Pediatr Radiol (1993) 23: 177–180

Pediatric Radiology

CT of invasive pulmonary aspergillosis in children with cancer

A. Taccone[1], M. Occhi[1], A. Garaventa[2], L. Manfredini[2], C. Viscoli[3]

[1] Department of Radiology, Gaslini Children's Hospital, Genoa, Italy
[2] Division of Hematology and Oncology, Gaslini Children's Hospital, Genoa, Italy
[3] Department of Infectious Diseases, Gaslini Children's Hospital, Genoa, Italy

Received: 5 November 1992/Accepted: 20 December 1992

Abstract. In treating cases of malignancy, the use of chemotherapy carries a high risk of lower respiratory tract infections, especially fungal pneumonopathy. This complication is a major cause of mortality and is often difficult to diagnose because of non-specific clinical or radiological changes, but the early recognition of invasive fungal disease is imperative. CT is an important non-invasive method for the detection and evaluation of opportunistic fungal infections. In these patients an improved survival rate can be achieved when early detection by CT leads to the prompt institution of high-dose antifungal therapy. We illustrate the spectrum of CT findings of invasive pulmonary aspergillosis encountered in children with cancer. These patients had previously been treated with high-dose chemotherapy with or without bone marrow rescue, and underwent radiological examinations because of clinical evidence of pneumonopathy. Representative cases demonstrate the clinical applications of CT in the evaluation and management of invasive fungal disease.

Infection and graft-versus-host disease are major causes of mortality in patients undergoing bone marrow transplantation (BMT) or conventional chemotherapy for childhood malignancies [1, 2]. Most of these patients develop fever, neutropenia and other clinical signs of infection and often there is clinical and radiological evidence of pneumonia as a consequence of chemotherapy-induced immunosuppression [1–3].

Fungi are a common cause of opportunistic pulmonary infections, and the clinical and radiological manifestations of fungal pneumonia in immunocompromised patients have been described by several authors [4–6]. Their incidence ranges from 20% to 50% and the mortality rate is approximately 80%. In most cases fungal pneumonias occur in patients with prolonged granulocytopenia and/or those who have received antibiotic therapy for bacterial infections. *Aspergillus* spp. and *Candida albicans* are the most common infecting agents.

We reviewed retrospectively the CT images of febrile immunocompromised patients with documented invasive pulmonary Aspergillosis (IPA), to evaluate the usefulness of CT in the clinical assessment of infectious complications.

Materials and methods

Twenty patients with malignancy and pulmonary fungal infection were studied between June 1987 and November 1991. Fourteen (70%) of these developed IPA (Table 1). There were 8 males and 6 females, ranging in age from 7 to 18 years (mean 11 years 3 months).

Seven underwent bone marrow transplantation (BMT), performed for acute lymphoblastic leukemia (ALL, 5), or non-lymphoblastic acute leukemia (nLAL, 2). Seven patients were treated with high-dose chemotherapy, without bone marrow rescue, for ALL (2), Ewing's sarcoma (ES, 2), nLAL (2) or acute undifferentiated leukemia (AUL, 1).

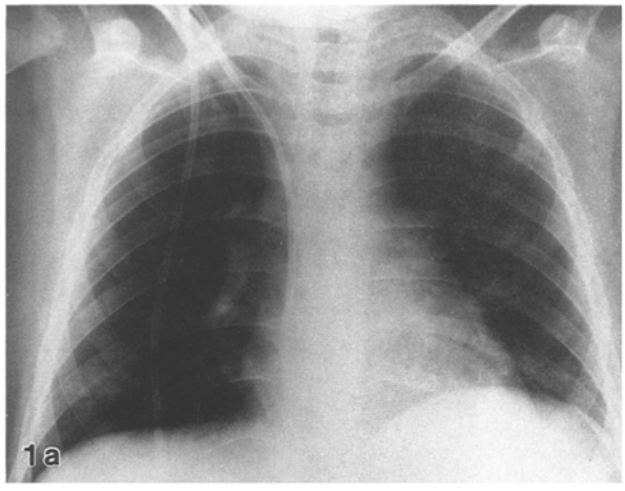
Three patients had fever and 11 had fever associated with cough (10) and/or dyspnea (3) and chest pain (4). The diagnosis of IPA was based on either histological findings (4 cases: 1 biopsy, 1 surgical drainage, 1 autopsy, 1 broncho-alveolar lavage) or culture results (10 cases: 4 sputum, 2 blood and 4 nose culture) (Table 1). All cases were associated with probative CT findings. Contiguous CT scans from the thoracic inlet to the diaphragm were obtained using a 10-mm section thickness, 3-s scanning time, 120 kV and 250 mAs. A section thickness of 5 mm was occasionally used at the hili and at the main regions of interest.

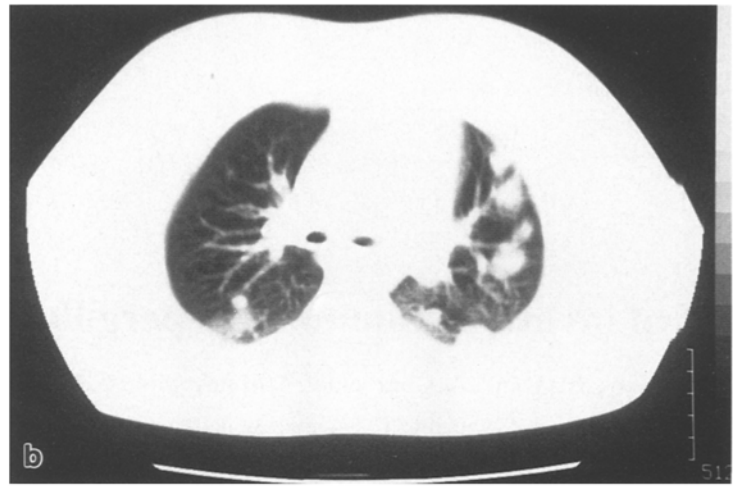
Results

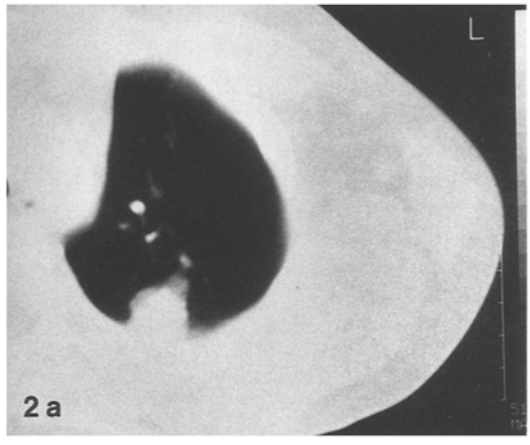
A summary of the clinical data and some of the typical CT findings in our patients is presented in Table 1. Two basic types of involvement were found: multiple nodules or fluffy masses (Fig. 1) and an infiltrate which looked like a mass lesion. An area of hyperlucency surrounding parenchymal opacities (halo sign) was found in two patients (Fig. 2).

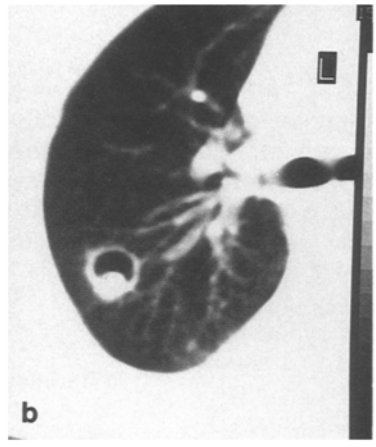
Cavitation occurred in 6 of the 14 patients. Three of the six cavities showed the air crescent sign (Figs. 2–4). In the

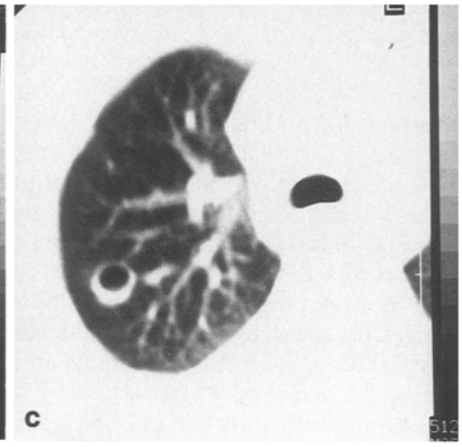
Correspondence to: A. Taccone, Servizio di Radiologia, Istituto "G. Gaslini", Largo G. Gaslini 5, I-16148 Genoa, Italy

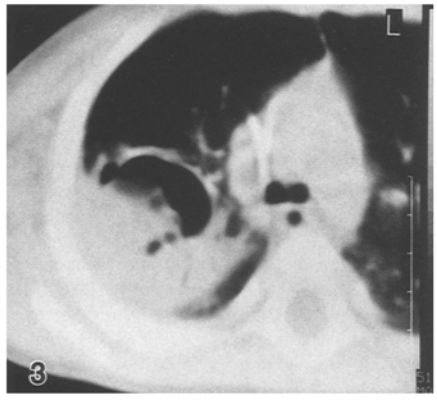

1a

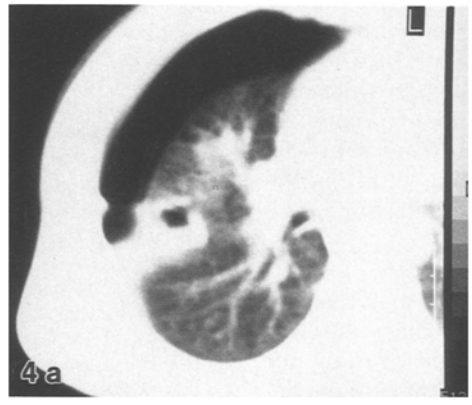

b

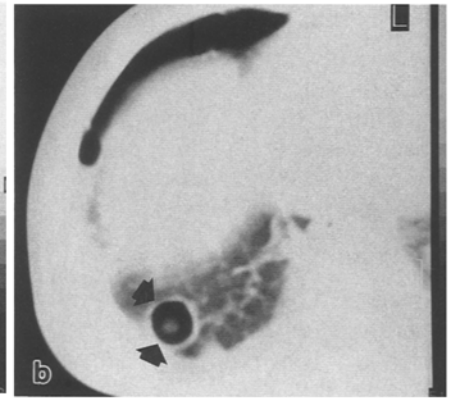

L
2a

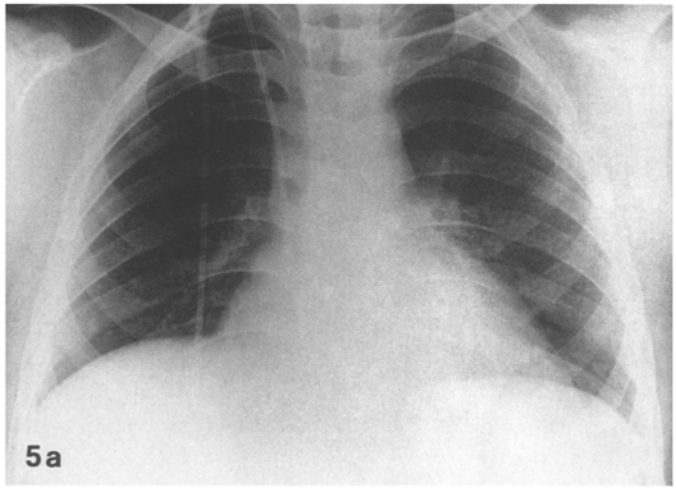

L
b


c


L
3


L
4a


L
b


5a

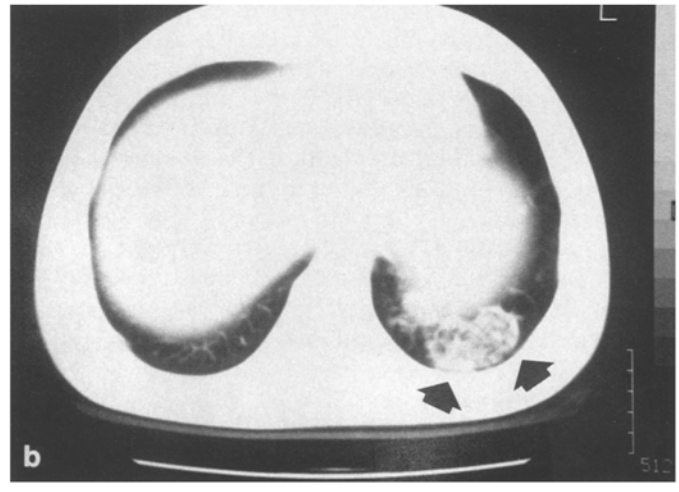

L
b

Table 1. Invasive pulmonary aspergillosis in children with cancer: clinical and CT findings

Case	Patient			Source of data	Days after therapy	WBC (mm^{-3})	Cough	Fever	Dyspnea	Chest pain	CT appearance
	Age	Sex	Diagnosis								
1	12	F	nLAL	Nose culture	15	< 500	–	+	–	–	Fluffy nodules
2	7	F	ALL	Sputum	30	< 500	–	+	–	–	Nodule with cavity
3	11	M	nLAL	Nose culture	36	< 100	+	+	–	–	Fluffy nodules
4	15	M	nLAL	Sputum	15	< 500	–	+	–	–	Hilar mass with hazy margin
5	11	F	AUL	Nose culture	30	13000	+	+	+	+	Nodules with cavity; pneumothorax
6	12	M	ALL	Nose culture	11	< 500	+	+	–	–	Fluffy nodules
7	13	M	ALL	Surgical finding	18	800	+	–	–	–	Mass with air crescent; nodule with cavitation
8	12	M	ALL	BAL	11	< 100	+	+	–	+	Nodules with sharp margin
9	15	M	ALL	Sputum	14	< 500	+	+	–	+	Mass with halo
10	8	F	nLAL	Sputum	30	500	+	+	–	–	Mass with air crescent
11	13	M	ES	Serum	10	< 100	+	+	+	+	Mass-lesion-like infiltrate; nodule with air crescent; nodule with cavity
12	10	M	ALL	Biopsy	25	< 500	+	+	–	–	Segmental pneumonia with air bronchograms
13	7	F	ES	Autopsy	15	< 500	+	+	+	–	Mass with halo
14	11	F	ALL	Serum	21	500	+	+	–	–	Mass with air crescent; pleural effusion

WBC, white blood cells; nLAL, non-lymphoblastic acute leukemia; ALL, acute lymphoblastic leukemia; AUL, acute undifferentiated leukemia; ES, Ewing's sarcoma; BAL, bronchoalveolar lavage

other three patients small cavities resembling septic emboli were noted. In 8 of the 14 patients no cavities developed during the period of observation. Pleural effusions were noted in one case. In one case pneumothorax resulting from pleural perforation of a cavitating lesion was also observed (Fig. 4).

In these cases the chest radiographs were considered normal or believed to show non-specific infiltrates prior to CT examination (Figs. 1, 5).

Fig. 1 a, b. Case 1. **a** Lesions are not clearly seen on chest radiographs. **b** CT scan demonstrates multiple small fluffy masses caused by septic emboli

Fig. 2 a–c. Case 11. **a** CT scan shows an infiltrate like a mass lesion with halo sign or surrounding zone of low attenuation in the left upper lobe. **b** Two weeks later, after white blood cell recovery, the CT scan shows a smaller spherical nodule in the right lung with an air crescent. **c** Residual cavitating lesion 1 month later. The mass-lesion-like infiltrate in the left upper lobe remained stable

Fig. 3. Case 14. Large infiltrate like a mass lesion in the right lung, air crescent cavitation within the mass, and extension into the pleural space

Fig. 4 a, b. Case 5. **a** Cavitating lesion with pneumothorax resulting from pleural perforation. **b** In the lower scan, a spherical nodule with target cavitation is seen. There is adjacent smaller consolidation *(arrows)*

Fig. 5 a, b. Case 4. **a** Normal chest radiograph. **b** Inhomogeneous infiltrate like a mass lesion in the right lower lobe *(arrows)*

Mixed fungal infections were present in three patients. The time between BMT and diagnosis, and the correlation between white blood cell count and the CT features, were evaluated (Table 1).

Discussion

Pulmonary fungal infections are an extremely serious complication in immunocompromised patients. This problem is frequently encountered in aplastic patients with continued fever in spite of antibiotics and chest films that are unchanged or show a questionable new infiltrate [6]. An early recognition of invasive fungal disease in such patients is essential and may improve survival. Definitive diagnosis frequently requires aggressive, invasive biopsy procedures that often cannot be performed because of marked thrombocytopenia or compromised respiratory status [5]. CT provides a more characteristic and recognizable pattern of parenchymal involvement of disease than plain radiography, especially in cases of IPA. CT scanning can detect multiple lesions, identify smaller nodules which are not appreciated on chest films, and reveal early target lesions or cavitation [5, 7].

The pathological features and natural history of IPA during the course of infection have been studied extensively [8–10]. Correlation of autopsy findings with premortem chest radiographs reveals that target lesion corre-

late with the early nodules or small fluffy infiltrates seen on plain films of patients with IPA [8].

It is speculative whether the pathologically identified peripheral ring of hemorrhage or hemorrhagic infarction surrounding target lesions corresponds to the halo zone of low attenuation surrounding IPA lesions seen in early CT scans. Since the resorption of sequestrum is required, it is not surprising that air crescent formation is a relatively late radiographic findings coinciding with the recovery of the white cells 2–3 weeks after treatment.

CT may also have a role in proven cases of infected emboli when a clinical response to appropriate therapy is slow or not forthcoming. In these cases, CT can be used to evaluate and follow the extent of disease and to detect potential complications such as lung abscess formation and extension into the pleural space [7]. Clearly, though, not every immunocompromised patient with septicemia needs a CT examination to detect the presence of significant lung infection; the conventional chest radiograph remains the screening test of choice.

The authors conclude that chest CT scanning has become an important method for evaluating the immunocompromised patient at high risk for opportunistic fungal infection. In the proper clinical setting, characteristic CT features of IPA can suggest the correct diagnosis, making a major contribution to better management of patients.

References

1. Brown AE (1990) Overview of fungal infection in cancer patients. Semin Oncol 17 (3): 2–5
2. Pizzo PA, Walsh TJ (1990) Fungal infections in the pediatric cancer patient. Semin Oncol 17 (3): 6–9
3. Anaissie E (1992) Opportunistic mycoses in the immunocompromised host: experience at a cancer centre and review. Clin Infect Dis 14 (1): S43–53
4. Mori M, Galvin JR, Barloon TJ, Gingrich RD, Stanford W (1991) Fungal pulmonary infections after bone marrow transplantation: evaluation with radiography and CT. Radiology 178: 721–726
5. Kuhlman JE, Fishman EK, Siegelman SS (1985) Invasive pulmonary aspergillosis in acute leukemia: characteristic findings on CT: the CT halo sign and the role of CT in early diagnosis. Radiology 157: 611–614
6. Kuhlman JE, Fishman EK, Burch PA, Karp JE, Zerhouni EA, Siegelman SS (1988) CT of invasive pulmonary aspergillosis. AJR 150: 1015–1020
7. Kuhlman JE, Fishman EK, Corey T (1990) Pulmonary septic emboli: diagnosis with CT. Radiology 174: 211–213
8. Herbert PA, Bayer AS (1980) Invasive pulmonary aspergillosis. Chest 80: 220–225
9. Orr DP, Myerowitz RL, Dubois PJ (1978) Pathoradiologic correlation of invasive pulmonary aspergillosis in the compromised host. Cancer 41: 2028–2039
10. Gefter WB, Albelda SM, Talbot GH, Stanton LG, Cassileth PA, Miller WT (1985) Invasive pulmonary aspergillosis and acute leukemia. Radiology 157: 605–610

Literature in pediatric radiology

Continued from p. 168

Clinical Pediatrics *(Philadelphia)*

Severe pulmonary hypertension without significant pulmonary parenchymal disease in a pediatric patient with acquired immunodeficiency syndrome. Rhodes, J. et al. (Div. of Ped. Cardiol., Floating Hosp. for Infants and Children, 750 Washington St., Box 171, Boston, MA 02111 (617) 956-5030, USA) 31: 629 (1992)

Investigative Radiology *(Philadelphia)*

Children with acquired immune deficiency syndrome. Wood, B.P. (Dept. of Rad., MS # 81, Children's Hosp., PO Box 54700, Los Angeles, CA, USA) 27: 964 (1992)

Journal of Bone and Joint Surgery. American Volume *(Boston)*

Multiple fractures in a child: the osteoporosis pseudoglioma syndrome. McDowell, C.L. et al. (1126-B Prifessional Dr., Williamsburg, VA 23185, USA) 74-A: 1247 (1992)

Tibia vara. Martinez, A.G. et al. (Weinstein, S.L., Dept. of Orthop., Univ. Hosp. and Clinics, 1012 Carver Pavilion, Iowa City, IA 52242, USA) 74-A: 1250 (1992)

Journal of Computer Assisted Tomography *(New York)*

The benign fibroosseous lesion: its association with paranasal sinus mucoceles and its MR appearance. Som, P.M. Lidov, M. (Dept. of Rad., Box 1234, Mount Sinai Med. Center, One Gustave L. Levy Place, New York, NY 10029-6574, USA) 16: 871 (1992)

Airway obstruction by right aortic arch with right-sided patent ductus arteriosus: demonstration by MRI. Friese, K.K. et al. (Higgins, C.B., Dept. of Rad., Box 0628, Univ., San Francisco, CA 94143, USA) 16: 888 (1992)

CT and MRI of arachnoid cyst with complicating intracystic and subdural haemorrhage. Eustace, S. et al. (Inst. of Rad. Sciences, Mater Misericordiae Hosp., Eccles St., Dublin 7, Ireland) 16: 995 (1992)

Journal of Neurosurgery *(Baltimore)*

Bilateral morning glory syndrome associated with sphenoid encephalocele. Itakura, T. et al. (Dept. of Neurol. Surg., Med. College, 7-27 Wakayama City, Japan) 77: 949 (1992)

Neurosurgical treatment of hypothalamic hamartomas causing precocious puberty. Albright, A.L., Lee, P.A. (Dept. of Neurosurg., Children's Hosp., 3705 Fifth Av., Pittsburgh, PA 15213, USA) 78: 77 (1993)

Journal of Nuclear Medicine *(New York)*

Brain SPECT in neonates following extracorporeal memprane oxygenation: evaluation of technique and preliminary results. Park, C.H. et al. (Div. of Nucl. Med., Dept. of Radiation Oncol. & Nucl. Med., Thomas Jefferson Univ. Hosp., 11th & Walnut St., Philadelphia, PA 19 107, USA) 33: 1943 (1992)

PET scanning of iodine-124-3F9 as an approach to tumor dosimetry during treatment planning for radioimmunotherapy in a child with neuroblastoma. Larson, S.M. et al. (Memorial Sloan-Kettering Cancer Center, 1275 York Av., New York, NY 10021, USA) 33: 2020 (1992)

Tracking the natural history of infantile hydronephrosis with diuretic renography. O'Tuama, L.A. et al. (Div. of Nucl. Med., Children's Hosp., Harvard Med. School, Boston, MA) 33: 2098 (1992)

Journal of Pediatrics *(St. Louis)*

Soft tissue swelling and acute skull fractures. Kleinman, P.K., Spevak, M.R. (Dept. of Rad., Univ. Med. Center, 55 Lake Av., North, Worcester, MA 01655, USA) 121: 737 (1992)

Symptomatic hyperammonemia caused by a congenital portosystemic shunt. Kitagawa, S. et al. (Div. of Gastroenterology and Nutrition, Univ. Med. School, 6431 Fannin St., No. 3142, Houston, TX 77030, USA) 121: 917 (1992)

Cerebral artery aneurysms in children infected with human immunodeficiency virus. Husson, R.N. et al. (Pizzo, P.A., Ped. Branch, Nat. Cancer Inst., Bldg. 10, Room 13N240, 9000 Rockville Pike, Bethesda, MD 20892, USA) 121: 927 (1992)

Idiopathic arterial calcification of infancy: prenatal and postnatal effects of therapy in an infant. Bellah, R.D. et al. (Dept. of Rad., The Children's Hosp., 34th St. and Civic Center Blvd., Philadelphia, PA 19104, USA) 121: 930 (1992)

continued on p. 188