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FULL PAPER

Non-osseous incidental findings in low-dose whole-body CT in patients with multiple myeloma

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Objective: The purpose of this study was to identify the frequency and grading of non-osseous incidental findings (NOIF) in non-contrast whole-body low-dose CT (LDCT) in patients with multiple myeloma.

Methods: In the time period from 2010 to 2013, 93 patients with multiple myeloma were staged by non-contrast whole-body LDCT at our radiological department. LDCT images were analysed retrospectively for NOIF, which also included unsuspected extramedullary manifestation of multiple myeloma. All NOIF were classified as major or clinically significant, moderate or possibly clinically significant and minor or not clinically significant. Medical records were analysed regarding further investigation and follow-up of the identified NOIF.

Results: In the 93 patients, 295 NOIF were identified (on average, 3.2 NOIF per patient). Most of the NOIF (52.4%) were not clinically significant, 25.8% of the NOIF were possibly clinically significant and 21.8% of the NOIF were

clinically significant. Clinically significant NOIF were investigated further by CT after intravenous administration of contrast medium and/or by ultrasound or MRI. In 34 of these cases, extramedullary relapse of myeloma, occult carcinoma or infectious/septic incidental findings were diagnosed (11.5% of all NOIF). In the remaining 10.3% of the NOIF classified as clinically significant, various benign lesions were diagnosed.

Conclusion: LDCT detected various non-osseous lesions in patients with multiple myeloma. 36.6% of the patients had clinically significant NOIF. Therefore, LDCT examinations in patients with multiple myeloma should be evaluated carefully for the presence of NOIF.

Advances in knowledge: LDCT identified several NOIF. A total of 36.6% of patients with multiple myeloma had clinically significant NOIF. Radiologists should analyse LDCT examinations in patients with multiple myeloma not only for bone lesions, but also for lesions in other organs.

CT is used for screening or staging in several malignancies.^{1–8} As reported previously, the staging CT examination also provides additional information regarding the general health status of the patient or so-called incidental findings (IF).^{1,3,6,7} Several IF on CT examinations were described in the literature.^{1–6} According to previous reports, IF can be classified into five different categories: Group “0”, limited examination, that is, evaluation of IF are severely limited; Group “1”, normal findings or anatomic variant; Group “2”, clinically unimportant findings, such as liver or kidney cysts; Group “3”, likely unimportant findings; and Group “4”, potentially important findings, such as solid renal masses or lymphadenopathy.⁵ In another publication, a three-part classification of IF according to their clinical importance was proposed, namely major, moderate and minor IF.¹

Most of the IF are clinically non-significant, such as colonic diverticula or simple cysts.^{1–7} However, serious IF, such

as aortic aneurysm or dissection, thrombosis, pulmonary embolism and second primary tumours, can also occur,^{1,3,6,7} and some of them may be not visible on low-dose CT (LDCT).

Most reports regarding IF are based on contrast-enhanced CT.^{1,7,9–11} There are only a few reports regarding IF in LDCT.¹² They described IF in screening programmes for lung cancer and based the findings on thoracic LDCT only.¹² In addition, non-contrast LDCT has been established for staging of bone lesions in multiple myeloma.^{13–16} However, radiologists should analyse LDCT examinations not only for bone lesions but also for lesions in other organs, which may include extramedullary manifestation of multiple myeloma as well as unrelated IF.

Although IF in multiple myeloma have also been described previously,¹⁴ to the best of our knowledge, there exists no

Table 1. Localization of non-osseous incidental findings (IF) detected in low-dose CT

Localization	<i>n</i> (%)
Cardiovascular IF	86 (29.2)
Gastrointestinal IF	72 (24.4)
Pulmonary IF	70 (23.7)
Renal IF	27 (9.1)
IF in the thyroid gland	23 (7.8)
Genital IF	7 (2.4)
Breast IF	6 (2.0)
IF in CNS	2 (0.7)
Skeletal muscle IF	2 (0.7)
Total	295 (100)

CNS, central nervous system.

analysis focused on frequency and distribution of non-osseous IF (NOIF) on whole-body LDCT. Therefore, the purpose of this study was to identify the frequency and grading of NOIF in non-contrast whole-body LDCT in patients with multiple myeloma.

METHODS AND MATERIALS

This retrospective study has been approved by the institutional ethics committee of the Martin-Luther-University Halle-Wittenberg, Halle, Germany.

For the 4-year time period from 2010 to 2013, we identified 93 patients in the database of the radiological department of the university hospital (Martin-Luther-University Halle-Wittenberg, Halle, Germany) who underwent staging of multiple myeloma by non-contrast whole-body LDCT, which has been used as the standard procedure for staging these patients at our institution. According to the clinical records, the diagnosis of multiple myeloma was established in all cases by bone marrow biopsy. None of the patients had a known history of extramedullary manifestation of myeloma. There were 41 females and 52 males with a median age of 64 years, ranging from 32 to 87 years.

LDCT was performed by using a multislice CT scanner (Somatom® Sensation 64; Siemens Healthcare, Erlangen, Germany). The imaging parameters were 120 kVp, 36 mAs, collimation of 64×0.6 mm and pitch of 0.8. The scan length included the following body regions: head, neck, chest, abdomen/pelvis, upper limb and the proximal half of the lower limb. The acquired images were reconstructed in transversal, sagittal and coronal views with a slice thickness of 3.0 mm. All images were reconstructed with a manufacturer-presented kernel, using a standard

Table 2. Identified non-osseous incidental findings (NOIF) in our patients

Clinically relevant NOIF	<i>n</i> (%)	Possibly clinically relevant NOIF	<i>n</i> (%)	Not clinically relevant NOIF	<i>n</i> (%)
Solid hepatic lesions	6 (2.0)	Pulmonary fibrosis	25 (8.5)	Liver cysts	15 (5.1)
Pleural mass	1 (0.3)	Emphysema	5 (1.7)	Liver calcifications	2 (0.7)
Muscle enlargement	1 (0.3)	Ascites	2 (0.7)	Kidney cysts	22 (7.5)
Solid renal mass	1 (0.3)	Cardiomegaly	43 (14.6)	Renal parenchymal reduction	4 (1.4)
Abdominal lymph node swelling	1 (0.3)	Pulmonary cement embolism	1 (0.3)	Colonic diverticula	12 (4.1)
Pneumonia	11 (3.7)			Hiatal hernia	7 (2.4)
Pleural effusion	16 (5.4)			Splenic cysts	2 (0.7)
Pulmonary nodules	2 (0.7)			Pancreatic calcifications	2 (0.7)
Aortic aneurysm	1 (0.3)			Bronchiectasis	4 (1.4)
Thyroid mass/enlargement	23 (7.8)			Gallstone	11 (3.7)
Prostatic enlargement	2 (0.7)			Uterine myoma	2 (0.7)
				Ovarian cyst	2 (0.7)
				Scrotal hydrocoele	1 (0.3)
				Pulmonary calcifications	5 (1.7)
				Vasosclerosis	42 (14.2)
				Meningioma	2 (0.7)
				Mesenterial calcifications	12 (4.1)
				Breast calcifications	6 (2.0)
				Muscle lipoma	1 (0.3)
Total	65 (22.0)	Total	76 (25.8)	Total	154 (52.2)

Figure 1. Extramedullary manifestation in myeloma incidentally detected on low-dose CT (LDCT). (a) LDCT documenting a large lesion (arrow) at the liver. (b, c) On CT after intravenous administration of contrast medium, the mass (arrows) showed an inhomogeneous enhancement. Histological examination revealed an extramedullary manifestation of multiple myeloma.

reconstruction algorithm (kernel 60 “bone”; Siemens Healthcare). For the evaluation of bone structures a window of 450/1500 (center/width), for the evaluation of the lungs a window of -250/1600 and for the evaluation of soft tissue a window of 56/342 was used. Because of the retrospective nature of our study, no reconstructions with specific kernels for soft-tissue or lung images were available for the LDCT examinations.

LDCT images were analysed retrospectively by two radiologists (AS and DS) with 11 and 4 years’ general radiological experience and 8 and 2 years’ experience of whole-body CT evaluation, respectively. In this study, non-osseous findings were only analysed. Osseous IF such as typical degenerative

osteoarthritis were excluded from the analysis. For the purpose of our study, we counted extramedullary manifestation of myeloma in patients with unsuspected extramedullary involvement as “IF” on non-contrast LDCT, which constitutes an examination specifically designed for the assessment of bone lesions of myeloma.

All images were analysed in digital form using a picture archiving and communication system (PACS) workstation (Centricity™ PACS; GE Medical Systems, Milwaukee, WI).

All NOIF were classified according to Lumbreras et al¹ as major or clinically significant, moderate or possibly clinically significant

Figure 2. Extramedullary hepatic manifestation in myeloma incidentally detected on low-dose CT (LDCT). (a) LDCT documenting a hypodense lesion (arrow) in the liver. (b) On MRI (T_1 weighted image with fat saturation) after intravenous administration of contrast medium, the lesion (arrow) showed an inhomogeneous enhancement. Histological examination revealed an extramedullary manifestation of multiple myeloma.

and minor or not clinically significant. Consensus was obtained between the two radiologists for final classification of NOIF.

Furthermore, medical records were analysed regarding further investigation and follow-up of the identified NOIF.

RESULTS

In the 93 patients, 295 NOIF were identified (3.2 IF per patient). They were located in the chest ($n = 161$; 54.6%), abdomen/pelvis ($n = 107$; 36.2%), head/neck ($n = 25$; 8.5%) and extremities ($n = 2$; 0.7%). The most frequent were cardiovascular NOIF (29.2%), followed by gastrointestinal (25.4%) and pulmonary NOIF (23.4%) (Table 1).

Most of the NOIF (52.2%) were not clinically significant (Table 2), 25.8% were possibly clinically significant and 22.0% of the NOIF were clinically significant. All findings classified as clinically significant NOIF had been investigated further by CT with intravenous administration of contrast medium and/or by ultrasound (in all cases, further investigations were available in our database). Extramedullary relapse of plasmacytoma was suspected in five cases (5.4% of all patients and 1.7% of all NOIF) and confirmed in all these cases by CT- or ultrasound-guided biopsy. There were two cases with solid hepatic lesions (Figures 1 and 2), one case with intra-abdominal lymphadenopathy (Figure 3), one patient with infiltration of the forearm musculature and one case with a pleural mass.

In the cases with pulmonary nodules, no malignancy was diagnosed (one patient underwent thoracic CT-guided biopsy; in the other case, the pulmonary lesion remained unchanged in follow-up CT investigations for 2 years).

In all cases with thyroid IF, available investigations, including thyroid ultrasound with or without biopsy, revealed several benign disorders, such as colloid nodules, multinodular goitre or adenomatous hyperplasia.

In one patient with a solid mass of the right kidney, renal cell carcinoma was diagnosed (1.1% of all patients and 0.3% of all NOIF). In the cases with prostatic enlargement, clinical work-up identified benign hyperplasia and adenoma.

Other clinically relevant NOIF were pneumonia (Figure 4) (11 cases; 11.8% of all patients and 3.7% of all NOIF); pleural effusion, with a width ranging from 10 to 70 mm (16 cases; 17.2% of all patients and 5.4% of all NOIF); and aortic aneurysm (1 patient; 1.1% of all patients and 0.3% of all NOIF) (Table 3).

In two cases with diagnosis of extramedullary manifestation of myeloma (patient with forearm muscle infiltration and patient with abdominal lymph node involvement), additional radiotherapy was performed and the identified lesions decreased in size. The patient with detected renal cell carcinoma died 3 months after the diagnosis because of sepsis. All patients with pneumonia were successfully treated with antibiotics. In the patient with aortic aneurysm, no additional investigations were performed, and the disease was stable within 2 years of follow-up.

Figure 3. Low-dose CT showing a large paravertebral mass (arrow). Histological examination after CT-guided biopsy revealed an extramedullary (lymph nodes) manifestation of multiple myeloma.

DISCUSSION

LDCT without contrast medium has lower signal-to-noise ratio and lower contrast than that of CT with intravenous administration of contrast. Therefore, it may be presumed that CT would have identified more IF than LDCT. In fact, as reported previously in patients with lymphoma, fluorine-18 fludeoxyglucose-positron emission tomography (FDG-PET)/full-dose enhanced CT detected relevant IF that were missed on PET/low-dose CT.¹⁷ Our study, however, showed that LDCT identified multiple NOIF in patients with myeloma. In detail, we detected on average 3.2 NOIF per patient. This is more than in other studies.^{2,3,8} For example,

Figure 4. Low-dose CT showing pneumonia in the right lung associated with pleural effusion (arrow). The detected findings were clinically silent.

Table 3. Frequency of extramedullary relapse of myeloma and of clinically significant non-osseous incidental findings (IF)

IF	<i>n</i>	% of all patients	% of all IF
Extramedullary relapse of myeloma	5	5.4	1.7
Pneumonia	11	11.8	3.7
Pleural effusion	16	17.2	5.4
Renal cell carcinoma	1	1.1	0.3
Aortic aneurysm	1	1.1	0.3
Total	34	36.6	11.5

Furtado et al⁸ reported, in a large series of LDCT whole-body screening examinations, a ratio of 2.8 IF per patient. Furthermore, many of the reported IF (32%) in their study were located in the spine.⁸ They included predominantly degenerative changes and several benign osseous IF, such as vertebral haemangiomas.⁸ Without osseous IF, the IF ratio per patient was 1.9 in their analysis.⁸

In previous reports, most of the IF were not clinically significant.^{1–3,8,10} For example, in the study of Paluska et al,¹⁸ who analysed IF in trauma patients, significant IF were identified only in 3.1%. In another study, clinically significant IF were detected in 8% of 1409 patients.¹² Most studies report IF from screening investigations or from patients investigated for certain acute disorders, such as pulmonary embolism or trauma.^{1,8,18} There were only a few studies that analysed IF in CT in patients with oncological diseases.^{6,7,11}

In contrast to previous reports, in our study, 36.6% of the detected NOIF were classified as clinically significant. This may be related to the fact that our patients had malignant systemic disease and were immunosuppressed. It is well known that infection is a significant cause of morbidity and of death in patients with myeloma.^{19,20} They can develop several inflammatory diseases, such as pneumonia or pleural effusion, which often remain clinically latent. In fact, because of severe cell-mediated immunity defects, manifestations of infection in patients with myeloma may be masked, rendering the diagnosis of infection difficult.^{19,20} Moreover, immunosuppressive systemic therapy of multiple myeloma also increases the infectious morbidity.¹⁹ Therefore, it is very important that radiologists check LDCT for clinically significant NOIF, such as pneumonia. Our findings regarding infectious NOIF in our patients are in accordance with those of other authors. For instance, Ippolito et al¹⁴ detected potentially

therapy-relevant pulmonary disorders, such as parenchymal consolidation or pleural effusion, in 14.5% of the patients with myeloma.

In 5.4% of our patients, we identified occult extramedullary manifestation of myeloma. This finding is not surprising. Previous reports described extramedullary relapse in myeloma ranging from 3.4% to 23.0% of the investigated cases.^{14,16,21} As described previously, patients with extramedullary manifestations of myeloma had shorter progression-free survival and overall survival.²² In addition, Zeiser et al²³ suggested that patients with extramedullary manifestations of myeloma need an individualized diagnostic and therapeutic approach. Therefore, all whole-body examinations in myeloma, including LDCT, should be checked for the presence of extramedullary relapses.

There were several reports describing the localization of IF.^{1,8,9} According to the literature, most IF were located in the abdomen and pelvic region.^{1,8} In our cases, however, most NOIF were detected in the chest. This is related to the fact that we only analysed non-osseous IF and most previously reported IF in the abdomen or pelvis were incidentally detected bone disorders.⁸ Furthermore, 29% of our patients had significant inflammatory pulmonary or pleural disease. Other commonly known thoracic NOIF were breast calcifications or thyroid gland enlargement.

In conclusion, our study shows that LDCT without intravenous administration of contrast medium detected various non-osseous lesions in patients with multiple myeloma. The ratio of NOIF per patient was 3.2. Furthermore, 36.6% of the patients had clinically significant NOIF. Therefore, LDCT examinations in patients with multiple myeloma should be evaluated carefully for the presence of NOIF.

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