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Case report

Bone and skeletal muscle metastases from gastric adenocarcinoma: unusual radiographic, CT and scintigraphic features

J. A. Narváez[1], **J. Narváez**[2], **M. T. Clavaguera**[2], **X. Juanola**[2], **C. Valls**[1], **J. Fiter**[2]

[1] Department of CT and MR Imaging, Hospital Duran i Reynals, Ciudad Sanitaria y Universitaria de Bellvitge, L'Hospitalet de Llobregat, Autovía de Castelldefels km. 2'7, E-08907 Barcelona, Spain
[2] Department of Rheumatology, Hospital Prínceps d'Espanya, Spain

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Abstract. Skeletal metastatic lesions arising from gastric cancer are uncommon and usually of the osteolytic type. In order to gain a better understanding of its radiological spectrum, we report two atypical cases of skeletal metastases from gastric adenocarcinoma presenting with unusual radiographic, CT and scintigraphic features. In one patient multiple ossifying skeletal muscle metastases and bone metastases with spiculated periosteal reaction occurred as a presenting manifestation of the malignant disease. The other patient developed widespread osteosclerotic metastases with a superscan pattern on bone scintigraphy.

Key words: Gastric adenocarcinoma – Skeletal metastases – Muscle metastases – Periostitis – Super bone scan

Introduction

Bone metastases from gastric cancer are generally of the osteolytic type, although diffuse osteoblastic lesions are occasionally described as an unusual feature of this tumour.

Spiculated or sunburst periosteal reaction is an uncommon response to bone metastases and, when present, may erroneously suggest the presence of a primary bone tumour. Reported cases of periosteal sunburst reaction in metastatic lesions from adenocarcinoma of the stomach are exceptionally rare. Furthermore, skeletal muscle is one of the most unusual sites of metastasis from any malignancy.

We report two histologically proven cases of far-advanced gastric adenocarcinoma presenting with unusual imaging features: ossifying skeletal muscle metastases, spiculated periosteal reaction, widespread osteosclerotic lesions and super bone scan pattern. Our cases, as well as a review of the literature, may broaden our perception of the the imaging appearance of these lesions.

Correspondence to: J. A. Narváez

Case reports

Case 1

A 60-year-old man was referred with a 6-month history of weight loss, diffuse bone pain and serum elevation of

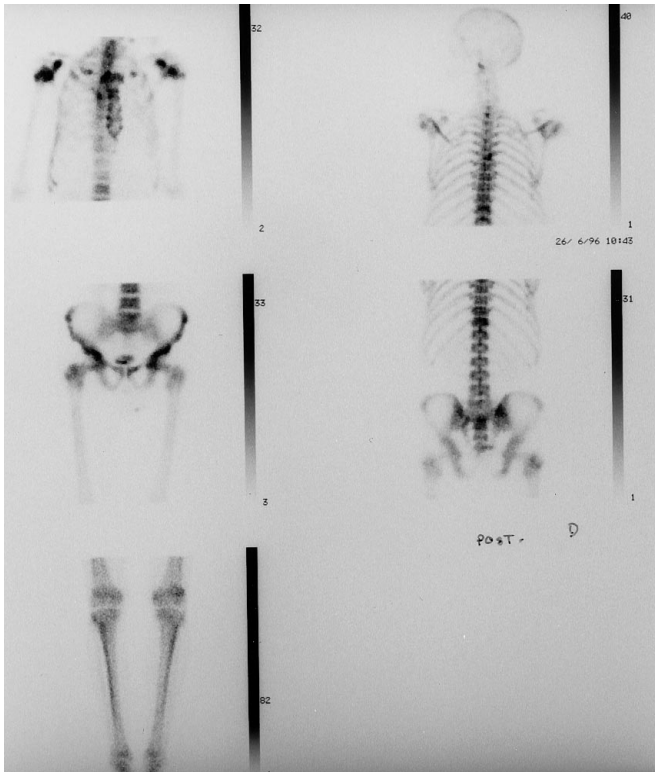
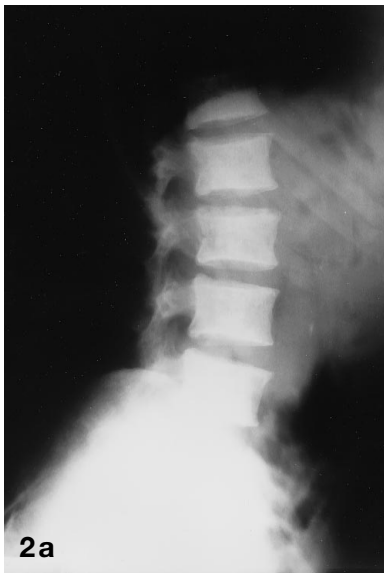
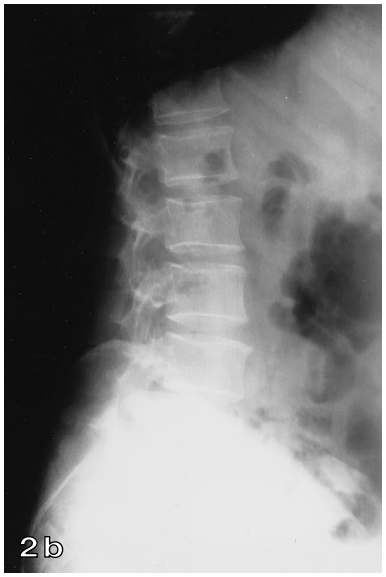
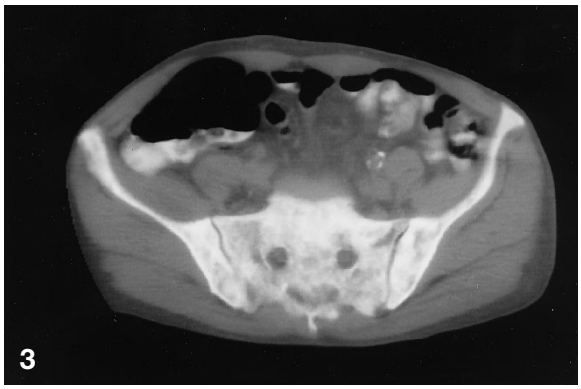
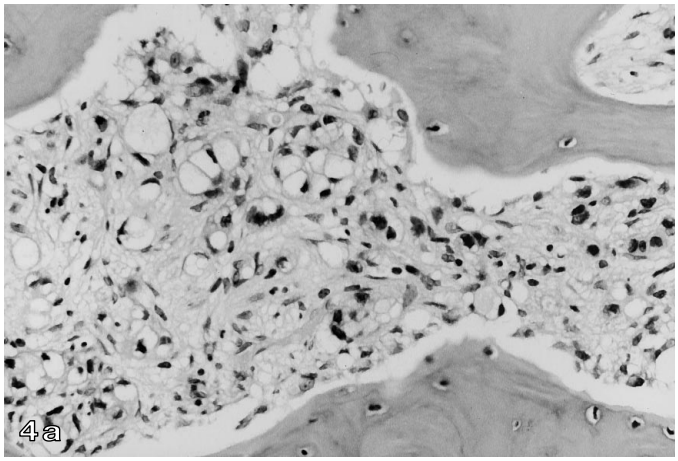


Fig. 1. Case 1. Superscan: increased accumulation of the radiopharmaceutical agent diffusely throughout the skeleton, with minimal activity in the soft tissues and kidneys









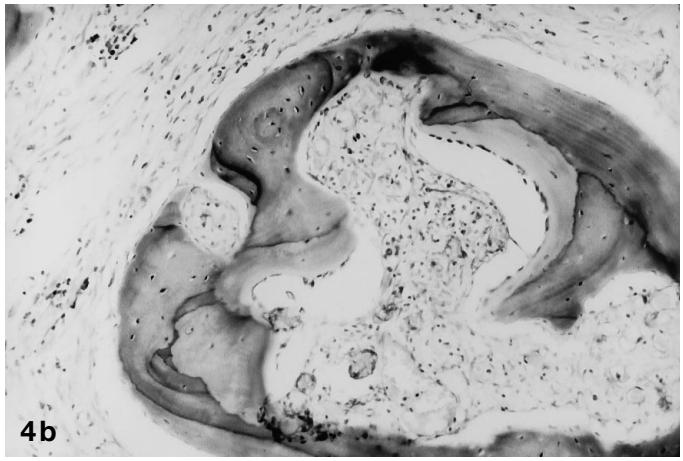


Fig. 2 a, b. Case 1. **a** Lateral view of lumbar spine shows widespread osteosclerotic lesions. **b** Two years previously its radiological aspect was normal

Fig. 3. Case 1. CT scan demonstrating a uniform increase in radiodensity of pelvic bones

Fig. 4 a, b. Case 1. **a** Haematoxylin and eosin stained and **b** Giemsa stained. Bone biopsy of the pelvis: the bone marrow is packed with carcinomatous deposits with signet rings cells

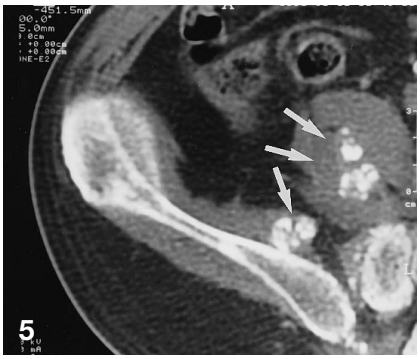
alkaline phosphatase. Two years previously, a diagnosis of gastric adenocarcinoma had been established, and a partial gastrectomy was performed. The conclusive stage was pT3 pN1 M0, and complementary chemotherapy (FAMTX regimen: 5-fluorouracil, doxorubicin and methotrexate) was administered, with apparent complete remission. At time of admission bone pain was mild, more intense at night, and relieved dramatically with low doses of acetaminophen. Physical examination showed no abnormal signs apart from some discomfort when the patient moved around on the examination couch. Laboratory studies disclosed an elevated erythrocyte sedimentation rate (76 mm/h) with normocytic normochromic anaemia and increased alkaline phosphatase (12.5 μkat/L; normal: 0.6–2 μKat/L); serum calcium, phosphate, liver function tests, and protein immunoelectrophoresis were normal.

A ^{99m}Tc bone scintigraphy showed a "superscan" pattern: diffusely increased skeletal uptake of the radiotracer, with minimal activity in the soft tissues and kidneys (Fig. 1). Radiographs performed at admission revealed widespread osteoblastic skeletal lesions predominating in the axial skeleton: ribs, pelvis, thoracic and lumbosacral spine (Fig. 2) and the proximal femora and humeri. A CT scan of the chest and abdomen confirmed the diffuse chalky sclerosis in the axial skeleton without evidence of extraosseous metastases (Fig. 3).

A biopsy of the pelvis was performed; the histological examination showed an infiltrating adenocarcinoma with signet ring cells (Fig. 4), suggesting a diffuse type of gastric cancer. Local recurrence was ruled out by endoscopic examination.

Case 2

A 49-year-old man with no significant past medical history was referred with a 3-month history of right-sided lumbar sciatica. Systemic questioning revealed asthenia and discrete weight loss.



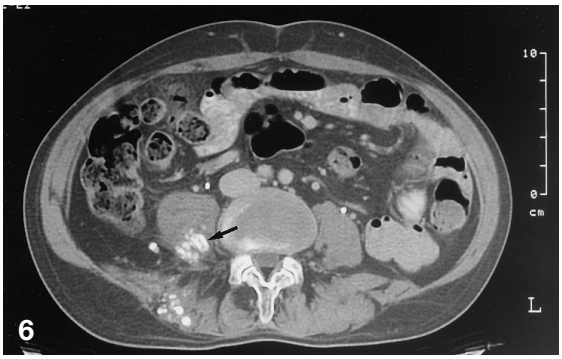


Fig. 6. Case 2. CT scan showed enlargement of right psoas muscle with multiple calcifications. One oval-shaped calcification *(arrow)* clearly depicts more dense periphery and radiolucent center corresponding to cortical and medullar bone. Note other ossified nodules at right posterior paraspinal muscles. None of these muscle lesions have adjacent bone involvement

Fig. 5. Case 2. CT scan shows an ill-defined osteolytic lesion of right iliac wing with sunburst periosteal reaction. Note the presence of ossified metastases in the right iliacus and psoas muscles *(arrows)*

Laboratory abnormalities included an elevated erythrocyte sedimentation rate (81 mm/h), mild normocytic normochromic anaemia and increased serum alkaline phosphatase (3.3 μkat/L).

Roentgenographic and CT examination revealed multiple mixed osteolytic–osteosclerotic lesions on lumbar spine and pelvis, some of them with sunburst periosteal reaction (Fig. 5). Computed tomography also disclosed a number of partially ossified skeletal muscle metastases, without adjacent bone involvement, in the right psoas and posterior paravertebral muscles (Fig. 6).

Biopsy of one paraspinal muscular lesion was compatible with adenocarcinoma. Further investigations revealed a gastric adenocarcinoma.

Discussion

The incidence of skeletal metastasis from gastric cancer ranges from 2 to 17.5% [1]. Clinical manifestations related to such osseous metastases more frequently are a late complication occurring years after total removal of the primary tumour. They are usually osteolytic or, less commonly, mixed osteolytic–osteosclerotic, although diffuse osteoblastic lesions may be an unusual feature of this tumour [2]. To our knowledge, only few histologically proven cases of osteoblastic metastases of gastric carcinoma have been reported previously [3–5], some of them with a radiological pattern of widespread sclerotic skeletal metastases similar to our first case [3].

The differential diagnosis of diffuse bone sclerosis includes widespread metastases, lymphoma, leukaemia and other infiltrative processes (myelofibrosis, osteosclerotic myeloma variants including the POEMS syndrome, mastocytosis), metabolic conditions (Paget's disease, renal osteodystrophy, axial osteomalacia), fluorosis and congenital dysplasias such as osteopetrosis and sclerosteosis [2]. Although diffuse sclerotic bone lesions are a well-recognized manifestation of metastatic disease, this pattern is most commonly encountered in patients with carcinoma of the prostate, and, less constantly, in carcinomas of the lung, breast, pancreas, colon and urinary bladder, malignant carcinoid tumour and medulloblastoma [6].

The factors that are involved in the production of sclerotic vs lytic lesions remain obscure. Reactive bone sclerosis, whether due to benign or malignant disease, reflects a relatively nonaggressive infiltrative process which permits time for osteoblastic repair. Therefore, the relatively indolent clinical course and the raised serum alkaline phosphatase in our first patient is not surprising. Elevation of serum alkaline phosphatase level in patients with skeletal metastasis reflects the magnitude of osteoblastic activity in the absence of liver disease [7].

The "superscan" found in our first case is a characteristic pattern defined as an increase in the ratio of skeletal to renal uptake in an isotopic bone scan with decreased or absent activity of the kidneys despite all other evidence indicating normal renal function. The uptake of radiopharmaceutical is uniformly intense in the skeleton, and minimal in soft tissue and the kidneys. Such scans are similar in appearance to normal scans except for a greater contrast between bone and soft tissue and an absence or considerable reduction of activity in the kidneys. The "superscan" condition has been reported in diffuse metabolic diseases (hyperparathyroidism, osteomalacia, Paget's disease, renal osteodystrophy, and hypervitaminosis D), haematologic diseases (multiple myeloma, lymphoma, systemic mastocytosis, aplastic anaemia, myelofibrosis, leukaemia, and Waldenström macroglobulinaemia), fibrous dysplasia, and metastatic carcinoma, particularly from the prostate or breast, and less commonly from bladder or lung [8–11], although a few cases of gastric carcinoma have also been reported [12–14]. Therefore, gastric carcinoma should also be considered on differential diagnosis when super bone scan is seen.

The interest in our second case involved the unusual presentation of gastric adenocarcinoma with bone metastases producing periosteal reaction and ossifying skeletal muscle metastases without adjacent bone involvement.

Spiculated periosteal reaction is generally a sign of underlying malignant process, commonly present in primary bone tumours such as osteosarcoma or Ewing sarcoma [2], whereas it is a rare finding in metastatic disease. As a general rule, periosteal new bone is either absent or of limited extent in metastatic lesions, a characteristic that differs from the extensive degree of periosti-

tis that generally accompanies primary malignant tumours of the skeleton. In a recent review of 70 cases with periosteal reaction to bone metastases [15], the most common primary tumour showing this response was prostatic carcinoma, followed by bronchial carcinoma, neuroblastoma and carcinoma of the colon or rectum. Only three examples of gastric cancer were reported. The majority of cases were associated with osteoblastic metastases.

Despite its high blood supply, the skeletal muscle is a rare site of haematogenous metastases from any malignancy. The incidence of metastases to skeletal muscle ranges from 1 to 6% [16–17], and they are usually associated with rapidly growing anaplastic neoplasms with numerous metastases in other tissues. In a large autopsy series of patients with gastric carcinoma [18], diaphragmatic involvement was found in 6% of cases, but no other muscle metastases were reported; half of these patients were nonoperative cases and probably, in most of them, diaphragmatic involvement resulted from direct extension rather than from haematogenous seeding. Furthermore, a review of the literature revealed additional case reports of skeletal muscle metastases from a primary gastric carcinoma [19–23].

The ossification of these metastases is also infrequent and has been identified in gastric carcinoma [20], other gastrointestinal malignancies, transitional cell carcinoma of the bladder, carcinoma of the breast and bronchogenic carcinoma [2]. The cause of this neoplasm-induced heterotopic ossification remains obscure, although it has been suggested that this process may be caused by the interaction of mucin-producing tumour implants, local haemorrhage and thrombosis, and the presence of large quantities of gamma-carboxyglutamic acid, an amino acid associated with the calcification of bone matrix formation [20].

Sometimes, as in our second case, bone or skeletal muscle metastases are the presenting manifestation of gastric carcinoma [3, 20]. Carstens and Resnick [3] reported a case of a patient with abdominal symptoms attributed to peptic ulcer disease, in whom the presence of diffuse sclerotic bone lesions raised up the suspicion of gastric carcinoma which was confirmed by endoscopic biopsy of benign-appearing antral ulcers. In the same way, Rosenbaum et al. [20] reported another case in whom back, hip and shoulder inflammatory pain due to skeletal muscle metastases of mucin-producing carcinoma was the initial complaint of an occult gastric adenocarcinoma diagnosed at autopsy.

In summary, our cases, as well as a review of the literature, suggest that the clinical spectrum and imaging appearance of metastatic bone disease from gastric carcinoma may broadly range from the most frequently encountered purely osteolytic or mixed osteolytic–osteosclerotic focal or diffuse lesions to atypical patterns of presentation, including widespread sclerotic skeletal metastases with superscan pattern on bone scintigraphy, skeletal muscle metastases with or without adjacent bone involvement and metastatic disease to bone with periosteal sunburst reaction. These features seem to be infrequent, but may be, as in our second case, the initial presentation of an occult primary gastric carcinoma.

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