

CASE REPORT

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A Young Woman with Autosomal Dominant Hyper Immunoglobulin E (job's) Syndrome Presenting with Acute Abdomen: a Case Report

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ABSTRACT

Background: Autosomal dominant hyper immunoglobulin IgE syndrome is a rare inherited condition that causes immune suppression. **Objective:** This case report describes a severe case of liver abscess, caused by a cavity-forming infection, secondary to Job's syndrome.

Case presentation: A 25-year-old female patient was emergently referred to the surgical department, for the evaluation of acute, right-sided, upper abdominal pain, fever, and chills. The patient reported a past history of recurrent pulmonary infections as well as a prior diagnosis of Job's syndrome. An abdominal CT scan revealed a large intrahepatic cystic mass, consistent with a hepatic abscess on the right liver lobe. The patient was started on a course of antibiotics and was admitted to the surgical ward for further treatment. After much deliberation, a multidisciplinary team comprised of general surgeons, gastroenterologists, and interventional radiologists, decided upon the guided drainage of the abscess. Two pigtail catheters were used to drain the cavities. Antibiotic use was de-escalated, the patient gradually recovered, and the reported abscesses were greatly reduced in size. After 14 days of treatment, the patient was successfully released home. **Conclusion:** In patients with a known history of the autosomal dominant hyper-IgE syndrome, presenting with acute abdominal pain, the liver abscess must be on the top of the differential diagnosis list.

Keywords: liver abscess drainage, hepatic abscess, job's syndrome.

1. BACKGROUND

Although one might think that genetic disease is a far cry from the ailments of everyday surgical practice, the modern surgeon must be prepared to effectively treat any and all causes of surgical pathology. This case report describes a severe case of liver abscess, caused by a cavity-forming infection, secondary to Job's syndrome. In this case, the patient was managed with image-guided drainage, due to the severe septic profile. Job's syndrome, is a rare autosomal dominant genetic disease, with a known incidence ranging from 0.01% to 0.0002% (1-3). It is most often known as a cause of inherited immune suppression, causing recurrent infections of the respiratory tract. The disease is caused by mutations within the JAK-STAT intracellular signaling pathway, known to be involved in the inflammatory response and immune system activation (4-7). The effective treatment of this patient required timely drainage intervention, not deviating from current guidelines regarding intra-abdominal source control in septic patients, despite the peculiar nature of the patient's history. At the same time, the optimal management of the patient required a multidisciplinary team of physicians, as well as a thorough knowledge of the underlying genetic immunosuppressive syndrome.

2. OBJECTIVE

The aim of this case report was to describe a severe case of liver abscess, caused by a cavity-forming infection, secondary to Job's syndrome.

3. CASE PRESENTATION

Patient Information: A 25-year-old female patient, presented at the emergency department complaining of severe abdominal pain. The patient's detailed medical history revealed a series of recurrent pulmonary infections

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for which she was treated, as well as a known diagnosis of Job's syndrome since childhood. The patient's family history included a similar history of Job's syndrome in one of their parents.

Clinical Findings: The patient was febrile on presentation with a temperature of 38.3°C, with otherwise normal vital signs. On physical examination, the patient reported pain on palpation of the right upper quadrant of the abdomen. Palpation of the liver revealed hepatomegaly as well as a palpable mass. The rest of the physical examination was insignificant.

Diagnostic assessment: Initial laboratory investigations of the patient while still in the Emergency Department included a complete blood count (CBC), a basic biochemical and electrolyte panel, a liver panel, C-reactive protein (CRP) measurements as well as an hCG measurement before undergoing any ionizing radiation-related imaging studies. White cell count was at 15,32 K/ μ l (range: 4,0–11 K/ μ l) with 70.6% neutrophils and 11.90 eosinophils. The rest of the CBC was at normal values, including hemoglobin, hematocrit, and platelet measurements. Electrolytes, hepatic enzymes, hCG levels, and the basic metabolic panel all came back normal in their entirety. C-reactive protein levels were at 11.30 mg/dL (range: <0.5 mg/dL), indicating a severe underlying inflammatory response, which coupled with the patient's acute, high fever, pointed towards an intra-abdominal pathology, possibly but not limited to, an infectious process. The patient was transported to the CT scan for an emergency abdominal series. The imaging studies revealed a large intrahepatic fluid collection (Figure 1A, B), that was accompanied by free intraperitoneal fluid, and a smaller collection in the right paracolic gutter. The patient underwent immediate CT-guided drainage of the major intrahepatic abscess. Peripheral blood cultures, as well as cultures of the fluid collection, were obtained, that identified *Staphylococcus aureus* as the abscess' causal agent.

Diagnosis: A differential diagnosis of the patient presenting with acute upper-right abdominal pain was necessary when the patient presented acutely in the Emergency Department. Prior to obtaining a detailed history, the physicians assessed for the presence of more common intra-abdominal pathologies, including biliary colic, acute cholecystitis, acute cholangitis, duodenal ulcer, or ureteral colic. After stabilization of the patient and initial fluid and empirical antibiotic collection, a more detailed history, revealed the presence of Job's syndrome, which turned the attention of the physicians towards a diagnosis of either a lower lobe pulmonary infection,

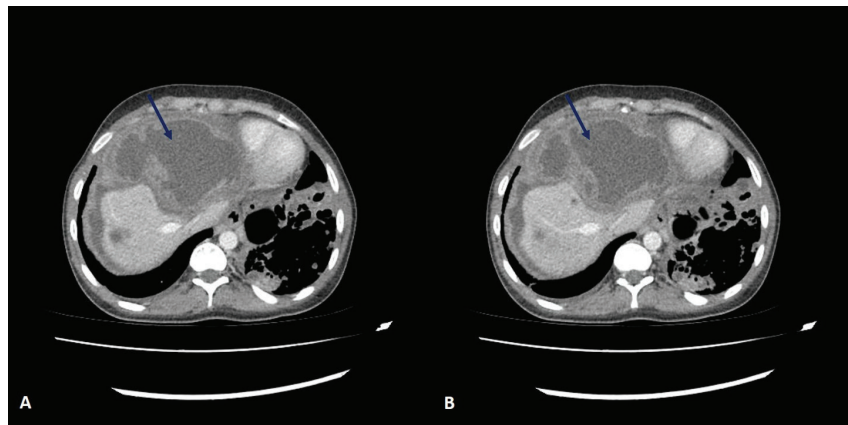


Figure 1. (A, B): The initial CT scan of the patient at presentation. Blue arrows indicate the hepatic abscess

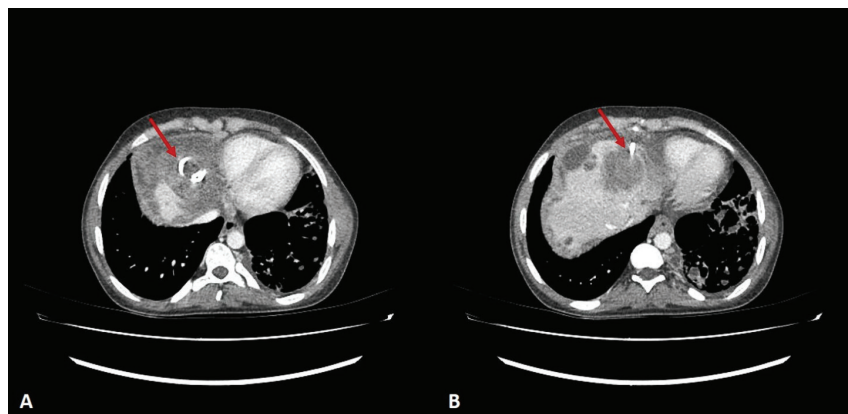


Figure 2.: (A, B): Abdominal CT scan of the patient after the first drainage. Red arrows indicate the indwelling pigtail catheter

with possible fungal involvement, or an intra-abdominal abscess formation, intra- or extra-hepatic. The nature of the differential diagnosis dictated timely CT scan investigations of the abdomen because since an intra-abdominal abscess was highly likely, the patient could be promptly treated by image-guided drainage since our institution has an on-call interventional radiology department.

Therapeutic interventions: After the initial CT scan that revealed hepatic abscess to be the cause of the acute abdomen, the patient was brought to the Interventional Radiology department, for immediate CT-guided drainage. The operation removed 500 ml of fluid, leaving an indwelling pigtail catheter for continuous drainage over the coming days (Figure 2A, B). The patient was administered empirical antibiotic treatment at the emergency department according to current views on intra-abdominal infections, which consisted of a combination of meropenem and tigecycline, as instructed by an infectious disease specialist. This decision was mainly based on the immune-compromisation history of the patient, as well as multiple previous antibiotic treatments for pneumonia, which meant a high possibility of colonization with multidrug-resistant bacteria. Meropenem monotherapy is well established as a single-agent regimen for intra-abdominal infections [8,9]. The adage of tigecycline is warranted in complicated

intra-abdominal infections, due to a favorable tissue penetration profile as well as a favorable efficacy against Gram-positive aerobes (10). After the first drainage, the patient remained in good clinical condition, with a low-grade intermittent fever that did not require antipyretic medication. Inflammatory markers were gradually subsiding (CRP: 17.6 and 15 mg/dL on the second and third day respectively). On the third day of hospitalization, the decision was made to also drain the fluid collection on the right paracolic gutter and a second pigtail catheter was placed, draining 1L of pus-filled fluid. Once the results of the sensitivity study for the isolated agent were available, trimethoprim/sulfamethoxazole was added to the antibiotic regimen with gradual de-escalation of empiric treatment, in accordance with current guidelines on targeted antimicrobial treatment. Pulmonology consultation recommended a chest CT scan for future reference, as well as initiation of anti-IgE monoclonal treatment that was previously prescribed for the patient, with good results. The patient remained afebrile for the remaining duration of her hospitalization. On the 14th day of hospitalization, and with minimal drainage from the indwelling catheters, both pigtail catheters were removed. The patient was discharged on the 15th day of hospitalization. Election of image-guided drainage over surgery was dictated from a multitude of position statements that recommend abscess drainage over open or laparoscopic surgery, whenever a liver abscess is not caused by an intra-abdominal pathology that requires surgical treatment. Indwelling catheters were preferred to simple drainage, due to the size and spread of the intrahepatic abscess.

Follow-up and outcome of interventions: At 4 weeks after discharge, the patient visited the outpatient department for the scheduled follow-up. Her clinical condition is excellent and has resumed all daily activities.

Informed Consent: the patient provided her full consent after oral explanation of our intention of publishing her case.

4. DISCUSSION

Autosomal dominant hyper immunoglobulin IgE syndrome is a rare inherited condition that causes immune suppression. The pathogenesis of the syndrome is most commonly attributed to missense variants of various domains in the STAT3 gene. The STAT3 protein is a major component within the JAK-STAT signaling pathway (1, 4-7, 11-13). The most widely known phenotypic effect of this genetic defect is the impaired function of the Th17 lymphocyte cells. Due to this impairment, neutrophil activation, chemotaxis, and proliferation are affected, leading to a decrease in the physiological inflammatory response to bacterial pathogens and increased susceptibility to infections. According to studies, the patients with Job's syndrome, are almost never neutropenic (7, 12, 13). The functionality of their neutrophils however is weakened, mainly concerning their chemotaxis and proliferation, which allow for infectious agents to cause recurrent disease. Furthermore, loss-of-function within the STAT3 gene has also been shown to cause

decreased levels of IL-17 and IL-9 among other inflammatory cytokines that account for reduced neutrophil proliferation and mobilization (2, 12-14). The observed elevation of serum IgE that is observed in patients with Job's syndrome is thought to be an accompanying abnormality that does not contribute to the disease's pathogenesis that seems to be linked with the relative deficit of IFN-gamma in these patients.

Usual manifestations of the syndrome, include a form of dermatitis, that is associated with recurrent skin abscesses, eczema, and anaphylactic reactions (1, 2, 14, 15). Other syndromic characteristics include face dysmorphias, retained childhood teeth, skeletal abnormalities, and growth retardation (1, 15). Sinopulmonary infections with high recurrence and severity are very common in patients with Job's syndrome. Data from one large registry of such patients indicate that the formation of lung abscesses was reported in 19% of the patients, an unusually high percentage when compared to the general population (3). Common microbial culprits include *S. aureus*, *Haemophilus influenza*, *C. Albicans*, *Pseudomonas*, *Pneumocystis jirovecii*, and *Aspergillus fumigatus*. Infectious processes and abscess formation can occur without the patient becoming febrile ("cold abscess"), in those with Job's syndrome, due to the impaired inflammation mechanisms (16). The formation of hepatic abscesses is uncommon occurrence in patients with Job's syndrome, with only a few case reports described in the literature (17-20). It should be noted, that in all cases, including ours, the hepatic abscess was managed as dictated by guidelines on liver abscess treatment, which included guided drainage and antibiotics.

5. CONCLUSION

In patients with a known history of the autosomal dominant hyper-IgE syndrome, presenting with acute abdominal pain, the liver abscess must be on the top of the differential diagnosis list. Despite being a genetic disease, Job's syndrome has the potential to require immediate surgical management by the general surgeon. Adherence to surgical guidelines, irrespective of the underlying cause of a liver abscess is crucial to ensure the best possible outcome.

- **Author's contribution:** G-I.V. and F.M. gave substantial contributions to the conception or design of the work in acquisition, analysis, or interpretation of data for the work. DI-C., I.P., K.T., L.T., E.L., I.P., P.P. had a part in article preparing for drafting or revising it critically for important intellectual content. K.B., and I.A. gave final approval of the version to be published and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
- **Conflicts of interest:** There are no conflicts of interest.
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REFERENCES

1. Chandesris MO, Melki I, Natividad A, et al. Autosomal dominant STAT3 deficiency and hyper-IgE syndrome: mo-

- lecular, cellular, and clinical features from a French national survey. *Medicine (Baltimore)*. 2012; 91: 10.1097/MD.0B013E31825F95B9
2. Woellner C, Gertz EM, Schäffer AA, et al. Mutations in STAT3 and diagnostic guidelines for hyper-IgE syndrome. *J Allergy Clin Immunol*. 2010; 125: 10.1016/J.JACI.2009.10.059
3. Gernez Y, Freeman AF, Holland SM, et al. Autosomal Dominant Hyper-IgE Syndrome in the USIDNET Registry. *J Allergy Clin Immunol Pract*. 2018; 6: 996-1001. 10.1016/J.JAIP.2017.06.041
4. Minegishi Y, Karasuyama H. Defects in Jak-STAT-mediated cytokine signals cause hyper-IgE syndrome: lessons from a primary immunodeficiency. *Int Immunol*. 2009; 21: 105-112. 10.1093/INTIMM/DXN134
5. Paulson ML, Freeman AF, Holland SM. Hyper IgE syndrome: an update on clinical aspects and the role of signal transducer and activator of transcription 3. *Curr Opin Allergy Clin Immunol*. 2008; 8: 527-533. 10.1097/ACI.0B013E3283184210
6. Van Scoy RE, Hill HR, Ritts RE, et al. Familial neutrophil chemotaxis defect, recurrent bacterial infections, mucocutaneous candidiasis, and hyperimmunoglobulinemia E. *Ann Intern Med*. 1975; 82: 766-771. 10.7326/0003-4819-82-6-766
7. Mogensen TH. STAT3 and the Hyper-IgE syndrome: Clinical presentation, genetic origin, pathogenesis, novel findings and remaining uncertainties. *JAK-STAT*. 2013; 2: 23435. 10.4161/JKST.23435
8. Mazuski JE, Tessier JM, May AK, et al. The Surgical Infection Society Revised Guidelines on the Management of Intra-Abdominal Infection. *Surg Infect (Larchmt)*. 2017; 18: 10.1089/SUR.2016.261
9. Solomkin JS, Mazuski JE, Bradley JS, et al. Diagnosis and management of complicated intra-abdominal infection in adults and children: guidelines by the Surgical Infection Society and the Infectious Diseases Society of America. *Clin Infect Dis*. 2010; 50: 133-64. 10.1086/649554
10. Eckmann C, Montravers P, Bassetti M, et al. Efficacy of tigecycline for the treatment of complicated intra-abdominal infections in real-life clinical practice from five European observational studies. *J Antimicrob Chemother*. 2013; 68, 2: 10.1093/JAC/DKT142
11. Grimbacher B, Holland SM, Gallin JL, et al. Hyper-IgE syndrome with recurrent infections - an autosomal dominant multisystem disorder. *N Engl J Med*. 1999; 340: 692-702. 10.1056/NEJM199903043400904
12. Heimall J, Freeman A, Holland SM. Pathogenesis of hyper IgE syndrome. *Clin Rev Allergy Immunol*. 2010; 38: 32-38. 10.1007/S12016-009-8134-1
13. Wolach O, Kuijpers T, Ben-Ari J, et al. Variable clinical expressivity of STAT3 mutation in hyperimmunoglobulin E syndrome: genetic and clinical studies of six patients. *J Clin Immunol*. 2014; 34: 163-170. 10.1007/S10875-014-9988-4
14. Szczawinska-Poplonyk A, Kycler Z, Pietrucha B, et al. The hyperimmunoglobulin e syndrome—Clinical manifestation diversity in primary immune deficiency. *Orphanet J Rare Dis*. 2011; 6: 1-11. 10.1186/1750-1172-6-76/TABLES/1
15. O'Connell AC, Puck JM, Grimbacher B, et al. Delayed eruption of permanent teeth in hyperimmunoglobulinemia E recurrent infection syndrome. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2000; 89: 177-185. 10.1067/MOE.2000.103129
16. Freeman AF, Kleiner DE, Nadiminti H, et al. Causes of death in hyper-IgE syndrome. *J Allergy Clin Immunol*. 2007; 119: 1234-1240. 10.1016/J.JACI.2006.12.666
17. Nandy S, Shah I. Liver abscess in a boy with hyper IgE syndrome. *J Fam Med Prim Care*. 2016; 5: 491. 10.4103/2249-4863.192353
18. Fanconi S, Seger RA, Willi U, et al. Oral chloramphenicol therapy for multiple liver abscesses in hyperimmunoglobulinemia E syndrome. *Eur J Pediatr*. 1984; 142: 292-295. 10.1007/BF00540256
19. Bhutani N, Sharma U, Kumar A, et al. Pediatric hyperimmunoglobulin E syndrome (Job's syndrome) with STAT3 mutation: A case report. *Ann Med Surg*. 2021; 66: 102452. 10.1016/J.AMSU.2021.102452
20. Freeman AF, Davis J, Anderson VL, et al. Pneumocystis jirovecii infection in patients with hyper-immunoglobulin E syndrome. *Pediatrics*. 2006; 118: 10.1542/PEDS.2006-0311