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CASE REPORT

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Association of hyper IgE with herpetic viral encephalitis and ecthyma gangrenosum in a male Egyptian patient

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Abstract

There are two forms of hyper-immunoglobulin E syndromes (HIES): a dominant form (AD-HIES) is caused by mutations in signal transducer and activator of transcription 3 (STAT3), and a recessive form (AR-HIES) is caused by mutations in dedicator of cytokinesis 8 (DOCK8). DOCK8 autosomal recessive hyper IgE syndrome (AR-HIES) patients have a more symptomatic neurologic disease than those with STAT3 deficiency. Involvement of the central nervous system in patients with HIES has been rarely reported. Being a rare primary immuno-deficiency, the disease may be underdiagnosed and under-reported. In the central nervous system abnormalities with definite neurologic manifestations, very few articles were published previously which may vary from hemiplegia to partial facial nerve paralysis in children and acute disseminated encephalomyelitis (ADEM), but viral encephalitis has not been reported. Herein, we describe a 21-year-old male with hyper-immunoglobulin E syndrome presented with fever, pneumonia, skin abscesses, and altered consciousness who proved to have herpetic viral encephalitis. The purpose of this study is to emphasize that neurologic complications with herpetic viral encephalitis may occur in patients with hyper IgE syndrome. In the case series, no cases of hyper IgE were described to have viral encephalitis, and to the best of our knowledge, this is the first description of herpes simplex encephalitis in a patient with hyper IgE syndrome.

Keywords Hyper IgE, AR HIES, AD-HIES, Recurrent herpes simplex infection, Herpetic viral encephalitis, Ecthyma gangrenosum

Background

Hyper-immunoglobulin E syndrome (HIES) is a rare disorder due to primary immunodeficiency characterized by recurrent infection of the skin and lungs, eosinophilia, and high-serum levels of IgE [1]. HIES is divided into autosomal dominant HIES (AD-HIES) and autosomal recessive HIES according to different inheritance genes [2]. Autosomal recessive hyper IgE (AR-HIES) is particularly common with intermarriage among close relatives, where its occurrence may exceed that of AD-HIES [3].

Autosomal recessive hyper immunoglobulin E (AR-HIES) similar to AD-HIES presents with eczema, skin abscesses, recurrent respiratory infections, candidiasis, and other fungal infections, patients with AR-HIES are distinguished from those with AD-HIES by the occurrence of severe, recurrent viral infections caused by pathogens such as Herpes simplex, Herpes zoster, and Molluscum contagiosum [3]. Patients with AR-HIES also have a high frequency of neurologic complications, including encephalitis and vascular brain lesions [4]. A small number of patients may have severe central nervous system lesions [5]. The mechanisms of those

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complications may include viral infections of the central nervous system and autoimmunity [4].

Reports on central nervous system involvement in hyper-immunoglobulin E syndromes are rare. In this case, we shed light on a rare association between herpes simplex encephalitis and hyper-immunoglobulin E syndrome.

Case presentation

A 21-year-old young man presented to the emergency room of Embaba Fever Hospital (Giza, Egypt), in a deep coma state after 1 week of admission in a general hospital with pneumonia and confusion. He is not a drug abuser and not a smoker, and he has a known history of recurrent sinusitis and skin allergy. Both parents are cousins. The history dated back 1 week before admission to the fever hospital. When he started to suffer from headache, fever, and shortness of breath, associated with generalized nodular eruptions all over his body, he became confused and vomited several times. He had been admitted to a general hospital, they started antibiotics after requesting a plain chest X-ray which revealed diffuse homogenous opacification on the left lung, and they attributed the vomiting and confusion to the severe pneumonic changes. By the second day, all eruptions changed into multiple abscesses, and over the next 5 days, he was no better and became comatose; his CT brain proved to be normal, and he was transferred to the fever hospital for suspected encephalitis. In the emergency room, a lumbar puncture was performed and CSF analysis was obtained, and the patient was admitted to the intensive care unit. He had a long history of pruritic vesicular eruptions, also burning sores and vesicles in the perioral area, especially during stressful conditions.

Examination

- Examination revealed a comatose teenager, GCS severe (7/15) E2V1M4, with no pallor, jaundice, or cyanosis, and pupils and round, regular, and reactive. He was febrile, temperature, 38 °C; blood pressure, 120/70 mmHg; heart rate, 110/m; and respiratory rate, 28/minute with oxygen saturation, 92%, at room temperature. Skin examination shows disseminated superficial abscesses over the face, trunk, and abdomen.

Two large ulcers with a black center and yellowish margin of pus over the scrotum (Fig. 1).

- The chest showed a diminished air entry on the left side and normal cardiac and abdominal examination.

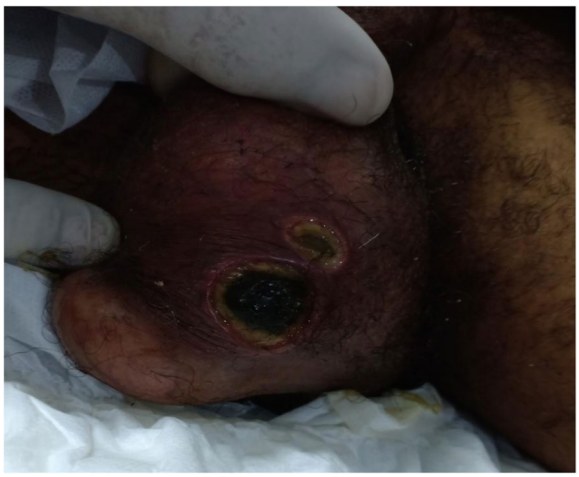

Fig. 1 Ecthyma gangrenosum: two scrotal ulcers with central necrosis (black gangrenous areas)

- Neurological examination shows a comatose patient with only withdrawal to pain and no lateralizing signs.

Investigations

- CBC shows leukocytosis; TLC, 24.000/Cmm; ALT, 49 U/L; AST, 100 U/L; ALP, 69 U/L; bilirubin, 0.8 mg/dl; creatinine, 1.7 mg/dl; urea, 54.1 mg/dl; and a normal electrolyte panel.
- CRP, 68 IU/L; ABG, normal; HIV Ab, negative
- Blood cultures for both aerobic and anaerobic organisms: negative
- A swab from the abscess: klebsiella sensitive to meropenem
- CSF obtained revealed: cells, 90 cells/cu mm
- Neutrophils, 20%; lymphocytes, 80%; glucose, 73 mg/dl; and protein, 160mg/dl
- Tuberculin skin test: negative, gene x-pert for TB, negative
- Aspergillus galactomannan test: negative
- CSF PCR for HSV1: positive
- The serum immunoglobulin profile was as follows: IgG: 820 mg/dl (normal 700–1600)
- IgA in serum: 191.4 mg/dl (normal), Ref. 70–400)
- IgM in serum: 123 mg/dl (normal), Ref. 40–230)
- IgE (total): (high) 1005 IU/ml (n. 0–100) IgG quantitative serum: 33.2 mg/dl (n. 13–152.7)
- Abdominal ultrasonography revealed a bilateral grade one nephropathy
- Chest X-ray: homogenous opacity with air bronchogram involving the whole left lung (Fig. 2)

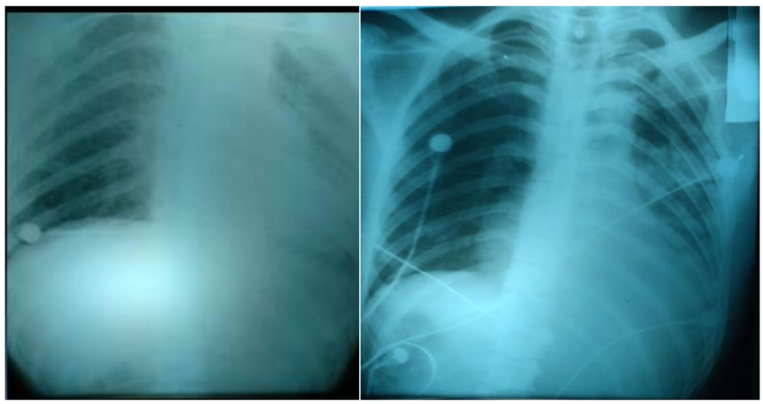

Fig. 2 Left-sided homogenous consolidation opacity with air bronchogram before and after antibiotic treatment

Laboratory			
Test range	Result	Unit	Reference range
Complete blood count			
Hemoglobin	14.3	gm/dl	11–16
Red cell count	4.8	million u/l	3.8–5.4
MCV	83.5.	fl	78–96
MCH	29.9	pg	26–32
MCHC	32	g/dl	31–36
RDW	13.4	%	11.5–14.5
Platelets	361.000	u/l	150–450
Total leucocytic count	24.100	u/l	$4–11^3$
Differential count			
Basophils	1	%	0–1
Eosinophils	0	%	0–3
Neutrophils	92.2	%	50–70
Lymphocytes	2.6	%	20–40
Monocytes	6	%	1–10
Test	Result	Unit	Reference range
Na	142	meq/l	135–145
K	3.2	meq/l	3–4.5
Ca total	8.9	mg/dl	9–11
Ca ionized	1.1	mmol/l	1.2–1.4
RBS	136	mg/dl	74–106
AST	100	u/l	15–37
ALT	49	u/l	14–63
ALP	69	u/l	44–147
Total bilirubin	0.8	mg/dl	0.20–1.00
Serum albumin	3.5	g/dl	3.4–5.4
Serum creatinine	1.7	mg/dl	0.55–1.3
Urea	54.1	mg/dl	20–40
CRP	68	mg/l	<6
Blood culture	no growth		No growth
Swab culture from the abscess			
	Growth of klebsiella		No growth
CSF analysis			
Cells	90	cu/mm	0–5
Neutrophils	20	%	0
Lymphocytes	80	%	0–5
Glucose	73	mg/dl	50–80
Protein	160	mg/dl	15–40
Gene X-Pert for TB	Negative		Negative
CSF PCR for HSV1	Positive		Negative
CSF PCR for HSV2	Negative		Negative
Aspergillus galactomannan test			
HIV antibody	Negative		Negative
	Negative		Negative
Tuberculin skin test	Negative		<5 mm induration
Serum immunoglobulin profile			
Serum IgG	820	mg/dl	700–1600
Serum IgA	191.4	mg/dl	70–400
Serum IgM	123	mg/dl	40–230
Serum IgE	1005	IU/ml	0–100
Serum IgG (quantitative)	33.2	mg/dl	13–152.7

Diagnosis

- Hyper IgE syndrome, Herpes simplex viral encephalitis (type 1), left-sided pneumonia, and ecthyma gangrenosum

Limitation

Genetic analysis was not done because of the non-availability of testing in our hospital and the poor financial condition of our patient.

Discussion

The etiology of most cases of autosomal recessive hyper IgE syndrome (AR-HIES) is unknown, but autosomal recessive inheritance is assumed because of consanguinity [3] autosomal recessive HIES (AR-HIES) manifests as severe eczema, recurrent bacterial and viral skin infections, and sinopulmonary infections. Patients with AR-HIES also have a high frequency of neurologic complications, including encephalitis (brain inflammation) and vascular brain lesions. The mechanisms of those complications may include viral infections of the central nervous system and autoimmunity [6]. Ecthyma gangrenosum is rare but pathognomonic for pseudomonal infection [7], and it is a cutaneous manifestation of sepsis. Although ecthyma gangrenosum is often due to pseudomonas, case reports indicate that the same frequency is associated with non-pseudomonal ecthyma gangrenosum (i.e., Fusarium [7], klebsiella [8]). Its association with hyper IgE denotes immune deficiency. The development of ecthyma gangrenosum lesions in individuals with sepsis is associated with a poor prognosis and is fatal in 20 to 77% of patients [8, 9].

Upon admission, the patient started IV acyclovir in a dose of 10mg/kg/dose/8 h for 3 weeks and meropenem 1gm/8 h for 2 weeks (doses adjusted according to the creatinine clearance) IV fluids, Ryle feeding for 1 week, and abscesses management surgically. Follow-up of the patient was satisfied within a few days, the consciousness level regained, pneumonia started to resolve, the skin lesions started to heal, and the ecthyma gangrenosum was managed surgically.

The patient survived and was discharged safely after 3 weeks of hospital admission with no neurological or post-meningitis sequelae.

Genetic analysis was not done because of the non-availability of testing in our hospital, and autosomal recessive inheritance is assumed because of intermarriage high consanguinity, and also, the patient had the common features of AR-HIES such as recurrent skin infections, recurrent sinusitis, and recurrent herpes simplex infections.

Conclusion

Neurologic complications with viral encephalitis may occur in patients with Hyper IgE syndrome. Ecthyma gangrenosum also occurs in immune-deficient patients including those with hyper IgE syndrome.

Abbreviations

HIES	Hyper-IgE syndrome
AD-HIES	Autosomal dominant hyper-IgE syndrome
AR-HIES	Autosomal recessive hyper-IgE syndrome
STAT3	Signal transducer and activator of transcription 3
DOCK8	Dedicator of cytokinesis 8
ADEM	Acute disseminated encephalomyelitis
HIV	Human immunodeficiency virus

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Authors' contributions

Hamdy Ibrahim collected the patient data and wrote the manuscript and the major contributor in writing the manuscript. Hamdi Ibrahim is the corresponding author. The authors read and approved the final manuscript.

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Consent for publication

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Competing interests

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