REVERSED HALO SIGN; THE CLINICAL MEANINGS AND THE FORMATION PROCESSES DURING NEUTROPENIA, A COHORT STUDY

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Objective:

During neutropenia, reversed halo sign (RHS) strongly suggests invasive pulmonary mold infection (IPMI), especially invasive pulmonary mucormycosis (IPM). However, due to its rarity (≤%4 of IPMI), there is only one paper referring its clinical meanings; 8 patients in M.D. Anderson cancer centre were retrospectively reviewed. And thus, much remains unknown. For the first time, we analyzed patients with RHS in a cohort study.

Methods:

Every patient with RHS was selected from a cohort study; the study was designed to detect earliest chest CT (CCT) signs of invasive pulmonary aspergillosis (IPA) and observe the progression process with a combination of routine serum galactomannan (GM) and routine CCT. From 1/4/2011 until 9/12/2013, all 221 patients with acute myelogenous leukemia (AML) and acute lymphocytic leukemia (ALL) receiving induction chemotherapy in our hospital were enrolled. Routine GM was conducted twice a week. Routine CCT was performed at the time of admission and weekly. Additional CCT was also conducted at the onset of pyrexia and for persisting pyrexia. All images were analyzed by senior radiologists.

Results:

According to EORTC/MSG criteria, 60 patients (27.1%) were diagnosed with IPMI; 59 (26.6%) IPA (all probable), 3 (1.3%) IPM (1 probable, 2 proven) with no other IPMIs. RHS was detected in 7 patients. The incidence of RHS were much higher than previous reports; 3.16% (7/221) overall and 11.6% (7/60) IPMI patients. Table1 shows the unique characteristics; higher age, higher male to female ratio (85.7%), higher IPA morbidity (85.7%) and complete incidence in IPM (3/3). Furthermore, with our unique CCT strategy, we could detect the earliest recorded CCT abnormalities suggesting IPMI; the median day was 7 (2-12). For 6 patients, RHS was not the earliest sign of IPMI; the median day of RHS appearance was 17 (6-22). Most significantly for the first time, we could detect whole RHS formation process including pre RHS signs in 5 patients. There are two separate RHS formation processes, which we termed, radial thickening process (RTP) and centripetal attenuating process (CAP). RTP begins from ground glass opacity (GGO) and then successive consolidation around GGO and radial expansion is observed. In contrast, CAP begins from consolidation and then successive centripetal attenuation resulting in RHS.

Conclusions:

By our original methods, we could analyze patient characteristics much more precisely and detect the formation process from a far earlier stage. This study is limited in number, however our results strongly indicate the difficulty of early and/or precise detection of RHS by chance and thus the importance of successive CTs; RHS detection is momentous for IPM.

Table 1

Patient	Sex	Age	Primary diagnosis	Day of IPMI diagnosis	Day of RHS diagnosis	Inpatient days	Number of CCTs	IPMI	Pattern	Status
1	M	83	AML	2	17	36	5	IPA	CAP	Alive
2	M	73	AML	2	19	36	6	IPA	-	Alive
3	M	70	AML	5	5	77	13	IPA	-	Alive
4	M	71	ALL	9	22	49	7	IPA	RTP	Alive
5	M	83	AML	11	14	67	12	IPM	RTP	Dead
6	M	80	AML	12	15	37	6	IPM, IPA	RTP	Dead
7	F	81	AML	2	6	25	6	IPM, IPA	RTP	Dead