21. Katz JN, Lipson SJ, Lew RA, et al. Lumbar laminectomy alone or with instrumented or noninstrumented arthrodesis in degenerative lumbar spinal stenosis. Patient selection, costs, and surgical outcomes. *Spine* 1997;22: 1123–31.
22. Fischgrund JS, Mackay M, Herkowitz HN, et al. 1997 Volvo Award winner in clinical studies. Degenerative lumbar spondylolisthesis with spinal stenosis: a prospective, randomized study comparing decompressive laminectomy and arthrodesis with and without spinal instrumentation. *Spine* 1997;22: 2807–12.
23. Carreon LY, Puno RM, Dimar JR II, et al. Perioperative complications of posterior lumbar decompression and arthrodesis in older adults. *J Bone Joint Surg Am* 2003;85:2089–92.
24. Deyo RA, Ciol MA, Cherkin DC, et al. Lumbar spinal fusion. A cohort study of complications, reoperations, and resource use in the Medicare population. *Spine* 1993;18:1463–70.
25. Deyo RA, Cherkin DC, Loeser JD, et al. Morbidity and mortality in association with operations on the lumbar spine. The influence of age, diagnosis, and procedure. *J Bone Joint Surg Am* 1992;74:536–43.
26. Ragab AA, Fye MA, Bohlman HH. Surgery of the lumbar spine for spinal stenosis in 118 patients 70 years of age or older. *Spine* 2003;28:348–53.
27. Thome C, Zevgaridis D, Leheta O, et al. Outcome after less-invasive decompression of lumbar spinal stenosis: a randomized comparison of unilateral laminotomy, bilateral laminotomy, and laminectomy. *J Neurosurg Spine* 2005;3:129–41.
28. Oertel MF, Ryang YM, Korinth MC, et al. Long-term results of microsurgical treatment of lumbar spinal stenosis by unilateral laminotomy for bilateral decompression. *Neurosurgery* 2006;59:1264–9; discussion 9–70.
29. Costa F, Sassi M, Cardia A, et al. Degenerative lumbar spinal stenosis: analysis of results in a series of 374 patients treated with unilateral laminotomy for bilateral microdecompression. *J Neurosurg Spine* 2007;7:579–86.
30. Cavusoglu H, Kaya RA, Turkmenoglu ON, et al. Midterm outcome after unilateral approach for bilateral decompression of lumbar spinal stenosis: 5-year prospective study. *Eur Spine J* 2007;16:2133–42.
31. Katz JN, Lipson SJ, Chang LC, et al. Seven- to 10-year outcome of decompressive surgery for degenerative lumbar spinal stenosis. *Spine* 1996;21: 92–8.
32. Atlas SJ, Keller RB, Wu YA, et al. Long-term outcomes of surgical and nonsurgical management of lumbar spinal stenosis: 8 to 10 year results from the maine lumbar spine study. *Spine* 2005;30:936–43.
33. Matsunaga S, Ijiri K, Hayashi K. Nonsurgically managed patients with degenerative spondylolisthesis: a 10- to 18-year follow-up study. *J Neurosurg* 2000;93:194–8.
34. Yoshida M, Minamide A, Maio K. The treatment strategy of lumbar spinal canal stenosis based on the natural course. *Spine Spinal Cord* 2005;18:879–85.

Arch Orthop Trauma Surg (2011) 131:59–64
DOI 10.1007/s00402-010-1102-7

ORTHOPAEDIC SURGERY

Evaluation of clinical problems associated with bone metastases from carcinoma from unknown primary sites

Manabu Hoshi · Susumu Taguchi · Keiko Hayakawa · Makoto Ieguchi · Hiroaki Nakamura

Received: 10 December 2009 / Published online: 22 April 2010

Abstract
Introduction This study focused on the evaluation of data concerning the clinical features of patients who were initially diagnosed with bone metastases of carcinoma from unknown primary sites that could not be detected, even using state of-the-art diagnostic modalities.
Method The oncologic outcome of these patients is discussed.
Patients The clinical records of seven patients who had presented with bone metastases of carcinoma from unknown primary sites were retrospectively reviewed. Clinical features, treatment and outcome were analyzed. Extraskeletal metastases were located in the lymph nodes, liver, skeletal muscle, kidney, adrenal gland, and pleura. Six cases were observed in the pelvis, three in the femur, three in the skull, two in the rib, two in the cervical spine, two in the thoracic spine, two in the lumbar spine, one in the humerus, one in the radius, one in the clavicle, one in the scapula and one in the sternum. Four patients received systemic chemotherapy including platinum.
Results At the last follow-up time of average 272 days, six patients were dead of disease and one patient was alive with disease. Although considerable progress has been made in the development of diagnostic modalities, including more recently FDG-PET, the primary tumor site cannot always be identified. Multiple bone and visceral organ metastases are often present in patients whose primary tumor was not detected.
Conclusion In the present study, it was found that systemic chemotherapy can appreciably increase the survival time of the patients with carcinoma metastases from unknown primary sites.

Keywords Unknown primary site · Bone metastasis · Treatment · Chemotherapy

M. Hoshi (✉) · S. Taguchi · K. Hayakawa · M. Ieguchi · H. Nakamura
Department of Orthopedic Surgery,
Osaka City University Graduate School of Medicine,
1-4-3 Asahi-machi, Abeno-ku, Osaka 545-8585, Japan
e-mail: hoshi@med.osaka-cu.ac.jp

Introduction

The prognosis of patients with various types of carcinoma has been gradually improved due to early diagnosis using modern imaging techniques and improved treatment protocols. Because of higher control rates of the primary tumor in recent decades, the prolonged survival of patients has significantly increased the risk of developing distant metastases. Carcinoma metastasis from unknown primary sites is frequently detected in the lymph nodes due to swelling [1] and bone is also a frequent target site. 10–15% of patients present with symptoms of occult cancer [2].

Identification of the primary site is critical in enabling a rapid start to treatment. Unfortunately, even with the recent progress in the development of variable diagnostic techniques, the primary tumor site cannot be determined always. Failure to locate the primary tumor using multimodal diagnostic approaches leads to increased treatment delays and costs. As a consequence, patients cannot undergo cancer-specific treatment and their overall prognosis is generally poor.

In the present study, the clinical features and oncological outcomes of a group of patients treated for carcinoma metastases in the bone were examined. Only patients whose primary site of carcinoma could not be detected using the latest diagnostic modalities were admitted into the study.

Patients in whom the primary location of the carcinoma could be identified were excluded.

Materials and methods

From March 1994 to 2009, seven patients with carcinoma metastases in the bone were treated and followed up. All patients were evaluated with physical examinations, various radiological evaluations and pathological investigation using biopsy. The primary site of the carcinoma in these patients could not be identified. There were three male and four female patients, with a mean age at diagnosis of 61.9 years (range 49–80 years), were followed up for a median period of 272 days (range 16–469 days). No patient was lost during follow-up. The clinical information reviewed in this study included performance status, laboratory date of tumor marker [alkaline phosphatase (ALP), lactate dehydrogenase (LDH), carcinoembryonic antigen (CEA)], anatomical site of bone metastases or extraskeletal metastases, histology and treatment modalities. Oncologic outcome at the last follow-up was also examined.

Results

The characteristics of patients with bone metastases from carcinoma originating from unknown primary sites are summarized in Table 1. At their first visit to our orthopedic department, the performance status was zero in two patients, one in two patients, two in one patient and three in two patients. Laboratory data showed elevated levels of ALP in five out of seven patients, LDH in four out of seven patients and CEA in four out of seven patients. Radiological imaging of patients, including FDG-PET, revealed that extraskeletal metastases were located in the lymph nodes in five cases (Fig. 1a), liver in two cases, skeletal muscle of the buttock in two cases (Fig. 1b, c), lower leg in two cases, kidney in one case, adrenal gland in one case and pleura in one case.

The incidence of bone metastases at different sites and the oncologic outcome of patients are summarized in Table 2. There were six cases of bone metastases in the pelvis (Fig. 1b, c), three in the femur, three in the skull, two in the ribs, two in the cervical spine, two in the thoracic spine, two in the lumbar spine, two in the humerus, one in the radius, one in the clavicle, one in the scapula and one in the sternum.

For histopathological diagnosis, six patients were biopsied. One patient underwent endoprosthetic replacement (Fig. 2a, b). Biopsy specimens and surgical specimens were identified as adenocarcinoma in three patients (Fig. 3a),

Table 1 Characteristics of patients with bone metastases from carcinoma of primary unknown site

		Number	%
Age	61.9 (mean)		
PS	0	2	28.6
	1	2	28.6
	2	1	14.3
	3	2	28.6
	4	0	
Laboratory			
ALP	Elevated	5	71.4
LDH	Elevated	4	57.1
CEA	Elevated	4	57.1
Extraskeletal metastases			
Lymph node		5	71.4
Liver		2	28.6
Kidney		1	14.3
Skeletal muscle		2	28.6
Adrenal gland		1	14.3
Pleura		1	14.3

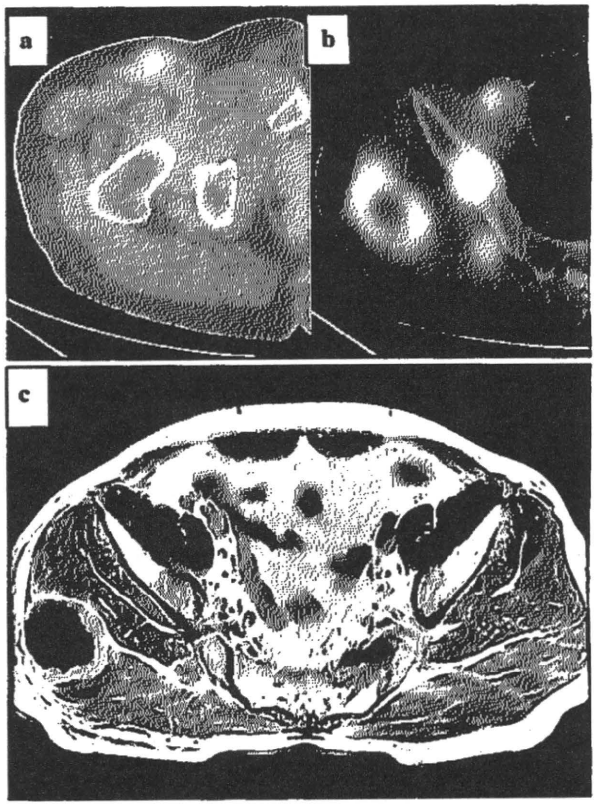


Fig. 1 Case 1. a PET/CT shows the lymph node swelling in the right inguinale. b PET/CT demonstrates the abnormal uptakes in intrapelvic lymph node, ilium, and buttocks. c Axial T2 weighted MRI shows the bone metastases of the right ilium and soft tissue metastasis in buttock

Table 2 Bone metastases and oncologic outcome in carcinoma of unknown primary sites

Case	Age	Sex	Histology	Bone metastasis	Treatment	Follow-up (days)	Prognosis
1	54	M	Adenocarcinoma	Pelvis	CT (CBDCA + PTX, TS1), RT (pelvis)	131	AWD
2	75	F	Adenocarcinoma	Skull, rib, pelvis, thoracic	RT (pelvis, thoracic)	407	DOD
3	55	F	Adenocarcinoma	Femur, pelvis, clavicle	CT (TS1), surgery (femur)	469	DOD
4	49	M	Poorly differentiated carcinoma	Femur	RT (femur)	33	DOD
5	64	F	Signet ring cell carcinoma	Skull, cervix, lumbar, thoracic, rib, pelvis	CT (CBDCA + PTX)	420	DOD
6	80	F	Poorly differentiated carcinoma	Carpal, lumbar, pelvis	RT (pelvis)	16	DOD
7	56	M	Signet ring cell carcinoma	Scapula, sternum, pelvis, femur, skull, cervix, lumbar, humerus	CT (CBDCA + PTX, TS1 + GEM)	429	DOD

RT Radiation therapy, *CT* Chemotherapy, *CBDCA* carboplatin, *PTX* paclitaxel, *GEM* gemcitabine hydrochloride, *DOD* Die of disease, *AWD* Alive with disease

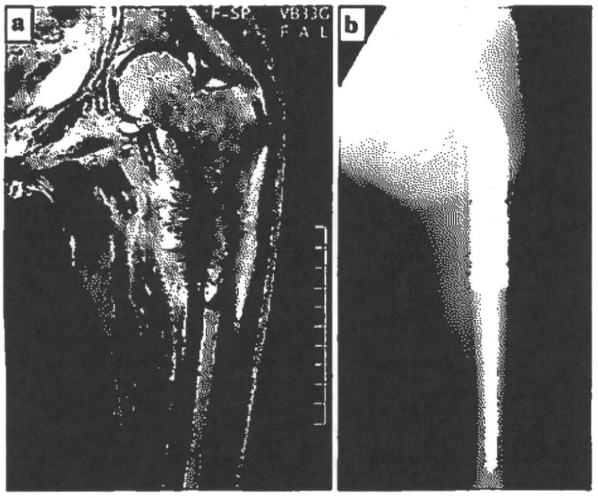


Fig. 2 Case 3. a Coronal T2 view of MRI shows the bone metastases of proximal femur. b Plain film shows the endoprosthetic replacement after tumor resection

signet ring cell carcinoma in two patients (Fig. 3b) and poorly undifferentiated carcinoma in two patients (Fig. 3c).

After diagnosis of metastatic cancer, three patients had major health problems. Two patients were in frail health, due to age (cases 2 and 6). One patient (case 4) had severe chronic renal failure. Four patients (cases 1, 3, 5 and 7) received systemic chemotherapy, and their regimen consisted of three sessions of carboplatin (CBDCA). The median survival time was 429 days for patients receiving chemotherapy, and 33 days for patients that did not undergo chemotherapy.

Three patients received local radiation therapy. One patient (case 3) showed prominent sclerotic changes after radiation therapy, indicating efficacy in treating the cancer (Fig. 4). In another patient (case 6), health suddenly deteriorated during radiation treatment and death followed after 10 days. At an average follow-up time of 272 days, six patients were DOD and only one patient was AWD. The median survival time of all patients was 420 days.

Discussion

Carcinoma metastases originating from an unknown primary site have been defined by Pavlidis et al. [3] as cancer occurring in patients who present with histologically confirmed metastatic disease, in whom a detailed medical history, complete physical examination, histopathological review of biopsy material with use of immunohistochemistry, chest radiography, CT of abdomen and pelvis failed to identify the primary site. The incidence of carcinoma metastases from unknown primary sites is approximately 3% of all malignant neoplasms. The common sites of occurrence of these metastases are the lymph nodes, liver, lung and bone [1].

Patients with bone metastases are often referred to an orthopedic oncologist by general physicians for investigation of the location of the primary tumor site. There is a need to identify the primary site as quickly as possible, in order to finalize the diagnosis and begin treatment. The incidence of carcinoma metastases in bone originating from unknown primary sites in the gastro-intestinal tract is relatively low. However, lung, prostate and breast cancer metastases occur more frequently in bone. As a consequence, endoscopy of the digestive tract is not the first choice for the primary investigation [4, 5]. This is due to the fact that it is neither time- nor cost-effective to do so and can delay treatment.

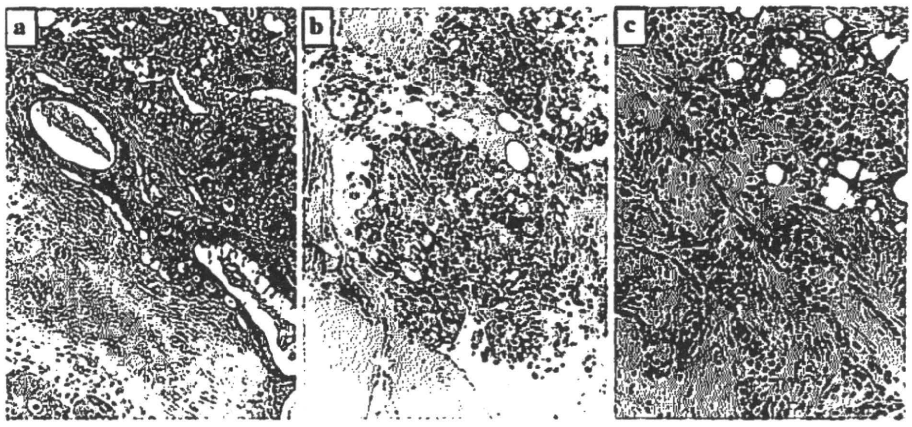


Fig. 3 a Histopathology confirms adenocarcinoma (Case 3), b signet ring cell carcinoma (Case 5), and c poorly differentiated carcinoma (Case 6) (magnification ×200)

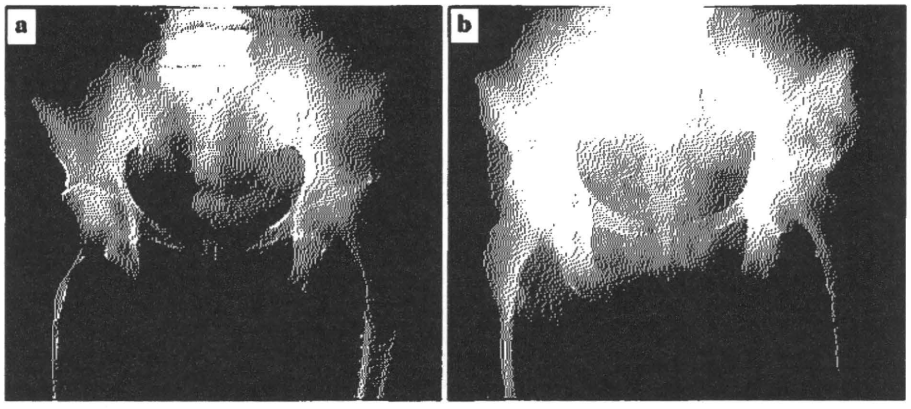


Fig. 4 Case 2. a Plain film shows the osteolytic lesion of bone metastases in the left ilium. b Plain film shows the prominent sclerotic change after local radiation therapy

If radiological imaging fails to confirm the location of the primary carcinoma site, biopsy is essential to rule out the possibility of the metastases being primary malignant bone tumors and to predict the cancer origin. In the present study, histopathological analysis revealed that the carcinoma types were adenocarcinoma in three cases, signet ring cell carcinoma in two cases and poorly differentiated carcinoma in two cases. Pavlidis et al. [3] reported that the histopathological types of carcinomas from primary unknown sites were mainly adenocarcinoma, followed by squamous cell carcinoma and poorly differentiated carcinoma. Prognosis of the patient differs depending on the type of carcinoma. Non-adenocarcinomas such as squamous cell carcinoma and neuroendocrine carcinoma have more favorable prognostic factors [1].

To investigate the location of the primary site of a carcinoma, FDG-PET imaging is being increasingly used. However, the efficacy of this approach is disputable. FDG-PET cannot be used to detect the presence of bone metastases, but can contribute in detecting extraskeletal metastases. Kole et al. [6] demonstrated that 27% of primary sites could be identified using FDG-PET after unsuccessful results using conventional diagnostic tools. In a review by Sève et al. [7] the detection rate of previously unknown primary tumor sites was found to be 41% using FDG-PET. We have been successful in using this modality for detecting primary carcinoma tumors at previously unknown sites.

At the first examination, multiple metastases, including bone and extraskeletal metastases, were already present in most cases. Systemic chemotherapy is the first choice of management for carcinoma metastases from unknown primary sites. Although systemic cancer chemotherapy should essentially be carried out according to conventional therapy protocols, an optimal standard chemotherapy regimen for carcinoma metastases from unknown primary sites has yet to be established. Multidrug regimens are generally administered as a first choice option. Previous reports [8–14] concerning representative systemic chemotherapy for carcinoma metastases from unknown primary sites, involving more than 50 patients, are summarized in Table 3.

Over the last two decades, the median survival time of patients with carcinoma metastases has been extended by approximately 7 months, due to the introduction of systemic chemotherapy using platinum. The administration of chemotherapy depends upon the general condition of the patient, but factors related to the therapeutic efficacy of chemotherapy may outweigh this consideration. More recently,

Table 3 Previous report on chemotherapy for carcinoma of unknown primary site

Authors	Year	No. of patients	Regimen	Response rate (%)	Survival median (months)	Reference
Bécouarn et al.	1989	85	5Fu/DOX/CDDP/HMM	21	7	[8]
Briasoulis et al.	1998	62	CBDCA/EPI/VP16	37.1	10	[9]
Greco et al.	2000	71	CBDCA/PTX/VP16	48	11	[10]
Briasoulis et al.	2000	77	CBDCA/PTX	38.7	13	[11]
Greco et al.	2002	120	CBDCA/PTX/GEM	25	9	[12]
Piga et al.	2004	102	CBDCA/DOX/VP16	26.5	9	[13]
Pittman et al.	2006	51	CBDCA/GEM	30.5	7.8	[14]

the administration of variable drug combinations, such as gemcitabine (GEM) and paclitaxel (TAX) in combination with platinum, has delivered improved response rates of 25–48%, and the median survival time has been increased to 9–11 months.

It appears that the patients diagnosed with carcinoma metastases from unknown primary sites have relatively limited life expectancy. The median survival time of patients involved in the present study was only 420 days. Hess et al. [1] reported that in their analysis of 1,000 patients, the median survival time was 11 months. Poor prognostic factors were age >61.5 years, the presence of liver metastases and tumor histologies other than neuroendocrine carcinoma and adrenal metastases [1]. In addition, the effect of bone metastases on survival depends on whether patients also have liver metastases. These factors may be important in the orthopedic oncologists' decision about whether or not to perform palliative surgery.

The limitation of the present study is that the number of patients was small and the power of the study is so limited, and the present study included the patients who were treated in a long span of 15 years, from March 1994 to 2009. In recent decades, early diagnosis using modern imaging techniques, such as whole body MRI and PET/CT, contribute to detect origin of primary sites in some cases [15]. And the extensive investigation with histopathological technology, immunohistochemistry [16, 17], electron microscopy [18] also gave some improvement for detection of primary site. Especially the therapeutic modality is also improving. Therefore, we may not evaluate the accurate up to date clinical features and result of the patients initially diagnosed with bone metastases from carcinoma with primary sites.

More recently, molecular gene profiling of carcinoma metastases biopsy samples has contributed to the detection of the primary site, and patients with metastases identified as originating from the colon have had a better response to their therapy [19]. It is now believed that in the future, such genetic analysis of biopsy samples will enable the delivery of cancer-specific treatments without the need for other costly and time-consuming diagnostic techniques.

Conflict of interest statement The authors declare that they have no conflict of interest.

References

1. Hess KR, Abbruzzese MC, Lenzi R, Raber MN, Abbruzzese JL (1999) Classification and regression tree analysis of 1,000 consecutive patients with unknown primary carcinoma. Clin Cancer Res 5:3403–3410
2. Rougraff BT (2003) Evaluation of the patient with carcinoma of unknown origin metastatic to bone. Clin Orthop Relat Res 415:105–109
3. Pavlidis N, Briasoulis E, Hainsworth J, Greco FA (2003) Diagnostic and therapeutic management of cancer of an unknown primary. Eur J Cancer 39:1990–2005
4. Katagiri H, Takahashi M, Inagaki J, Sugiura H, Ito S, Iwata H (2000) Determining the site of the primary cancer in patients with skeletal metastasis of unknown origin: a retrospective study. Cancer 88:1759–1761
5. Nottebaert M, Exner GU, von Hochstetter AR, Schreiber A (1989) Metastatic bone disease from occult carcinoma: a profile. Int Orthop 13:119–123
6. Kole AC, Nieweg OE, Pruim J, Hoekstra HJ, Koops HS, Roodenburg JL, Vaalburg W, Vermey A (1998) Detection of unknown occult primary tumors using positron emission tomography. Cancer 82:1160–1166
7. Sève P, Billotey C, Broussolle C, Dumontet C, Mackey JR (2007) The role of 2-deoxy-2-[F-18]fluoro-d-glucose positron emission tomography in disseminated carcinoma of unknown primary site. Cancer 109:292–299
8. Bécouarn Y, Brunet R, Barbé-Gaston C (1989) Fluorouracil, doxorubicin, cisplatin and altretamine in the treatment of metastatic carcinoma of unknown primary. Eur J Cancer Clin Oncol 25:861–865
9. Briasoulis E, Tsavaris N, Fountzilas G, Athanasiadis A, Kosmidis P, Bafaloukos D, Skarlos D, Samantas E, Pavlidis N (1998) Combination regimen with carboplatin, epirubicin and etoposide in metastatic carcinomas of unknown primary site: a Hellenic cooperative oncology group phase II study. Oncology 55:426–430
10. Greco FA, Burris HA 3rd, Erland JB, Gray JR, Kalman LA, Schreeder MT, Hainsworth JD (2000) Carcinoma of unknown primary site. Cancer 89:2655–2660
11. Briasoulis E, Kalofonos H, Bafaloukos D, Samantas E, Fountzilas G, Xiros N, Skarlos D, Christodoulou C, Kosmidis P, Pavlidis N

(2000) Carboplatin plus paclitaxel in unknown primary carcinoma: a phase II Hellenic cooperative oncology group study. J Clin Oncol 18:3101–3107
12. Greco FA, Burris HA 3rd, Litchy S, Barton JH, Bradof JE, Richards P, Scullin DC Jr, Erland JB, Morrissey LH, Hainsworth JD (2002) Gemcitabine, carboplatin, and paclitaxel for patients with carcinoma of unknown primary site: a Minnie Pearl Cancer Research Network study. J Clin Oncol 20:1651–1656
13. Piga A, Nortilli R, Cetto GL, Cardarelli N, Fedeli SL, Fiorentini G, D'Aprile M, Giorgi F, Parziale AP, Contu A, Montironi R, Gesuita R, Carle F, Cellerino R (2004) Carboplatin, doxorubicin and etoposide in the treatment of tumours of unknown primary site. Br J Cancer 90:1898–1904
14. Pittman KB, Olver IN, Koczwara B, Kotasek D, Patterson WK, Keefe DM, Karapetis CS, Parnis FX, Moldovan S, Yeend SJ, Price TJ, Adelaide Cancer Trials and Education Collaborative (ACTEC) (2006) Gemcitabine and carboplatin in carcinoma of unknown primary site: a phase 2 Adelaide Cancer Trials and Education Collaborative study. Br J Cancer 95:1309–1313
15. Nakanishi K, Kobayashi M, Takahashi S, Nakata S, Kyakuno M, Nakaguchi K, Nakamura H (2005) Whole body MRI for detecting metastatic bone tumor: comparison with bone scintigrams. Magn Reson Med Sci 4:11–17
16. Yam LT, Winkler CF, Janckila AJ, Li CY, Lam KW (1983) Prostatic cancer presenting as metastatic adenocarcinoma of undetermined origin. Immunodiagnosis by prostatic acid phosphatase. Cancer 51:283–287
17. Battifora H (1984) Recent progress in the immunohistochemistry of solid tumors. Semin Diagn Pathol 1:251–271
18. Herrera GA, Reimann BE (1984) Electron microscopy in determining origin of metastatic adenocarcinomas. South Med J 77:1557–1566
19. Varadhachary GR, Talantov D, Raber MN, Meng C, Hess KR, Jatkoe T, Lenzi R, Spigel DR, Wang Y, Greco FA, Abbruzzese JL, Hainsworth JD (2008) Molecular profiling of carcinoma of unknown primary and correlation with clinical evaluation. J Clin Oncol 26:44424–44448

Mod Rheumatol (2010) 20:598–601
DOI 10.1007/s10165-010-0336-0

CASE REPORT

Use of infliximab in a patient with pyoderma gangrenosum and rheumatoid arthritis

Masahiro Tada · Takeshi Nakanishi · Chika Hirata · Tadashi Okano · Yuko Sugioka · Shigeyuki Wakitani · Hiroaki Nakamura · Tatsuya Koike

Received: 10 May 2010 / Accepted: 25 June 2010 / Published online: 4 August 2010

Abstract Pyoderma gangrenosum (PG) is characterized by ulcerative skin lesions. Infliximab (IFX) may promote PG healing in patients with inflammatory bowel disease, but whether IFX is effective for treating PG in patients with rheumatoid arthritis (RA) has not reported. We report the case of a 53-year-old woman with PG complicated by RA who was treated using IFX therapy. This case suggests that IFX therapy might offer effective treatment for such patients.

Keywords Infliximab · Pyoderma gangrenosum · Treatment · Rheumatoid arthritis · Tumor necrosis factor α

Introduction

Pyoderma gangrenosum (PG) is an immune-mediated inflammatory condition characterized by chronic ulcerative skin lesions, commonly on the lower extremities [1–3]. The cause of PG remains unknown. PG reportedly occurs in approximately 1–2% of patients with inflammatory bowel disease (IBD) [4], such as Crohn's disease (CD). Conversely, 36–50% of patients with PG have IBD [1, 3, 5]. However, cases of PG complicated by rheumatoid arthritis (RA) are rare. The mainstay of PG treatment remains immunosuppression, and the most commonly used medicines are corticosteroids and cyclosporine [2, 6]. Local treatments include dressing, debridement, and topical pharmacotherapy [7]. Infliximab (IFX), a monoclonal antibody against tumor necrosis factor (TNF)-α, has been approved for use in the treatment of moderate to severe CD [8, 9] and for RA when used in combination with methotrexate (MTX) [10]. IFX effectively blocks the inflammatory processes underlying CD and produces clinical and histological improvements. Recent case reports have suggested that IFX may promote healing of PG lesions in patients with IBD [11–14]. However, whether IFX is effective for treating PG in patients with RA has not been reported. We describe herein the case of a woman with PG complicated by RA and who was successfully treated using IFX.

Case report

A 53-year-old Japanese woman was referred to our hospital with joint tenderness and swelling in the wrists and fingers. She fulfilled the 1987 criteria of the American College of Rheumatology (ACR) for RA [15] at 35 years old in 1989. She had been treated with 4 mg/week of MTX and 6 mg/day of auranofin since 1997, and the condition of her disease had been stable. She had never taken prednisolone. The patient had a history of schizophrenia, but mental status was well-controlled by alprazolam (Constan; Takeda Pharmaceutical Co., Ltd., Osaka, Japan). Bilateral resection arthroplasty of the metatarsophalangeal joint had been performed for hallux valgus and crow toes in 2004, followed by partial arthrodesis of the left wrist in 2006. In April 2008, an ulcerous lesion

M. Tada · T. Okano · Y. Sugioka · S. Wakitani · H. Nakamura
Department of Orthopaedic Surgery, Osaka City University Medical School, 1-4-3 Asahimachi, Abeno-ku, Osaka 545-8585, Japan

T. Nakanishi · C. Hirata
Department of Dermatology, Osaka City University Medical School, 1-4-3 Asahimachi, Abeno-ku, Osaka 545-8585, Japan

T. Koike (✉)
Department of Rheumatosurgery, Osaka City University Medical School, 1-4-3 Asahimachi, Abeno-ku, Osaka 545-8585, Japan
e-mail: tatsuya@med.osaka-cu.ac.jp

appeared on the left lower limb. This area gradually became larger, and RA activity increased at the same time. There was no trigger for RA exacerbation. MTX was not increased to >4 mg because she had a liver function disorder despite taking folic acid 5 mg/week. In the Steinbrocker classification, functional class was estimated to be class III and stage was assessed as stage III. In June 2008, she consulted a dermatologist regarding an ulcerous lesion (15 × 9 cm) in which all layers of the skin were almost completely necrotic (Fig. 1a, b). Skin biopsy was immediately performed, and she was diagnosed with PG after histopathological identification of superficial and deep perivascular leukocytoclastic dermatosis (Fig. 2). No diarrhea, abdominal pain, or other digestive symptoms were present, so a diagnosis of IBD was excluded. Serological examinations showed positive result for rheumatoid factor (RF) (176 IU/ml), anticyclic citrullinated peptide antibody (ACPA) (>100 U/ml), and autoantibody to galactose-deficient immunoglobulin G (IgG) (CARF) (432.6 AU/mi); negative results of antinuclear antibodies (ANA), anti-CLβ2GP1 (<0.7 U/ml), myeloperoxidase–antineutrophil cytoplasmic autoantibodies (MPO-ANCA) (<1.3 U/ml), and PR3-ANCA (<3.5 U/ml).

The patient received 200 mg of IFX (4.8 mg/kg) at 0, 2, and 6 weeks, and every 8 weeks thereafter, in combination with 4 mg/week of MTX. She had been applying sulfadiazine silver cream (1% Geben cream) to the ulcer lesion once daily and had undergone a checkup by a dermatologist. Signs of improvement were observed after the second course of IFX, and the ulcer lesion was obviously reduced. The area of the ulcer lesion was 9 × 4 cm at 3 months after initiating treatment with IFX (Fig. 1c, d). At the same time, swelling and tenderness of bilateral metacarpophalangeal, proximal interphalangeal, and ankle joints were decreased and disappeared. Before initiating treatment with IFX, laboratory evaluation revealed white blood cell count 13,200/μl, C-reactive protein (CRP) 5.61 mg/dl, erythrocyte sedimentation rate (ESR) 57 mm in 1 h, matrix metalloproteinase 3 109 ng/ml, Disease Activity Score of 28 Joints-CRP4 (DAS28-CRP4) 5.24, and DAS28-ESR4 6.43 [16]. After 3 months of treatment, CRP had decreased to 0.26 mg/dl, DAS28-CRP4 to 2.78, ESR to 21 mm, and DAS28-ESR4 to 3.87. This patient was classified as a moderate responder according to European League Against Rheumatism criteria [17]. As of the time of this writing, 2 years after the first treatment with IFX, ulcers have completely disappeared (Fig. 1e, f) and RA remains very well controlled. Maintenance treatment with IFX in combination with MTX has been continued to control RA and PG activity.

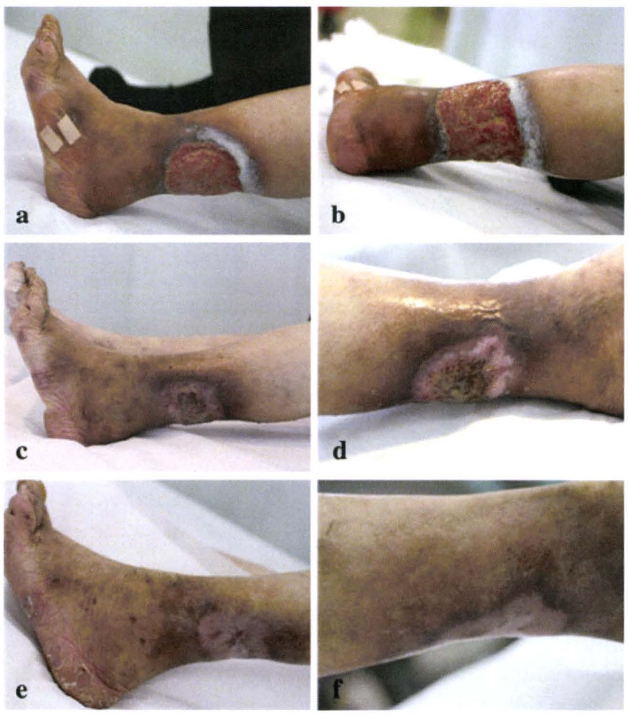


Fig. 1 Pyodermic lesion of the left lower limb. **a**, **b** Before treatment with infliximab, the area of the ulcer lesion was 15 × 9 cm. All layers of the skin showed almost complete necrosis. **c**, **d** Lesion at 3 months after initiating infliximab infusion. While the ulcer remains, the area of the lesion has been reduced to 9 × 4 cm. **e**, **f** Lesion at 2 years after first treatment with infliximab. The ulcer lesion has disappeared completely

Discussion

This case illustrates the benefits of IFX in healing RA-associated PG lesions. The etiopathogenesis of PG is still not well understood. However, the disease is associated with systemic diseases such as IBD and myeloproliferative diseases. TNF-α is known to play an integral role in the development of such diseases. PG has frequently been reported to occur in patients with IBD [1, 3, 5]. However, cases of PG in patients with RA are rare. Clinically, PG is classified into ulcerative, pustular, bullous, and vegetative types [18]. The case reported here was typical of ulcerative PG. Diagnosis mainly depends on recognizing evolving clinical features and histopathological findings, as no specific investigations are available to reach the diagnosis. Other diseases such as occlusive vascular disease, vasculitis, infection, and drug-induced tissue damage must be excluded before a definitive diagnosis can be reached. In this case, the patient showed none of those diseases and was diagnosed with PG on the basis of characteristic skin findings. She also had no symptoms of IBD. Histopathological findings that may be useful to exclude other pathologies are not specific. With reference to findings in PG, perivascular dermal infiltrate of neutrophils is seen, generally extending to the subcutis and associated with a

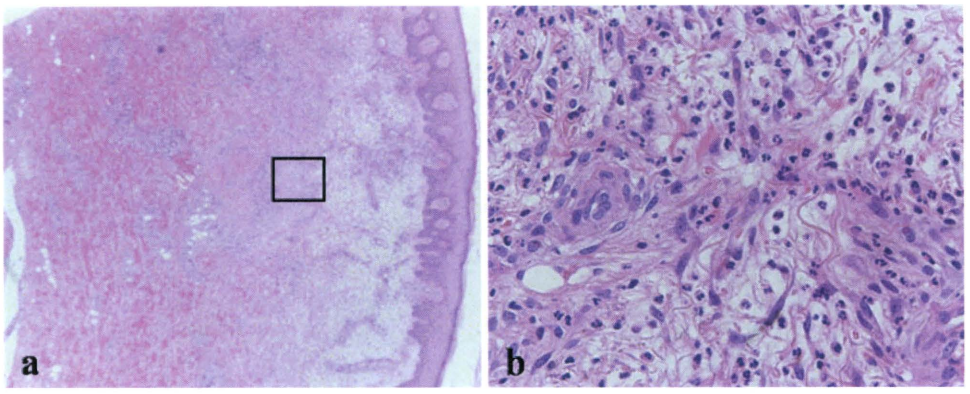


Fig. 2 Histopathology of a biopsy skin specimen from the left lower limb. **a** Perivascular dermal infiltration of neutrophils is apparent, extending to the subcutis and associated with mixed interstitial infiltration of lymphocytes and histiocytes. **b** Higher magnification of the area indicated in **a**. H&E stain: **a** ×40; **b** ×400

mixed interstitial infiltrate of lymphocytes and histiocytes [18].

Conventional PG management involves local and systemic therapy. The combination of both therapies is important in achieving PG control. Local treatment includes dressings, corticosteroid creams, topical sulfadiazine silver cream, and necrotic tissue debridement [7]. The mainstays of systemic treatment include corticosteroids and immunosuppressive agents. High-dose corticosteroids have been recommended in the acute phase [7] but are associated with significant side effects. Cyclosporine is commonly used in patients with steroid-resistant PG and has been reported as effective [6]. Other drugs such as azathioprine, tacrolimus, MTX, and cyclophosphamide have been used with success [2]. These drugs also show problematic side effects, including myelosuppression, nephrotoxicity, and hepatotoxicity.

A number of recent case reports have demonstrated good PG response to treatment with IFX [11–14] or etanercept [19]. In particular, IFX therapy has been shown to be effective and safe for IBD-associated PG in a retrospective study [20] and a randomized placebo-controlled trial [21]. However, whether biologics represent effective treatment for RA-associated PG remains unclear. Otherwise, IFX therapy has been a great advance in treating RA patients [10]. In Japan, several studies have shown the effectiveness of this treatment in terms of clinical [22] and radiographic results [23] and activities of daily life [24]. The typical IFX dose has been 5 mg/kg for IBD-associated PG, without combined MTX. In the case reported here, 200 mg of IFX (4.8 mg/kg) was used in combination with MTX at 4 mg/week. IFX dose was similar to that used in IBD-associated PG. This case study suggests that IFX might offer potential as an effective therapy for PG patients with RA.

TNF inhibitors have been reported to induce cutaneous vasculitis. Fujikawa et al. [25] recently reported three patients with anti-TNF therapy-induced cutaneous vasculitis. These patients developed a red rash on the extremities and fever. Skin biopsy of the rash showed leukocytoclastic vasculitis in two patients. The underlying mechanisms are unknown, but cutaneous vasculitis and ulcer may be worsened with the use of TNF inhibitors. Vandevyvere et al. [26] presented a case of a patient with RA who developed PG under IFX and persistent cutaneous inflammation when switching to etanercept. Additional case studies and large prospective studies are needed to establish the appropriate use of IFX for PG patients with RA.

In conclusion, we report a case in which IFX therapy was successful for a patient with PG and RA. IFX administration may be useful not only for PG patients with IBD but also for PG patients with RA.

Conflict of interest Dr. Koike has received research grants and/or speaking fees from Takeda Pharmaceutical, Mitsubishi Tanabe Pharma Corporation, Chugai Pharmaceutical, Eisai, Abbott Japan, Teijin Pharma, Banyu Pharmaceutical and Ono Pharmaceutical. The other authors declare no conflict of interest.

References

1. Callen JP. Pyoderma gangrenosum. Lancet. 1998;351:581–5.
2. Wollina U. Clinical management of pyoderma gangrenosum. Am J Clin Dermatol. 2002;3:149–58.
3. Bennett ML, Jackson JM, Jorizzo JL, Fleischer AB Jr, White WL, Callen JP. Pyoderma gangrenosum. A comparison of typical and atypical forms with an emphasis on time to remission. Case review of 86 patients from 2 institutions. Medicine (Baltimore). 2000;79:37–46.
4. Bernstein CN, Blanchard JF, Rawsthorne P, Yu N. The prevalence of extraintestinal diseases in inflammatory bowel disease: a population-based study. Am J Gastroenterol. 2001;96:1116–22.
5. von den Driesch P. Pyoderma gangrenosum: a report of 44 cases with follow-up. Br J Dermatol. 1997;137:1000–5.
6. Friedman S, Marion JF, Scherl E, Rubin PH, Present DH. Intravenous cyclosporine in refractory pyoderma gangrenosum complicating inflammatory bowel disease. Inflamm Bowel Dis. 2001;7:1–7.
7. Wenzel J, Gerdsen R, Phillipp-Dormston W, Bieber T, Uerlich M. Topical treatment of pyoderma gangrenosum. Dermatology. 2002;205:221–3.
8. Present DH, Rutgeerts P, Targan S, Hanauer SB, Mayer L, van Hogezand RA, et al. Infliximab for the treatment of fistulas in patients with Crohn's disease. N Engl J Med. 1999;340:1398–405.

9. Targan SR, Hanauer SB, van Deventer SJ, Mayer L, Present DH, Braakman T, et al. A short-term study of chimeric monoclonal antibody cA2 to tumor necrosis factor alpha for Crohn's disease. Crohn's Disease cA2 Study Group. N Engl J Med. 1997;337: 1029–35.
10. Lipsky PE, van der Heijde DM, St Clair EW, Furst DE, Breedveld FC, Kalden JR, et al. Infliximab and methotrexate in the treatment of rheumatoid arthritis. Anti-Tumor Necrosis Factor Trial in Rheumatoid Arthritis with Concomitant Therapy Study Group. N Engl J Med. 2000;343:1594–602.
11. Ljung T, Staun M, Grove O, Fausa O, Vatn MH, Hellstrom PM. Pyoderma gangrenosum associated with crohn disease: effect of TNF-alpha blockade with infliximab. Scand J Gastroenterol. 2002;37:1108–10.
12. Tan MH, Gordon M, Lebwohl O, George J, Lebwohl MG. Improvement of pyoderma gangrenosum and psoriasis associated with Crohn disease with anti-tumor necrosis factor alpha monoclonal antibody. Arch Dermatol. 2001;137:930–3.
13. Grange F, Djilali-Bouzina F, Weiss AM, Polette A, Guillaume JC. Corticosteroid-resistant pyoderma gangrenosum associated with Crohn's disease: rapid cure with infliximab. Dermatology. 2002;205:278–80.
14. Ferkolj I, Hocevar A, Golouh R, Dolenc Voljc M. Infliximab for treatment of resistant pyoderma gangrenosum associated with Crohn's disease. Acta Dermatovenerol Alp Panonica Adriat. 2006;15:173–7.
15. Arnett FC, Edworthy SM, Bloch DA, McShane DJ, Fries JF, Cooper NS, et al. The American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis. Arthritis Rheum. 1988;31:315–24.
16. Prevoo ML, van 't Hof MA, Kuper HH, van Leeuwen MA, van de Putte LB, van Riel PL. Modified disease activity scores that include twenty-eight-joint counts. Development and validation in a prospective longitudinal study of patients with rheumatoid arthritis. Arthritis Rheum. 1995;38:44–8.
17. van Gestel AM, Prevoo ML, van 't Hof MA, van Rijswijk MH, van de Putte LB, van Riel PL. Development and validation of the European League Against Rheumatism response criteria for rheumatoid arthritis. Comparison with the preliminary American College of Rheumatology and the World Health Organization/ International League Against Rheumatism Criteria. Arthritis Rheum. 1996;39:34–40.
18. Bhat RM. Management of pyoderma gangrenosum—an update. Indian J Dermatol Venereol Leprol. 2004;70:329–35.
19. McGowan JW, Johnson CA, Lynn A. Treatment of pyoderma gangrenosum with etanercept. J Drugs Dermatol. 2004;3:441–4.
20. Regueiro M, Valentine J, Plevy S, Fleisher MR, Lichtenstein GR. Infliximab for treatment of pyoderma gangrenosum associated with inflammatory bowel disease. Am J Gastroenterol. 2003;98: 1821–6.
21. Brooklyn TN, Dunnill MG, Shetty A, Bowden JJ, Williams JD, Griffiths CE, et al. Infliximab for the treatment of pyoderma gangrenosum: a randomised, double blind, placebo controlled trial. Gut. 2006;55:505–9.
22. Tanaka Y, Takeuchi T, Inoue E, Saito K, Sekiguchi N, Sato E, et al. Retrospective clinical study on the notable efficacy and related factors of infliximab therapy in a rheumatoid arthritis management group in Japan: one-year clinical outcomes (RECONFIRM-2). Mod Rheumatol. 2008;18:146–52.
23. Takeuchi T, Yamanaka H, Inoue E, Nagasawa H, Nawata M, Ikari K, et al. Retrospective clinical study on the notable efficacy and related factors of infliximab therapy in a rheumatoid arthritis management group in Japan: one-year outcome of joint destruction (RECONFIRM-2J). Mod Rheumatol. 2008;18:447–54.
24. Nagasawa H, Kameda H, Sekiguchi N, Amano K, Takeuchi T. Improvement of the HAQ score by infliximab treatment in patients with RA: its association with disease activity and joint destruction. Mod Rheumatol. 2009;19:166–72.
25. Fujikawa K, Kawakami A, Hayashi T, Iwamoto N, Kawashiri SY, Aramaki T, et al. Cutaneous vasculitis induced by TNF inhibitors: a report of three cases. Mod Rheumatol. 2010;20: 86–9.
26. Vandevyvere K, Luyten FP, Verschueren P, Lories R, Segaert S, Westhovens R. Pyoderma gangrenosum developing during therapy with TNF-alpha antagonists in a patient with rheumatoid arthritis. Clin Rheumatol. 2007;26:2205–6.

Vertebroplastyとkyphoplasty

鈴木亨暢* 中村博亮*
Suzuki Akinobu Nakamura Hiroaki
(*大阪市立大学大学院医学研究科整形外科学)

はじめに

椎体形成術は，椎体骨折や脊椎腫瘍による不安定な椎体に対して，骨セメント(polymethyl methacrylate：PMMA)やリン酸カルシウムペースト(calcium phosphate cement：CPC)などを注入することにより，疼痛緩和と脆弱化した罹患骨の補強を得ようとする低侵襲治療である．椎体形成術はその手技によってvertebroplastyとkyphoplastyの2つに大別される．Vertebroplastyはおもに経皮的にPMMAを注入するもので，1987年にGalibertら[1]により報告された．椎体血管腫への骨セメントの注入が最初の臨床的実用とされている．本方法は局所麻酔下におこなうことができるという利点があるが，単に経皮的に注入するだけでは楔状化した椎体の変形を戻すことは困難であり，セメントの高圧注入による椎体外・脊柱管内への漏洩も危惧される．Kyphoplastyはこれらの欠点を改善する目的で考案された方法で，2001年にGarfinら[2]によってはじめて報告された．このkyphoplastyは全身麻酔下に経皮的もしくは小切開にて椎体内にバルーンを挿入し，バルーンを拡張させ椎体内に空洞を形成した後，骨セメントを充填する方法である．この操作により椎体高を再獲得し，形成された空洞に注入圧をかけずに高粘度の重合が進んだ骨セメントを充填できることが利点となる．

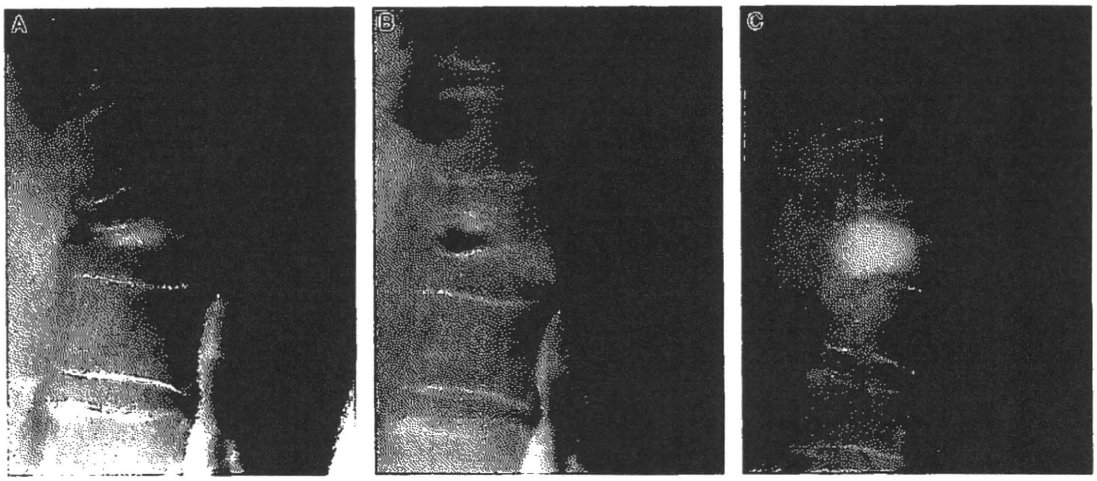
関連語
- vertebroplasty
- kyphoplasty
- 骨粗鬆症性椎体骨折

適応

椎体形成術の適応は各施設により大きく異なっている．一般的には，1)保存療法抵抗性の骨粗鬆症性椎体骨折による疼痛を有する症例，もしくは2)骨溶解性の良性もしくは悪性腫瘍による疼痛を有する症例が適応とされ，疼痛のない骨折や保存療法によく反応する椎体骨折，全身もしくは局所の感染を有する症例，補正できない出血傾向を有する症例などは適応外と考えられている[3]．過去には椎体後壁損傷や脊髄・馬尾症状がある場合は禁忌ともいわれていたが，現在では慎重におこなえば可能であるとされている．手技の簡便さから適応が拡大される傾向にあるが，重篤な合併症を起こしうる手技であり，その適応は十分に考慮されなければならない．

充填材料

一般的にはPMMAもしくはCPCが用いられることが多い．これらはいずれも充填時には液状であるため操作性が良い．PMMAの場合，硬化後の強度はきわめて高い(100MPa)が，重合熱が発生すること，重合前のモノマーに毒性があること，強度が高すぎて隣接椎の椎体骨折が発生しやすいことなどが問題点としてあげられる．CPC



図❶ 骨粗鬆症性椎体骨折後偽関節に椎体形成術を施行した1例
症例は64歳女性，背部痛を主訴とし，座位保持不能であった．術前X線中間位では椎体の楔状化が見られたが(A)，仰臥位では椎体内にVacuum Cleftを認め骨折部の癒合不全を認めた(B)．椎体形成術を施行した後，背部痛は消失し独歩可能となった(C)．

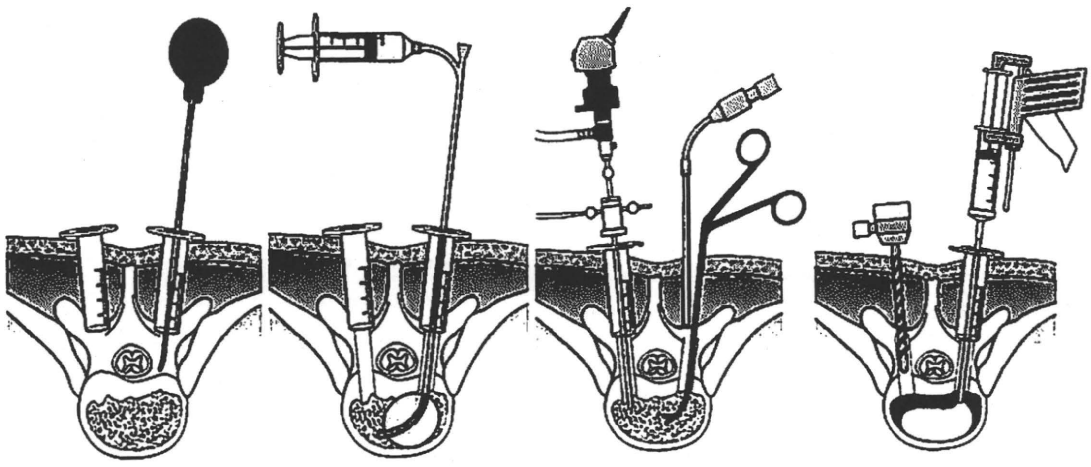
は生体親和性が良く，重合熱もあまり発生しない．強度はPMMAより低く(80MPa)椎体強度に近いため，隣接椎骨折は生じにくいとされているが，血液混入などにより強度が低下し圧潰しやすいという問題点もある．その他，切開手術ではあるが，hydroxyapatiteのブロックなどを使用した椎体形成術の報告も存在する．

合併症

いずれの手技においても問題となるのが，セメントの椎体外漏出である．セメント漏出があっても無症状のケースが多いが，血管内漏出が生じた場合には肺塞栓などの危険性があり，また脊柱管内・椎間孔部への漏出が生じた場合には神経損傷や根性疼痛を生じる可能性がある．Vertebroplastyおよびkyphoplastyの合併症に関するsystematic reviewによると，無症候性のセメント漏出はvertebroplastyで75%，kyphoplastyで14%であり，症候性のセメント漏出ではvertebroplastyで1.48%，kyphoplastyで0.04%と，いずれもkyphoplastyにおいて発生頻度は低いと報告されている[4]．また，新規椎体骨折も重要な合併症の一つである．その発生頻度は20%前後と報告されているが，この発生頻度が自然発生の椎体骨折の頻度を上回るかどうかは議論の余地がある．しかし，椎体形成術後の新規骨折は隣接椎に多い(vertebroplastyにて51.6%，kyphoplastyにて74.8%[4])ことから，骨セメントなどによる椎体強度やアライメントの変化がこれらの骨折に関与している可能性は高い．

当施設における適応・方法

筆者らの施設では，遷延化する強い腰背部痛を有する骨粗鬆症性椎体骨折後の偽関節症例を対象として，内視鏡とバルーンを用いて椎体形成術をおこなっている[5](図❶)．偽関節(または癒合不全)の診断は受傷後3～6ヵ月経過し，動態X線側面像(とくに仰臥位側面像と立位前屈像)にて椎体骨折部に異常可動性を有するものとしている(図❶A,B)．手術は全身麻酔下にて4点支持フレームを使用して，腹臥位でおこなう．イメージ透視下にて罹患椎の椎弓根を確認し，その背側に約2cmの小皮切を加えた後，10ccのプラスチック注射筒を創部の深さに合わせて切断し，レトラクターとして設置する(図❷A)．再度透視下にてオウル・プローブを用いて経椎弓根的に偽関節部までの骨孔を作成した後，偽関節腔にバルーン(8Fr)を挿入する(図❷B)．バルーンを膨らませて十分に偽関節腔のスペースを確保した後，内視鏡を挿入する．内視鏡視下に偽関節腔内の肉芽組織を掻爬し(図❷C)，造影剤を注入してその椎体外への漏出が無いことを確認し，CPCを充填する(図❷D)．CPCは最高強度に達する



図❷ 当科における椎体形成術の方法
約2cmの小皮切を加えた後，10ccのプラスチック注射筒を適切な長さに切断してレトラクターとして設置し，経椎弓根的に偽関節腔までの骨孔を作成(A)．偽関節腔にバルーン(8Fr)を挿入し，バルーンを膨らませて充分に偽関節腔内にスペースを確保する(B)，内視鏡視下に偽関節腔内の肉芽組織を掻爬し(C)，造影剤を注入して椎体外への漏出が無いことを確認して，CPCを充填する(D)．

のに72時間を要するため，術後3日間を臥床安静とした後，フレームコルセットを着用して離床させている．当院で椎体形成術を単独で施行し，6ヵ月以上followが可能であった25症例(男性3例，女性22例，平均年齢72.7歳)では手術前背部痛はvisual analogue scale(VAS：100mm法)にて平均73.5であったのに対し，退院時平均19.0，最終経過観察時24.2と有意な疼痛の改善を認めた．肺塞栓などの全身合併症は認められなかったが，1例で術中のCPCの脊柱管内への漏出が認められた．また，隣接椎体の新規骨折は4例に認められた．

最近の動向

2009年8月*N Engl J Med*に衝撃的な2論文が掲載され，波紋をよんだ．2本の論文とも1年以内に発生した，疼痛を有する椎体骨折患者(平均年齢はいずれも75歳前後)を対象としたrandomized controlled trialであり，vertebroplastyをおこなった群とsham procedure(実際に局所麻酔をおこない，セメントを開封してその臭いを患者に感じさせる)をおこなった群とで，疼痛の程度，腰痛，QOLに関するスコアを比較検討したものである[6,7]．Kallmesら[7]の研究では3，14，30，90日と1年のtime pointで，Buchbinderら[6]の研究では7，21，90日と6ヵ月のtime pointで検討をおこなっているが，驚くべきことに，両研究とも疼痛およびその他のスコアはいずれのtime pointにおいてもvertebroplasty群とsham procedure群で有意な差を認めなかった．Sham procedure群も早期より除痛効果があったことから局所麻酔に意味があったのではないか，あるいは患者のselection biasがあったのではないかなど，臨床的な経験から両論文に対して多数の疑問の声が上がっている[8]．実際，sham procedureではなく通常おこなわれる保存療法を対照群としたRCTにおいて，vertebroplasty[9]もしくはkyphoplasty[10]は早期の除痛獲得に有用であるとした報告も存在する．つまり骨粗鬆症性椎体骨折に対する椎体形成術の有効性についてはいまだ明確な答えが出ていないといえる．椎体形成術にも重篤な合併症は起こりえること，新規の骨粗鬆症性椎体骨折は保存療法で良好な経過をたどる症例が多いことなどを考えると，やはり適応には慎重になる必要がある．一方，転移性脊椎腫瘍に対するkyphoplastyに関するmeta analysisでは，Level Ⅲながらも除痛に有効であると報告されている[11]．また転移性脊椎腫瘍に対する椎体形成術に関してはラジオ波焼灼術との組み合わせ[12]や，ラジオアイソトープ含有セメントを用いた椎体形成術[13]など，抗腫瘍効果も考慮に入れた方法が報告されている．

椎体形成術はすでに世界で広くおこなわれているが，

適応症例の基準や手技・方法，また有効性に関してもいまだ確立されているとはいえない．保存療法を含めた大規模調査や異なった手技間での比較検討をおこなうことなどが今後の課題であると考えられる．

文　献

1) Galibert P, Deramond H : Percutaneous acrylic vertebroplasty as a treatment of vertebral angioma as well as painful and debilitating diseases. *Chirurgie* **116** : 326-334, 1990
2) Garfin SR, Yuan HA, Reiley MA : New technologies in spine : kyphoplasty and vertebroplasty for the treatment of painful osteoporotic compression fractures. *Spine (Phila Pa 1976)* **26** : 1511-1515, 2001
3) Denaro L, Longo UG, Denaro V : Vertebroplasty and kyphoplasty : reasons for concern?*Orthop Clin North Am* **40** : 465-471, viii, 2009
4) Lee MJ, Dumonski M, Cahill P *et al* : Percutaneous treatment of vertebral compression fractures : a meta-analysis of complications. *Spine (Phila Pa 1976)* **34** : 1228-1232, 2009
5) Hoshino M, Nakamura H, Konishi S *et al* : Endoscopic vertebroplasty for the treatment of chronic vertebral compression fracture. Technical note. *J Neurosurg Spine* **5** : 461-467, 2006
6) Buchbinder R, Osborne RH, Ebeling PR *et al* : A randomized trial of vertebroplasty for painful osteoporotic vertebral fractures. *N Engl J Med* **361** : 557-568, 2009
7) Kallmes DF, Comstock BA, Heagerty PJ *et al* : A randomized trial of vertebroplasty for osteoporotic spinal fractures. *N Engl J Med* **361** : 569-579, 2009
8) Andersson GB : Surgery : vertebroplasty : one solution does not fit all. *Nat Rev Rheumatol* **5** : 662-663, 2009
9) Rousing R, Andersen MO, Jespersen SM *et al* : Percutaneous vertebroplasty compared to conservative treatment in patients with painful acute or subacute osteoporotic vertebral fractures : three-months follow-up in a clinical randomized study. *Spine (Phila Pa 1976)* **34** : 1349-1354, 2009
10) Wardlaw D, Cummings SR, Van Meirhaeghe J *et al* : Efficacy and safety of balloon kyphoplasty compared with non-surgical care for vertebral compression fracture (FREE) : a randomised controlled trial. *Lancet* **373** : 1016-1024, 2009
11) Mendel E, Bourekas E, Gerszten P *et al* : Percutaneous techniques in the treatment of spine tumors : what are the diagnostic and therapeutic indications and outcomes? *Spine (Phila Pa 1976)* **34** : S93-100, 2009
12) Schaefer O, Lohrmann C, Markmiller M *et al* : Technical innovation. Combined treatment of a spinal metastasis with radiofrequency heat ablation and vertebroplasty. *AJR Am J Roentgenol* **180** : 1075-1077, 2003
13) Cardoso ER, Ashamalla H, Weng *et al* : Percutaneous tumor curettage and interstitial delivery of samarium-153 coupled with kyphoplasty for treatment of vertebral metastases. *J Neurosurg Spine* **10** : 336-342, 2009

都会 腰椎疾患患者への手術適応と手術の実際

寺井秀富，中村博亮　大阪市立大学大学院医学研究科整形外科学

2009年度版国民衛生の動向によれば，腰痛を主訴とした年齢階級別通院者率は55～64歳では1,000人当たり54.7人であるのが，75～84歳の年齢層では144.5人と加齢に伴い3倍近くに急増していることがわかる。その理由は現時点で明らかでないが，他の整形外科的疾患である肩こりや関節痛，骨粗鬆症と比較してもその増加率は顕著である(図1)。一方，10年前には2,200万人であった65歳以上の人口は，10年後の2020年には3,500万人，全人口の約30%に達すると見込まれている(図2)。この比率から換算すると，腰痛を主訴に通院する患者数は今後の10年間で100万人以上増加するであろうと予想される。この増加率は，今後10年間で輩出される整形外科医・脊椎外科医で対応可能な患者数をはるかに上回る。それゆえ高齢者の腰椎疾患に対する治療法の確立は社会的にも，医学的にも早急に確立されなければならない問題の1つである。

ここでは高齢者(75歳～)，超高齢者(85歳～)の腰椎疾患に関する手術療法について，疾患の特徴，手術適応，術式選択などについて述べる。

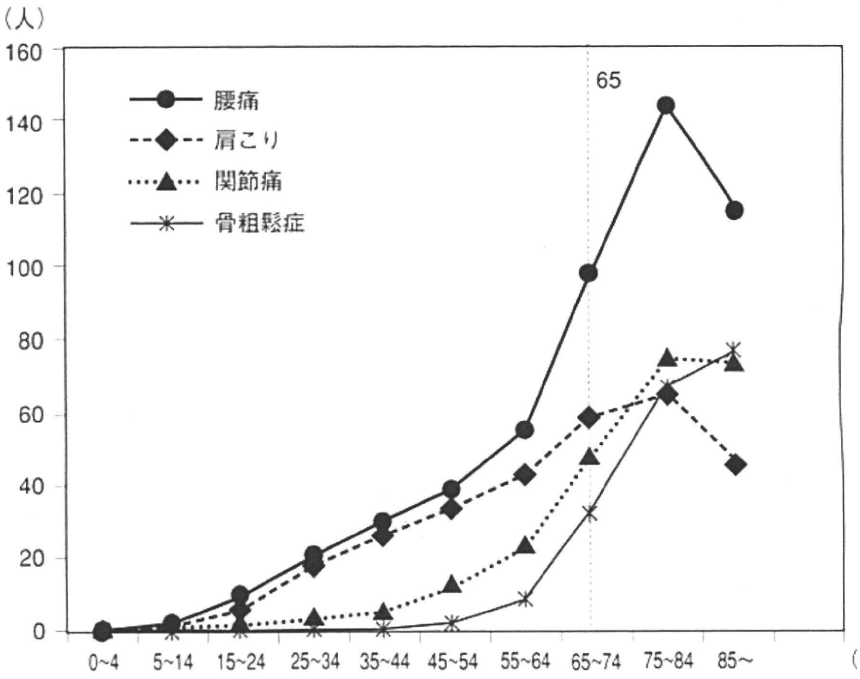
高齢者腰椎疾患の特徴

高齢者における腰椎疾患の特徴は変形と骨粗鬆症を伴うことである。椎間板変性，椎間関節の破綻，骨粗鬆性椎体骨折などが高率，また複合して認められる。これらはすべり症や変性側弯症，腰椎後弯症，または分類不能な脊柱不安定性の原因となっており，高齢者に腰痛が多い原因の1つであると考えられる。

あまり知られていないが，強直性脊椎骨増殖(diffuse idiopathic skeletal hyperostosis；DISH)も70歳以上の高齢者で有病率が急激に増加する。70歳代の男性では実に4割近くにDISHが認められるという海外の報告もある[1,2]。DISHにより脊柱に部分的な不撓性が生じると，固定術後の隣接椎間障害と類似した脊柱不安定性の出現や，いわゆるglobal kyphosisの原因となる。

0286-5394/10/¥400/論文/JCOPY

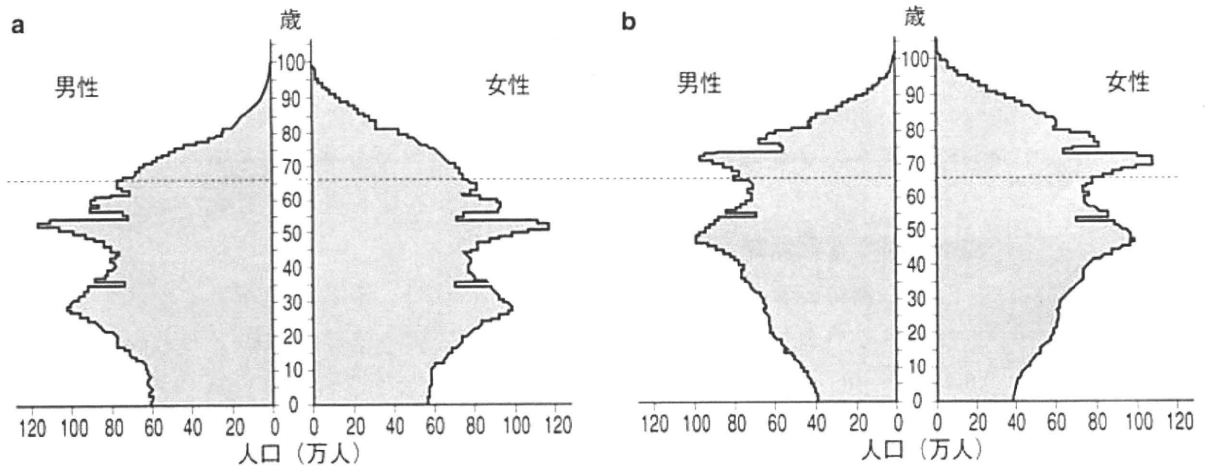
図1 年齢階級別通院者率（人口1,000人当たり）



（国民衛生の動向：2009年）

図2 人口ピラミッド データ

a：2000年は65歳以上が2,200万人（17%）。
b：2020年は65歳以上が3,500万人（28%）。



（国立社会保障・人口問題研究所HPより）

高齢者腰椎疾患患者に対する手術適応

高齢者は内科的疾患の合併率が高く，その有無と程度により全身麻酔に対するリスクは個人差が大きい。基本的に安全に全身麻酔を実施できる全身的予備能があれば，手術適応については非高齢の患者と大きな相違はないと考えられる。中・高年の患者と比較すると，もともと活動性は高くなく連続歩行距離も短い。腰部脊柱管狭窄症に関しては，若年者と比べるとより短時間の歩行で間欠跛行が

出る状態でないと手術を希望しない。すなわち，手術を希望するほどの症状がある高齢者はより重症であるといえる。

ただし，高齢者ではrestless legs syndromeが馬尾性間欠跛行の訴えと似ていることがあるので注意を要する。

変性側弯や椎体不安定性，椎体骨折後偽関節による腰背部痛を伴っている場合は，歩行すらままならないこともあり，正確な間欠跛行の程度を聴取できないこともあるので注意しなければならない。腰痛が主訴の場合でも手術適応はあるが，それが手術で解消できるかどうかの判断は難しい。病歴の詳細な聴取と神経学的所見，動態撮影や神経根ブロックなどから考えて総合的に判断する必要がある。しかし，高齢者腰痛に対する手術加療に関するエビデンスは少なく，術者の経験的な判断要素が大きい。

術式の選択

術式を決定するうえで最も重要な条件は高率に症状がとれる手術法であること，かつ周術期の合併症を避け早期の離床とリハビリテーションを可能にせしめる術式であることである。高齢者は全身麻酔を受けるだけでもリスクがある。それゆえ，症状の軽快を見込めない手術を行って経過をみるということは，症状が軽減しないばかりでなく，全身状態の悪化によりかえってADLの低下を招くおそれがある。それゆえ上記の条件に見合う術式がない場合，もしくは技術的にできない場合は，ほかの保存療法を模索するべきである。余命から考えると，術後の長期臥床や再手術は最も忌避すべき事項であるといえる。

術式の判断材料として重要な要素は患者の症状と全身状態である。まずは症状，神経所見から必要な術式を決定し，それが患者の全身状態と照らし合わせて可能かどうかを検討する。脊柱変形や不安定性がなく，除圧で対処できる場合は内視鏡下手術など低侵襲手術のよい適応である[3]。

しかし組織侵襲の小ささばかりにとらわれて，手術時間が長くなってしまうことは避けなければならない。手術時間短縮の観点からは高齢者への内視鏡下手術は十分にトレーニングを積み，短時間で行えるようになってから行うべきである。

腰背部痛を伴い，その原因が脊柱不安定性にある場合は固定術も検討されなければならない。神経圧迫症状がメインの場合，脊柱不安定性が症状発現に寄与しているかどうかで固定の必要性は違ってくる。脊柱不安定性の判断はミエログラフィ，脊柱動態撮影を行って判断する。高齢者では一見すべり症や椎間楔状化が認められても，変性の進行により椎体間での再安定化が得られていることがあるので注意が必要である。術式選択のプロセスについては長谷川ら[4]の文献も参考にされたい。

高齢者の脊椎固定術は骨脆弱性のためにスクリューの固着力が弱い。強固なインプラントの固定を得るためにはペディクルスクリューだけでなくsublaminar wiring techniqueやフックを自在に扱うことができなければいけない。また椎体骨折後偽関節に対しては椎体形成術の技術を習得しておくと，侵襲の大きい前方固定を回避できることができる場合があり術式選択の幅が広がる[5]。

現在まで術式別の術後経過についてさまざまな報告がなされているが，高齢者・超高齢者では日常の生活レベルも骨脆弱性も異なるので一概に既存の論文の結果をあてはめて考えることはできない。長期経過を優先する術式と同一に論じることができないということを理解する必要がある。術者の技量も手術方針を決定するうえで重要な因子となる。高齢者の脊椎インストゥルメンテーション手術における手術侵襲の安全域について佐野[9]が詳述している。高齢者の脊椎疾患はさまざまな疾患要素を含んだ応用問題であり，手術中の臨機応変な判断と対処が必要になることも多い。トレーニングレベルにあるものはさまざまな手技に習熟した指導医のもとで経験を積む必要がある。

症例供覧

【症例1】

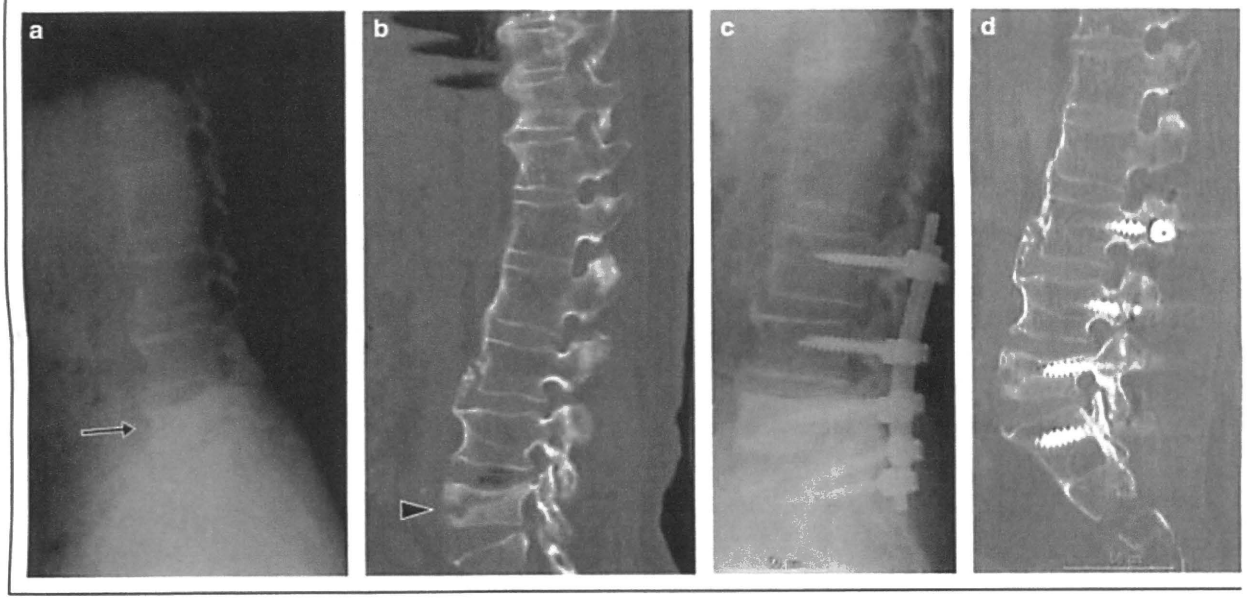
75歳，男性(会社勤務)1年前に転倒し，約6カ月後に腰痛が出現，徐々に増悪して1年ほどで疼痛のため寝起きが困難となった。仰臥位または立位の保持姿勢では疼痛は軽微であった。神経症状は認められなかった。立位単純X線側面像ではDISHとL5椎体の骨硬化を認めたが病変の存在は判然としなかった(**図3a**)。仰臥位側面像，CTによりL5椎体骨折後偽関節と判明した(**図3b**)。偽関節腔内への腸骨移植とL3-S1までの固定術を施行。術後1年で完全に骨癒合が得られ，疼痛は軽快し職場復帰を果たした(**図3c，d**)。

図3 【症例1】L5椎体骨折後偽関節

75歳，男性。

a：初診時X線側面像。**b**：初診時CT。立位側面像ではDISHとL5椎体の骨硬化像を認めるが病変ははっきりしない(矢印)。CTにてL5椎体骨折後偽関節と判明した(矢頭印)。

c：術後X線側面像。**d**：術後CT。L5偽関節腔内を掻爬後に腸骨移植を行い，当該椎間を含めた4椎体を固定した。約半年で骨癒合が得られ，術前の寝起きができないという症状は軽快し職場に復帰した。



【症例2】

85歳，女性。独居。以前から腰下肢痛があり近医にて投薬，ブロックなどの保存療法を受けていた。受診時には10m以下の混合性間欠跛行を認めた。神経根ブロックを施行し，責任高位はL3/4と判断したが，変性側弯が強くL2-5の椎弓切除術とPLFを施行した。術後ドレーントラブルから術後血腫となり同日緊急血腫除去術を施行。右下肢のdrop footを生じたが術前の両下肢痛は消失したため患者満足度は高く，短下肢装具装着にてADLは自立している**(図4)**。

【症例3】

75歳，女性。独居。骨粗鬆性椎体骨折後の後弯症，椎間不安定性による腰痛，根性疼痛に対し短縮骨切り術を予定していた。手術の3週間前に自宅で転倒し，新たな椎体骨折を生じたため，手術まで入院・臥床安静としていたところ認知症症状が出現した**(図5a〜c)**。当初予定していた固定椎間を延長せざるをえず，T10-L5までの後方固定術，L3のpedicle subtraction osteotomy，T12椎体への椎体形成術を施行した。術前の疼痛は消失し，坐位保持は可能となったが，認知症症状のためリハビリが思うように進まず，ADL改善という点では問題を残した**(図5d〜f)**。

図4 【症例2】腰椎変性側弯症

85歳，女性。

a：術前臥位X線正面像。**b**：術前ミエログラム(立位) **c**：術後X線正面像(立位)。

術前の画像診断においてL3/4椎間で臥位6mm，立位で12mmと増強する側方すべりと同部位を中心とした脊柱管狭窄を認めた(矢印)。術前L1-4間での立位正面像でのCobb角は29°であったが，術後9°にまで改善した。JOAスコアも術前12点から術後1年で20点にまで改善した。現在腰痛に関しての愁訴はなく，drop footを認めるもののADLは自立している。