Eur J Pediatr (1984) 142:292–295

Oral chloramphenicol therapy for multiple liver abscesses in hyperimmunoglobulinemia E syndrome

S. Fanconi[1], R. A. Seger[1], U. Willi[1], R. Otto[2], H. Spiess[3], F. H. Kayser[4], and W. H. Hitzig[1]

[1] Department of Pediatrics, Divisions of Hematology-Immunology and of Radiology, University Zürich
[2] Department of Radiology, University of Zürich
[3] Neuroradiologisches Institut, Talstrasse, Zürich
[4] Department of Medical Microbiology, University of Zürich

Abstract. In a patient with Hyper-IgE-syndrome multiple liver abscesses developed in spite of prophylactic treatment with trimethoprim and sulfamethoxazol. Ultrasound confirmed the clinical diagnosis and percutaneous needle aspiration under ultrasonographic guidance and culture of the aspirated pus allowed specific antibiotic treatment by oral chloramphenicol alone without surgical drainage. The isolated Staph. aureus strain was resistant to trimethoprim and sulfamethoxazol.

Key words: Hyper-IgE-syndrome – Multiple liver abscesses – Percutaneous needle aspiration – Oral chloramphenicol

Introduction

The hyper-IgE syndrome is a rare immunodeficiency characterized by coarse facial features, eczematoid dermatitis and severe recurring staphylococcal abscesses of skin, ears, oral mucosa, sinuses, lungs, joints and viscera [3, 4, 7]. If the diagnosis is made late, osteoporosis leading to pathological fractures [6] and pneumatoceles resulting in putrid lung abscesses or aspergilloma formation [3] may develop. The major laboratory abnormalities of the disorder are eosinophilia in blood, sputum and tissue, markedly elevated serum IgE and often IgD, impaired anamnestic (IgG) antibody responses, usually depressed cell-mediated immunity and variable presence of chemotactic defects [3, 11, 13, 22].

Despite many attempts at immunological therapy [6], the most successfull treatment of this debilitating disease still consists of long-term therapy with a β-lactamase resistant penicillin, incision and drainage of furuncles and surgical excision of abscesses and pneumatoceles [3, 7].

We present a patient with multiple liver abscesses diagnosed by ultrasound

Table 1. Hyper IgE syndrome: Clinical manifestations and treatment

Age in years	$^{7}/_{12}$	$^{11}/_{12}$	$^{12}/_{12}$	$^{17}/_{12}$	$1^{10}/_{12}$	2	$2^{10}/_{12}$	$3^{1}/_{12}$	$4^{2}/_{12}$	$5^{2}/_{12}$	$5^{7}/_{12}$	$6^{2}/_{12}$
Days spent in hospital	88	21	45	17	20	9	6	15	18	18	18	44
Infections:												
Dermatitis	● ■	● ■	● ■	● ■	● ■	●	●	●	●	●	●	
Otitis		●										
Penumonia		●			●				●	●		
Peritonitis								●				
Abscesses:												
Scalp	●	●	●	●	●	●		●		●	●	
Face	●		●			●					●	
Neck	●		●					●				
Axilla	●											
Arm				●								
Knee							●					
Toe						●						
Perianal			●					●				
Liver												●
Therapy	OP AB	OP AB AR	OP AB	AB	OP AB AR	OP AB	AB	OP AB	AB	AB	AB	AB

Key: ● = *Staphylococcus aureus* ■ = *Candida albicans*
OP = operation
AB = antibiotics
AR = artificial respiration

Corresponding author: R. A. Seger, Universitäts-Kinderspital, Steinwiesstrasse 75, CH-8032 Zürich, Switzerland

and computed tomography who was successfully treated with oral chloramphenicol alone after diagnostic percutaneous needle aspiration under ultrasonographic guidance.

Case report

H.L., a $6^{2}/_{12}$-year-old son of unrelated and healthy parents, first became ill at the age of 10 days with pruritic dermatitis. This was followed by numerous candidal and staphylococcal infections summarized in Table 1.

He had coarse facial features and scaphocephaly, eosinophilia up to 12.45×10^{9}/l, IgE up to 4000 U/ml (normal range for his age 0–330 U/ml), normal IgG, IgA, IgM, low IgG 2 (9.8%, normal 29.4%), normal IgG 1, 3, and 4; normal C3, 4, 5, 6, 7, 8, and 9; variable, but usually normal T and B cell functions; normal neutrophil functions (NBT, chemotaxis, phagocytosis and killing of *Staphylococcus aureus* and *Candida albicans*); high IgE-antibodies against *Staphylococcus aureus* cell walls (20%, normal up to 10% [22]; normal Tetanus (1:32) and no Diphtheria antibody responses to boostering; delayed type skin tests to *Staphylococcus aureus* and *Candida albicans* were positive. These clinical and laboratory findings are typical of the hyper-IgE syndrome.

The patient had been treated for varying periods of time with flucloxacillin and other antibiotics. Since February 1981 he had been under prophylactic trimethoprim (6 mg/kg per day) and sulfamethoxazol (30 mg/kg per day) therapy.

Clinical findings

On admission his temperature was 36.8°C, pulse rate 82/min, weight 20.4 kg (25–50th percentile for age), length 116 cm (25–50th percentile for age) and head circumference 53 cm (50–75th percentile for age). The liver was tender and palpable 10 cm below the right costal margin and the spleen was palpable 1 cm below the left costal margin. There was no jaundice, ascites or abnormal physical signs in the right lower chest. Apart from coarse facial features and multiple scars from previous skin abscesses, the rest of the physical examination was normal.

Laboratory findings

Laboratory studies revealed a hemoglobin level of 83 g/l with hypochromia and microcytosis but without iron deficiency. Platelets were normal. The sedimentation rate (Westergren) was 58/109 mm and the WBC count was 2.6×10^{9}/l with 43.5% band forms, 9% segmented neutrophils, 10.5% eosinophils, 16% monocytes, 2% basophils, 18% lymphocytes, 0.5% plasmacells and 0.5% metamyelocytes.

Liver function tests revealed: SGOT 82 U/l (normal 6–46 U/l); SGPT 67 U/l (normal 3–46 U/l); gamma GT 124 U/l (normal 3–30 U/l); alkaline phosphatase 2101 U/l (normal 115–460 U/l); bilirubin 9 µmol/l (normal < 17 µmol/l); direct bilirubin 2 µmol/l (normal 0–5 µmol/l); albumin 19 g/l; γ-globulin 22 g/l; Quick and PTT within the normal range.

Microbiological studies showed: *Candida* precipitins 1:20; *Aspergillus* precipitins negative; repeated urine, aerobic and anaerobic blood cultures negative;

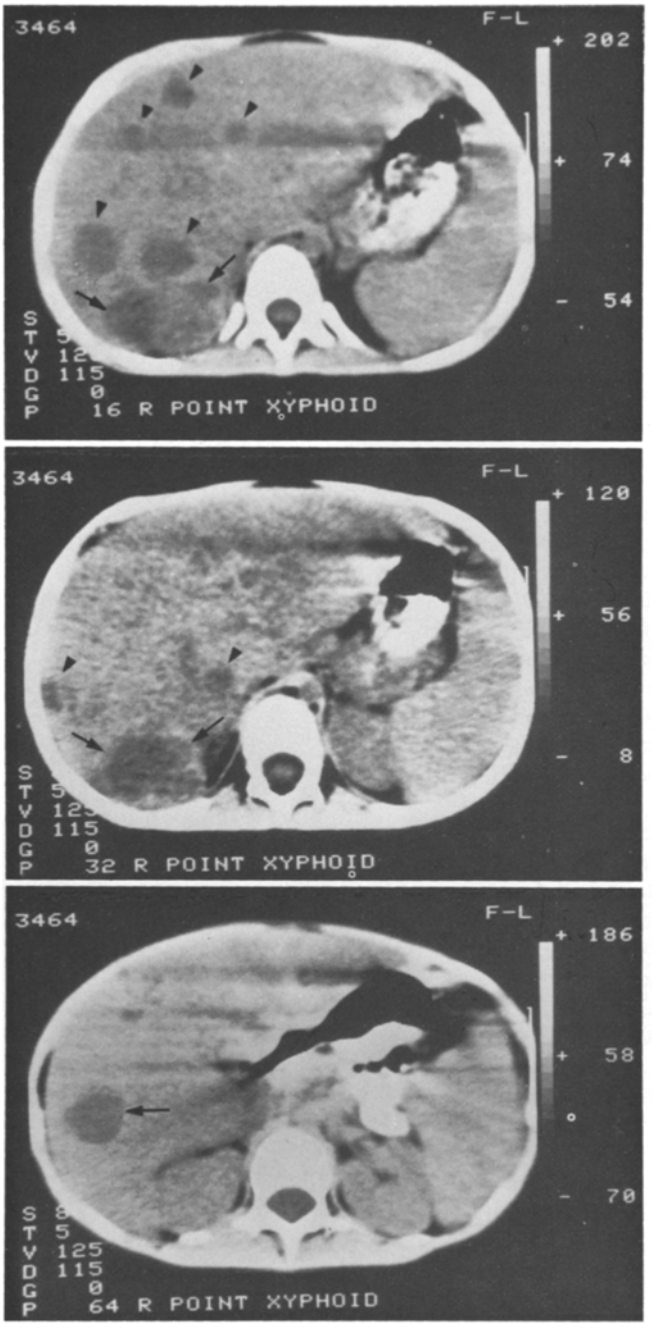

Fig. 1A–C. Three transverse CT scans show, at a few centimeters distance from each other, multiple liver abscesses (arrows and arrowheads). **A** and **B** Level above right kidney. Large abscess (arrows) in immediate suprarenal area. **C** Medium-size abscess (arrow) at level of right renal upper pole, laterally

throat and stool cultures normal flora; hepatitis serology negative. Urinalysis revealed a slight proteinuria, while creatinine and urea were within the normal range.

A chest X-ray showed residual infiltrations in the right upper lobe (pneumonia in 1979). There were no signs of osteoporosis on skeletal X-rays.

Special findings

Ultrasound examination showed multiple well-defined intrahepatic masses of 2–5 cm diameter.

Computed tomography confirmed the presence of multiple liver abscesses (Fig. 1). Diagnostic percutaneous needle aspiration of three sites under ultrasonographic guidance yielded a few milliliters of thick pus. Gram's stain revealed gram-positive cocci and leukocytes. Pus was cultured under aerobic and anaerobic conditions and yielded *Staphylococcus aureus*. Disc susceptibility testing [1] revealed susceptibility to β-lactamase resistant penicillins and cephalosporins, to erythromycin, to gentamicin and amikacin, to rifampicin and to chloramphenicol. The strain was resistant to sulphonamides and sulfamethoxazole-trimethoprim, to penicllin G and further β-lactamase labile penicillins and to the tretracyclines. Minimal inhibitory concentrations (MICs) were determined by the microdilution test procedure [10]. MICs of flucloxacillin and of rifampicin were 0.12 mg/l and 0.008 mg/l, respectively. Minimal bactericidal concentrations (MBCs) were 0.12 mg/l for flucloxacillin and 0.016 mg/l for rifampicin. Checkerboard titration revealed synergistic activity of the two drugs for the strain.

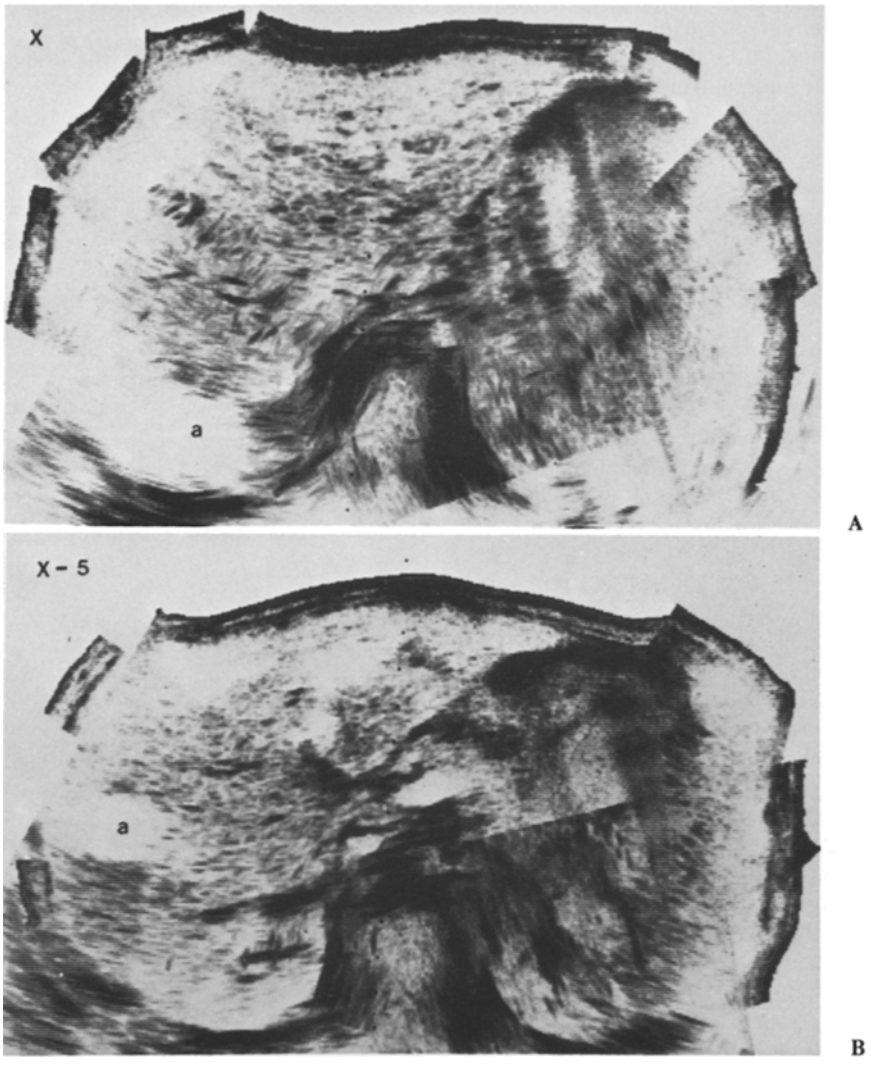

Fig. 2A and B. Transverse ultrasonographic scans following the first 6 weeks of treatment and before institution of oral chloramphenicol show persistance of multiple liver abscesses *(a)*. **A** Large suprarenal abscess. **B** Medium-size abscess at level of right renal upper pole, laterally. Smaller areas of low echogenicity within the liver may also represent abscesses (*X* = level of xyphoid; *X-5* = 5 cm below xyphoid)

Treatment and results

The patient was given intravenous moxalactam (50 mg/kg per day) and rifampicin (15 mg/kg per day) for 6 weeks in combination with amikacin (15 mg/kg per day) for 2 weeks, followed by flucloxacillin (50 mg/kg per day) for 4 weeks. Under this regimen the poor general condition, spiking fever, tender liver enlargement, elevated sedimentation rate anf liver abscesses (ultrasound control) persisted (Fig. 2) so that choramphenicol (100 mg/kg per day) was started. After 3 days fever disappeared and the child felt better. Three days later intravenous antibiotics were stopped and the patient could be discharged with oral chloramphenicol administration (100 mg/kg per day) only, the mean plasma concentration being 8 μg/ml before and 18.7 μg/ml after administration of the drug.

The patient was treated with oral chloramphenicol for a total of 6 weeks and afterwards prophylactic long-term flucloxacillin therapy (100 mg/kg per day) was instituted. At the end of chloramphenicol treatment laboratory examinations revealed an erythrocyte sedimentation rate of 8/20 mm, normal hemogram and liver enzymes. A percutaneous needle aspiration under ultrasonographic guidance yielded sterile pus. Computed tomography and an ultrasound scan 3 and 9 weeks after stopping chloramphenicol treatment showed, respectively, a single zone of low echogenicity with a diameter of 1–1.5 cm. Four months later liver palpation and ultrasonographic control were absolutely normal.

Discussion

Pyogenic hepatic abscess is an unusual infection in the pediatric age group and occurs most often in infants who had sepsis or umbilical infection or in older children with host defence defects [5, 8, 15]. The overall mortality varies between 27% and 75%, depending on age and the underlying disease [5, 8, 18–21, 24]. However, ultrasound computed tomography and radioisotope scanning are extremely effective and safe diagnostic procedures for abscess detection. In addi-

tion, percutaneous diagnostic needle aspirations under ultrasonographic or computed tomographic guidance are now widely employed. They are increasingly followed by percutaneous catheter drainage for definitive nonsurgiccal therapy [2, 5, 9, 12, 18–22].

In our patient multiple hepatic abscesses developed in spite of prophylactic treatment with trimethoprim and sulfamethoxazol. Computed tomographyy, ultrasound and percutaneous aspiration under ultrasonographic guidance confirmed the clinical diagnosis and culture of the aspirated pus allowed specific antibiotic treatment without surgical drainage. The isolated *Staphylococcus aureus* was resistent to trimethoprim and sulfamethoxazol and susceptible to cephalosporins, amikacin, rifampicin, chloramphenicol and β-lactamase resistant penicillins, the latter classically used for prophylaxis in the hyper-IgE syndrome. In spite of good in vitro sensitivity and synergistic activity of rifampicin and flucloxacillin, the symptomatology and volume of the abscesses (ultrasound measurements) did not improve.

It is unclear why rifampicin and flucloxacillin failed and oral chloramphenicol alone succeeded in treating the staphylococcal abscesses. Possibly rapid emergence of resistance, differences of in vivo and in vitro susceptibility, variable cellular uptake and intracellular activity played major roles.

It may be of relevance that chloramphenicol, a lipophilic antibiotic, penetrates neutrophil granulocytes and kills intracellular bacteria [14, 16, 17, 21, 23].

The successfull treatment of a potentially lethal infection with oral chloramphenicol alone, especially while monitoring the therapy by repeated ultrasounds and percutaneous punctures, offers new possibilities in the nonsurgical management of immunodeficient patients with liver abscesses and will need further studies.

Acknowledgements. We are grateful to Dr. R. Lüthy, Dept. Int. Medicine, University of Zürich, for measuring the plasma concentrations of chloramphenicol, to Dr. K. Schopfer, Inst. of Med. Microbiology, St. Gallen, for analysing the IgE-antibodies against *Staphylococcus aureus* and to Dr. F. Skvaril, Inst. of Exp. Tumor Research, University of Berne, for determining the IgG subclasses. We thank Dr. A. Kenny for editing and Mrs. Ricklin for secretarial assistance. R. A. Seger was supported by the Schweizerische Stiftung für Medizinisch-Biologische Stipendien.

References

1. Barry AL, Thormberry C (1980) Susceptibility testing: diffusion test procedures. In: Lennette EH, Balows A, Hausler WJ, Truant JP (eds) Manual of clinical microbiology. Am Soc Microbiol, Washington DC, pp 463–474
2. Berger LA, Osborne DR (1982) Treatment of pyogenic liver abscesses by percutaneous needle aspiration. Lancet 1: 132–136
3. Buckley RH, Sampson HA (1981) The hyperimmunoglobulinemia E syndrome. Clinical immunology up to date. In: Franklin EC (ed) Reviews for physicians. Churchill, Livingstone Edinburgh, pp 147–167
4. Buckley RH, Wray BB, Belmaker EZ (1972) Extreme hyperimmunoglobulinemia E and undue susceptibility to infection. Pediatrics 49: 59–70
5. Chusid MJ (1978) Pyogenic hepatic abscess in infancy and childhood. Pediatrics 62: 554–559
6. Däumling S, Buriot D, Hun Trung P, Griscelli C, Lalama MC, Belohradsky BH (1980) Das Buckley-Syndrom: Rezidivierende, schwere Staphylokokken-Infektionen, Ekzem und Hyperimmunoglobulinämie E. Infection 8: 248–254
7. Davis SD, Schaller JS, Wedgwood RJ (1966) Job's syndrome, recurrent, "cold", staphyloccocal abscesses. Lancet 1: 1013–1015
8. Dehner LP, Kissane JM (1969) Pyogenic hepatic abscesses in infancy and childhood. J Pediatr 74: 763–773
9. Ferrucci JT, Vansonnenberg E (1982) In: Remington JS, Swartz MN (eds) Role of ultrasound and computed tomography in the diagnosis and treatment of intra-abdominal abscess. Corrent clinical topics in infections diseases. Volume 3. McGraw-Hill, New York, pp 136–159
10. Gavan TL, Barry AL (1980) Microdilution test procedures. In: Lennette EH, Balows A, Hausler WJ, Truant JP (eds) Manual of Clinical Microbiology. Am Soc Microbiol, Washington DC, pp 459–462
11. Geha RS, Reinherz E, Leung D (1981) Deficiency of suppressor T cells in the hyperimmunoglobulin E syndrome. J Clin Invest 68: 783–791
12. Gerzof SG, Robbins AH, Johnson WC (1981) Percutaneous catheter drainage of abdominal abscesses. A five-year experience. N Engl J Med 305: 653–657
13. Hill HR, Ochs HD, Quie PG (1974) Defect in neutrophil granulocyte chemotaxis in Job's syndrome of recurrent "cold" staphylococcal abscesses. Lancet 2: 617–619
14. Jacobs RF, Wilson CB, Laxton JG (1982) Cellular uptake and intracellular activity of antibiotics against Haemophilus influenzae type b. J Infect Dis 145: 152–159
15. Kaplan SL, Feigin RD (1976) Pyogenic liver abscess in normal children with fever of unknown origin. Pediatrics 58: 614–616
16. Kauffman RE, Thirumoorthi MC, Buckley JA (1981) Relative bioavailability of intravenous chloramphenicol succinate and oral chloramphenicol palmitate in infants and children. J Pediatr 99: 963–967
17. Laferriere CI, Marks MI (1982) Chloramphenicol properties and clinical use. Pediatr Infect Dis 1: 257–264
18. Maher JA, Reynolds TB, Yellin AE (1979) Successful medical treatment of pyogenic liver abscess. Gastroenterology 77: 618–622
19. McFadzean AJS, Chang KPS, Wong CC (1953) Solitary pyogenic abscess of the liver treated by closed aspiration and antibiotics. A report of 14 consecutive cases with recovery. Br J Surg 42: 141–152
20. Perera MR, Kirk A, Noone P (1980) Presentation, diagnosis and management of liver abscess. Lancet 2: 629–632
21. Rubin RH, Swarzt MN, Malt R (1974) Hepatic abscess: changes in clinical, bacteriologic and therapeutic aspects. Am J Med 57: 601–610
22. Schopfer K, Baerlocher K, Price P (1979) Staphylococcal IgE antibodies, hyperimmunoglobulinemia E and Staphylococcus aureus infections. N Engl J Med 300: 835–838
23. Tuomanen EI, Powell KR, Marks MI (1981) Oral chloramphenicol in the treatment of Haemophilus influenzae meningitis. J Pediatr 99 (6): 968–974
24. Verlenden WL, Frey CF (1980) Management of liver abscess. Am J Surg 140: 53–59

Received July 26, 1983 /
Accepted February 20, 1984