule on the midline of the scalp (especially the occipital area), or less commonly on the upper face or paravertebral region. Most cases present in childhood or shortly after birth, but occasionally the lesion is initially noticed during adolescence or adulthood. The average age of five cases reported by Suster and Rosai [1] was 14.3 years-old (range: 4 months to 46 years). We report a case of MH of the scalp in a 78-year-old man.

The lesion manifested as a well-circumscribed solitary subcutaneous tumor of 5 × 5cm diameter on the right

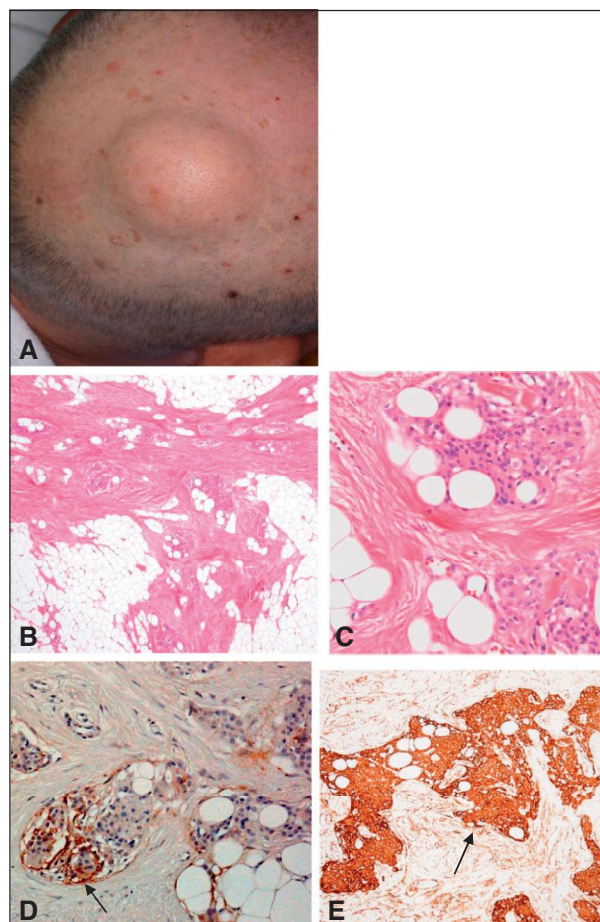


Figure 1. A well-circumscribed solitary subcutaneous tumor measuring 5 × 5cm in diameter on the right parieto-occipital scalp (A). Histopathology of the lesion showed mature adipose tissue, dense collagenous fibers and clusters of cuboidal, epithelioid cells (hematoxylin-eosin; ×40) (B) with scant eosinophilic cytoplasm, vesicular nuclei, and indistinct cell borders (hematoxylin-eosin; ×200) (C). EMA (D) and vimentin (E) positive meningeothelial cells (arrow).

parieto-occipital area of the scalp (figure 1A). It was firm, non-tender, non-movable and covered by normal hair-bearing skin. The patient said that it had been present as a small nodule since his childhood, but that its size had recently increased. There was no history of trauma to the area, and his other medical and familial history was not specific. A computed tomography (CT) scan of the head revealed a soft-tissue mass with inconsistent density. No bony defects or intracranial tumor was found. Lipoma was suspected, and surgical excision was performed.

Histopathologically, under low-power magnification, the lesion was composed of mature adipose tissue with stroma of dense collagenous fibers. Intermixed with the collagenous fibers were clusters of cuboidal, epithelioid cells (figure 1B). Under high-power magnification, these cuboidal, epithelioid cells had scant eosinophilic cytoplasm, and oval, vesicular nuclei. They had indistinct cell borders and formed nests between the collagen bundles showing a pseudo-infiltrative pattern (figure 1C). No mitoses or nuclear atypia was present. Immunohistochemically, these cells were positive for epithelial membrane