5. Bitter-Suermann D, Roth J. Monoclonal antibodies to polysialic acid reveal epitope sharing between invasive pathogenic bacteria, differentiating cells and tumor cells. *Immunol Res* 1987, **6**, 225–237.
6. Roth J, Zuber C, Wagner P, *et al.* Reexpression of poly(sialic acid) units of the neural cell adhesion molecule in Wilms' tumor. *Proc Natl Acad Sci USA* 1988, **85**, 2999–3003.
7. Kruse J, Mailhammer R, Wernecke H, *et al.* Neural cell adhesion molecules and myelin-associated glycoprotein share a common carbohydrate moiety recognized by monoclonal antibodies L2 and HNK-1. *Nature* 1984, **311**, 154–155.
8. Kunemund V, Jungalwala FB, Fischer G, Chou DKH, Keilhauer G, Schachner M. The L2/HNK-1 carbohydrate of neural cell adhesion molecules is involved in cell interactions. *J Cell Biol* 1988, **106**, 213–223.
9. Mountain CF. Staging in lung cancer, UICC 1987. *Chest* 1986, **89**, 225S–233S.
10. Gazdar AF, Carney DN, Russell EK, *et al.* Establishment of continuous, clonable cultures of small-cell carcinoma of the lung which have amine precursor uptake and decarboxylation cell properties. *Cancer Res* 1985, **40**, 3502–3507.
11. Ibsen S, Berezin V, Norgard-Pedersen B, Bock E. Quantification of the D2 glycoprotein in amniotic fluid and serum from pregnancies with foetal neural tube defects. *J Neurochem* 1983, **41**, 363–366.
12. Frosch M, Gorgen I, Boulnois GJ, Timmis KN, Bitter-Suermann D. NZB mouse system for production of monoclonal antibodies to weak bacterial antigens: isolation of an IgG antibody to the polysaccharide capsules of escherichia coli K1 and group B meningococci. *Proc Natl Acad Sci USA* 1985, **82**, 1194–1198.
13. De Ley L, Broers J, Ramaekers F, Berendsen H, Wagenaar Sj Sc. Monoclonal antibodies in clinical and experimental pathology of lung cancer. In: Fleuren GJ, Ruiter DJ, Warnaar SO, eds. *Application of Monoclonal Antibodies in Tumour Pathology*. Amsterdam, Martinus Nijhoff, 1987.
14. Kibbelaar RE, Moolenaar CEC, Michalides RJAM, Bitter-Suermann D, Addis B, Mooi WJ. Expression of the embryonal neural cell adhesion molecule in lung carcinoma. Diagnostic usefulness of monoclonal antibody 735 for the distinction between small cell lung cancer and non-small cell lung cancer. *J Pathol* 1989, **159**, 23–28.
15. Patel K, Moore SE, Dickson G, *et al.* Neural cell adhesion molecule (NCAM) is the antigen recognised by monoclonal antibodies of similar specificity in small-cell lung carcinoma and neuroblastoma. *Int J Cancer* 1989, **44**, 573–578.
16. Laemmli UK. Cleavage of structural proteins during the assembly of the head of bacteriophage T_4. *Nature* 1970, **227**, 680–685.
17. Schol DJ, Mooi WJ, Gugten van der AA, Wagenaar SjSc, Hilgers J. Monoclonal antibody 123c3, identifying small cell lung carcinoma phenotype in lung tumours, recognizes mainly, but not exclusively, endocrine and neuron-supporting normal tissues. *Int J Cancer* 1988 (Suppl. 2) 34–40.
18. Mooi WJ, Dingemans KP, Van Zandwijk N. Prevalence of neuroendocrine granules in small cell lung carcinoma. Usefulness of electron microscopy in lung cancer classification. *J Pathol* 1986, **149**, 41–48.
19. Mooi WJ, Van Zandwijk N, Dingemans KP, Koolen MGJ, Wagenvoort CA. The "grey area" between small cell and non-small cell lung carcinomas. Light and electron microscopy versus clinical data in 14 cases. *J Pathol* 1986, **149**, 49–54.
20. Sadoul R, Hirn M, Deagostini-Bazin H, Rougon G, Goridis G. Adult and embryonic mouse neural cell adhesion molecules have different binding properties. *Nature* 1983, **304**, 347–349.

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Listeria monocytogenes Brain Abscesses in a Girl with Acute Lymphoblastic Leukaemia after Late Central Nervous System Relapse

Claudio Viscoli, Alberto Garaventa, Giuseppe Ferrea, Graziana Manno, Agostino Taccone and Alberto Terragna

A case of *Listeria monocytogenes* bacteraemia and meningitis with intracerebral abscesses in a girl with acute lymphoblastic leukaemia in relapse is reported. The clinical features included subacute onset with fever and marked irritability followed by seizures, meningism and confusion. The pathogen was isolated from blood and cerebrospinal fluid. Computerised tomography of the brain showed two intracerebral parenchymal localisations, in the left frontal lobe and in the right occipital lobe, respectively. The patient survived this severe infection without neurological sequelae. 2 months later she underwent allogeneic bone marrow transplantation without major complications. This case report should alert pediatric oncologists about the possible occurrence of severe intracerebral listerial infections in the immunocompromised child and suggests that this infection can be treated successfully and should not necessarily preclude continuation of antineoplastic treatments.
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INTRODUCTION

MENINGITIS IS the most common clinical form of infection caused by *Listeria monocytogenes*, accounting for about 50% of cases [1]. Nevertheless, this intracellular pathogen has never been associated with brain abscesses in immunocompromised children younger than 15 years of age [2, 3]. We describe the case of a young girl with acute lymphoblastic leukaemia in relapse, who developed listerial bacteraemia and meningitis with intracerebral parenchymal localisations.

CASE REPORT

A 6-year-old girl with a 4-year history of acute lymphoblastic leukaemia had a central nervous system relapse in December 1987. She received intensive chemotherapy with vincristine, prednisone, doxorubicin, L-asparaginase and weekly intrathecal methotrexate. On 14 January 1988 she was admitted to G. Gaslini Children's Hospital, Genova, Italy, with high fever and generalised seizures. The mother reported a 2-week history of aspecific behavioral abnormalities. The physical examination

showed no meningism or focal neurological signs. The absolute granulocyte count was 1.4×10^9/l, with normal platelet count. Computerised tomography of the brain was normal. Spinal fluid cell count and glucose and protein content were normal, and cultures from blood and cerebrospinal fluid were negative. Due to persistent fever and decreasing granulocyte count, empiric antibiotic therapy with ceftazidime and amikacin was then started, but the patient remained persistently febrile without any sign of neurological involvement, apart from marked irritability. On day 6 slight meningeal signs appeared, with confusion, right facial palsy and clonal left Achilles reflex. Spinal fluid examination showed the presence of 95×10^6/l mononuclear cells with decreased glucose (0.19 g/l) and slightly increased protein concentrations (0.43 g/l). Blood and spinal fluid cultures yielded *L. monocytogenes* type 1 ("O" Antisera, Difco Laboratories). In concomitance, a contrast-enhancing lesion in the left frontal lobe and a hypodense lesion in the right occipital lobe with tetraventricular hydrocephalus became evident at computerised tomography (Fig. 1, a and b). The patient's neurological condition progressively deteriorated to deep confusion and stupor. On day 7 the initial regimen was modified to ampicillin, vancomycin and netilmicin; 6 days later vancomycin was replaced with rifampin. This intravenous antibiotic regimen was administered for 29 days. Along with bone marrow recovery, an initial increase in spinal fluid cell count (500×10^6/l mononuclear cells) was observed, followed by progressive normalisation. By day 30 after the onset of fever the girl was afebrile and in good general condition. Both spinal fluid and brain computerised tomography were normal and therefore antineoplastic treatment was progressively resumed. In June 1988 the patient underwent allogeneic bone marrow transplantation from a HLA identical brother. Conditioning regimen included vincristine, cyclophosphamide and total body irradiation. Cyclosporine and short-term intravenous methotrexate were administered after bone marrow transplantation for prophylaxis of graft vs. host disease. While severely granulocytopenic the patient developed two episodes of fever of unknown origin and was successfully treated with empiric antibiotic therapy. After discharge, she developed mild graft vs. host disease and received additional immunosuppressive therapy with prednisone, without complications. She is presently in good general condition and shows no signs of either malignant disease or neurological deficit.

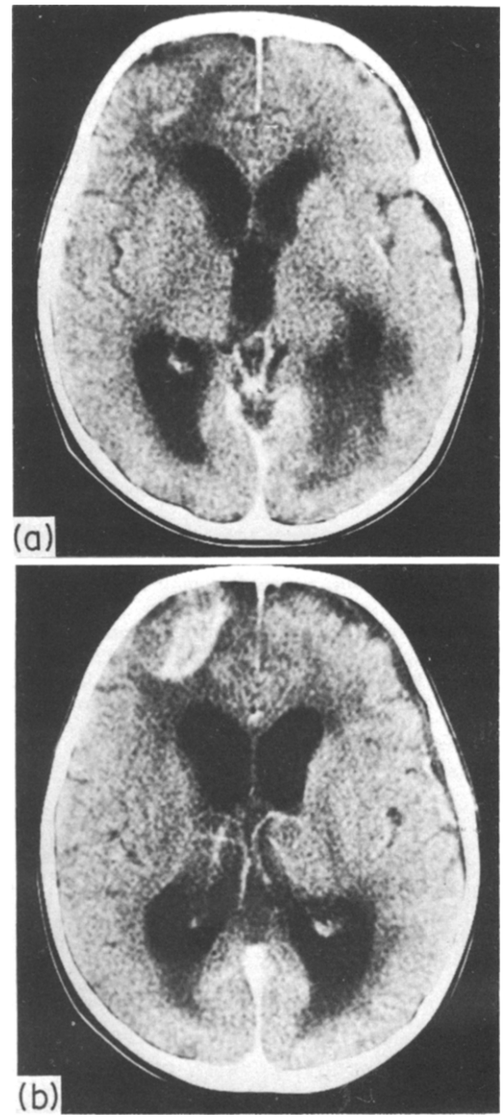

Fig. 1. Computerised tomography: (a) Hypodense lesion in the right occipital lobe; (b) contrast-enhancing lesion in the left frontal lobe.

DISCUSSION

The pattern of infections caused by *L. monocytogenes* has been recently reviewed [4]. Septicaemia and meningoencephalitis are the commonest clinical manifestations of nonperinatal listeriosis, while the development of intracerebral parenchymal localisations seems to be rare [1]. Food-borne infections due to *L. monocytogenes* are increasingly reported both in the USA and in Europe [5–7], but this pathogen seems to be relatively uncommon in neutropenic cancer patients [8, 9], despite the high incidence of gram positive infections which is now being observed in this patient population [10]. Although T-cell mediated, lymphokine-dependent activation of mononuclear phagocytes appears to play a crucial role in immune response against *Listeria* sp., quite unexpectedly this infection occurs infrequently among HIV-infected patients, too [11, 12]. However, once exposed to this microorganism, immunocompromised patients have a higher probability of developing the disease than normal subjects [4].

The gastrointestinal tract is the most probable portal of entry, but exposure does not necessarily mean disease, because the pathogen can be isolated from stool culture in absence of any clinical manifestation. In this paediatric case stool culture was negative and the source of the infection remained unknown. No other case of *Listeria* infection was seen in our hospital, nor in the city of Genova in that period. Blood–brain barrier disruption due to leukaemic infiltration and intrathecal therapy might have played a role in the development of meningitis and intracerebral localisations, while the effect of the cranial irradiation, performed 18 months before, appears to be less evident [13].

The clinical and radiological presentation of brain abscesses due to this pathogen does not appear to be distinct from that of brain abscesses of other aetiologies, thus precluding diagnosis

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without isolation and identification of the causative agent [1]. This is particularly important in light of the poor intrinsic activity of the cephalosporins and of the lack of intracerebral penetration of the aminoglycosides, a combination that is currently used as empirical treatment of fever and suspected infection in neutropenic cancer patients. Optimal treatment of listerial infections remains controversial. A combination of ampicillin and gentamicin is generally recommended, but other options are possible, including cotrimoxazole, rifampin and vancomycin [4].

In conclusion, the occurrence of brain abscesses due to *L. monocytogenes* in this 6-year-old girl should alert pediatricians against this entity. Despite the severity of the clinical course, this infection was treated successfully without any neurological sequela and did not preclude the continuation of the antineoplastic treatment, including allogeneic bone marrow transplantation.

1. Dee RR, Lorber B. Brain abscess due to *Listeria monocytogenes*: case report and literature review. *Rev Infect Dis* 1986, **8**, 968–977.
2. Pollock SS, Pollock TM, Harrison MJG. Infection of the central nervous system by *Listeria monocytogenes*: a review of 54 adult and juvenile cases. *Q J Med* 1984, **53**, 331–340.
3. Dykes A, Baraff LJ, Herzog P. *Listeria* abscess in an immunocompromised child. *J Pediatr* 1979, **94**, 72–74.
4. Gellin BG, Broome CV. Listeriosis. *JAMA* 1989, **261**, 1313–1320.
5. Fleming DW, Cochio SL, MacDonald KL, *et al.* Pasteurized milk as a vehicle of infection in an outbreak of lister. *N Engl J Med* 1985, **312**, 404–407.
6. Linnan MJ, Mascola L, Xiao DL, *et al.* Epidemic listeriosis associated with Mexican-style cheese. *N Engl J Med* 1988, **319**, 823–828.
7. Schlech WF, Lavigne PM, Bortolusse R, *et al.* Epidemic listeriosis: evidence for transmission by food. *N Engl J Med* 1983, **308**, 203–206.
8. Hantel A, Dick JD, Karp JE. Listeriosis in the setting of malignant disease. Changing issues in an unusual infection. *Cancer* 1989, **64**, 516–520.
9. Khardori N, Berkey P, Hayat S, Rosenbaum B, Bodey GP. Spectrum and outcome of microbiologically documented *Listeria monocytogenes* infections in cancer patients. *Cancer* 1989, **64**, 1968–1970.
10. Viscoli C, Van der Auwera P, Meunier F. Gram-positive infections in granulocytopenic patients: an important issue? *J Antimicrob Chemother* 1989, **21**, 149–156.
11. Armstrong D, Polsky B. Central nervous system infections in the compromised host. In: Rubin LH, Young LS. *Clinical Approach to Infections in the Compromised Host*, 2nd ed. New York, Plenum Medical, 1988, 165–191.
12. Oren-Harris J, Marquez J, Swerdloff MA, Magana IA. *Listeria* brain abscess in the acquired immunodeficiency syndrome. *Arch Neurol* 1989, **46**, 250.
13. Ochs J, Mulhern RK. Late effects of antileukemic treatment. *Pediat Clin North Am* 1988, **35**, 815–834.

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Postremission Chemotherapy in Adult Acute Non-lymphoblastic Leukaemia Including Intensive or Non-intensive Consolidation Therapy

Monica Giordano, Alberto Riccardi, Margherita Girino, Silvia Brugnatelli, Paolo Scivetti, Renata Luoni, Rosangela Invernizzi and Edoardo Ascari

From October 1983 to December 1988, 84 consecutive adult patients with acute non-lymphoblastic leukaemia (ANLL; median age = 51 yr) were uniformly treated to induce remission (CR) with intravenous vincristine and cytarabine sequentially followed by daunomycin and infusion cytarabine. From October 1983 to December 1985 consolidation was non-intensive (2 courses with the same drugs used for induction) (protocol ANLL83: 27 patients, median age = 45). From January 1986 to December 1988 consolidation was intensive (4 courses of vincristine and cytarabine sequentially followed by etoposide plus thioguanine or amsacrine) (protocol ANLL86: 57 patients, median age = 57). Excluding early deaths, the CR rate was 71.6%. Median CR, responsive patient survival and overall survival were 11.1, 15.3 and 8.5 mo, respectively. For protocol ANLL83 and ANLL86, median CR was 8.7 and 13.2 mo ($P < 0.05$) and median survival was 13.1 and 16.9 mo ($P < 0.05$) for responders and 8.0 and 9.2 mo (P not significant) for all patients. Intensive consolidation including drugs not previously used for induction seems to prolong CR duration and responder survival in adult ANLL.
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INTRODUCTION

A WAY OF administering postinduction therapy to adult acute non-lymphoblastic leukaemia (ANLL) patients after remission (CR) is consolidation therapy, where short intensive cyclic therapy is given for 3–6 months and may be followed or not by maintenance [1]. For consolidation, options can be made for both the choice of drugs administered (only those employed for induction can be used or new cytostatics may be added) and their dosage [1]. The prerequisites which define a consolidation course as being intensive or non-intensive are not clear-cut but, as a guideline, an intensive course should produce, in a CR patient, heavy cytopenia, i.e white blood cell (WBC) count of less than 1.0×10^9/l and a platelet count of less than 50×10^9/l about 2 weeks following its completion [2].