Jikeikai Med J 2010 ; 57 : 141-7

Case Report

Chronic Arthritis of the Knee due to Synovial Metastasis

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ABSTRACT

A 65-year-old man with advanced gastric adenocarcinoma complained of left knee pain and swelling lasting for 2 months. Laboratory studies demonstrated mild inflammation and hemorrhagic joint effusion. Magnetic resonance imaging revealed hydrarthrosis and a tumor within the suprapatellar pouch. Diagnostic arthroscopy with multiple synovial biopsies indicated metastatic adenocarcinoma. Synovial metastasis is rare. To the best of our knowledge, this is the first case of synovial metastasis of adenocarcinoma to be reported in Japan, and only 47 cases have been reported worldwide. The diagnosis can be established with cytologic examination of the synovial fluid or histopathologic examination of the synovium. The knee is the most frequently affected joint, and adenocarcinoma is the main histopathological type. The mechanism of synovial metastasis remains unclear. In the present case, spread via a hematogenous route was considered most likely. Because disease metastatic to a joint carries a poor prognosis, with an average survival of less than 5 months, the possibility of joint metastasis should be considered in an elderly patient with a malignancy and chronic arthritis. Early cytological or pathological examinations are important because they allow better treatment and care. (Jikeikai Med J 2010 ; 57 : 141-7)

Key words : arthritis, joint metastasis, synovium, adenocarcinoma, knee

INTRODUCTION

Metastasis to synovial tissue is uncommon. Only 47 cases have been reported worldwide[1-41]. The diagnosis can be established with cytologic examination of the synovial fluid or histopathologic examination of the synovium[40]. Direct invasion of the synovium from a periarticular bony metastasis has been regarded the most likely mechanism[40,41]. We describe a case of chronic knee arthritis due to synovial metastasis of adenocarcinoma. In this case, the most likely mechanism was considered spread via a hematogenous route.

CASE REPORT

A 65-year-old man presented to the general surgery department of our hospital because of a weight loss of 5 kg during the previous 6 months. After he was admitted, and an endoscopic examination revealed carcinoma of the stomach (T4N3) (Fig. 1). Computed tomography (CT) of the abdomen with contrast enhancement showed multiple metastases to the liver (Fig. 2). The primary tumor could not be resected because of the advanced stage of the disease ; therefore, the patient underwent systemic chemotherapy. In addition to the weight loss, the patient also complained of left knee pain and swelling lasting for 2 months and was referred to the department of

Received for publication, August 18, 2010

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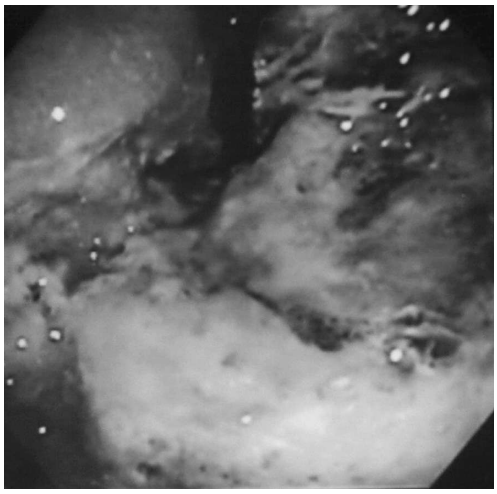
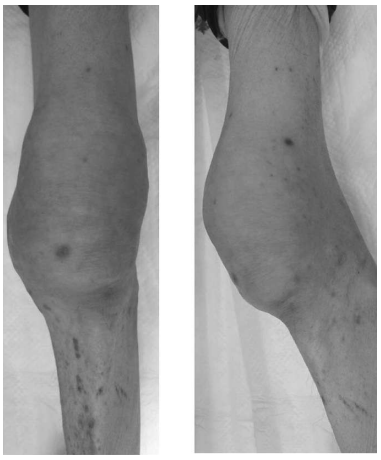


Fig. 1. Gastrointestinal fiberoptic endoscopy showed a stricture due to a tumor with ulcer at the gastric cardia.



(a) (b)

Fig. 3. Appearance of the left knee: (a) anteroposterior view, (b) lateral view

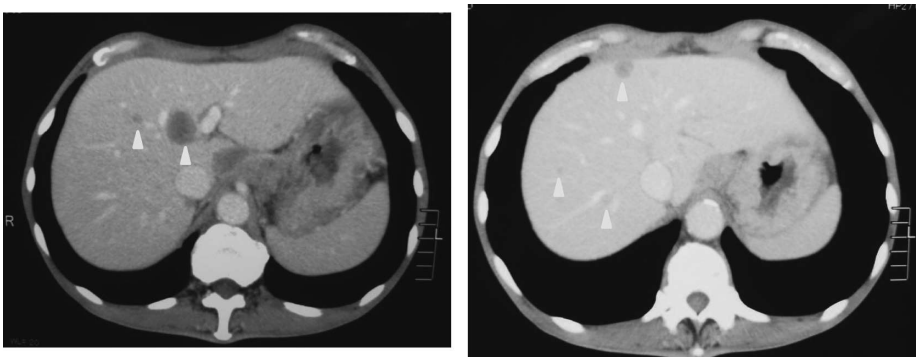


Fig. 2. A CT scan of the abdomen with contrast enhancement. Several nonenhanced tumors (▲) were detected in the liver.

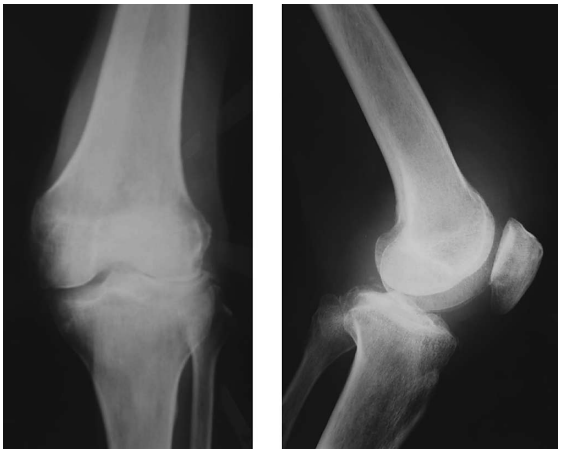


Fig. 4. Plain radiographs of the left knee with degenerative changes and swelling of the soft tissues.

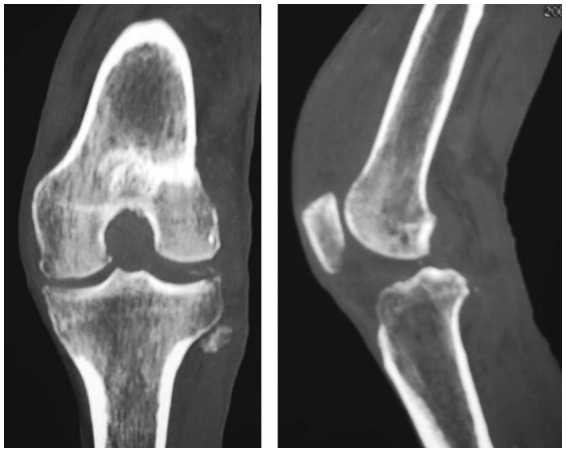
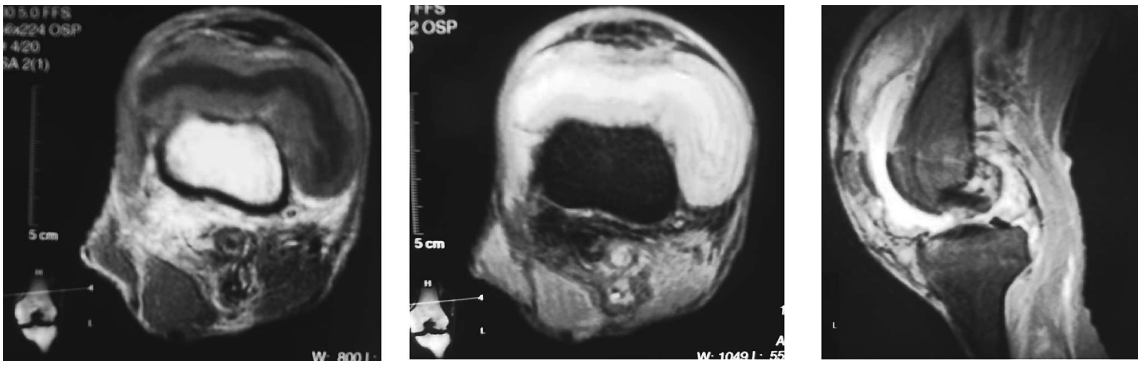


Fig. 5. A CT scan.



(a) (b) (c)

Fig. 6. A MRI scan showing a wide low-intensity isointense area in the suprapatellar pouch. Abnormal lesions could not found in the bone marrow. (a) T1-weighted image (b) (c) T2-weighted image

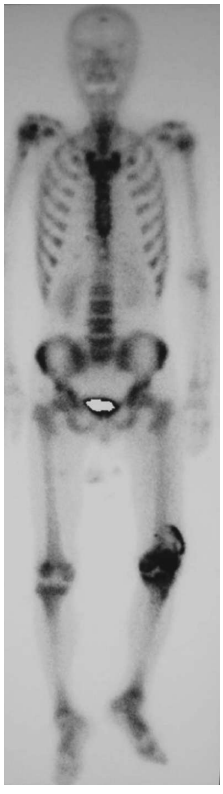


Fig. 7. A whole-body Tc-99m bone scan showing increased uptake around the left knee (periarticular bone and suprapatellar pouch)

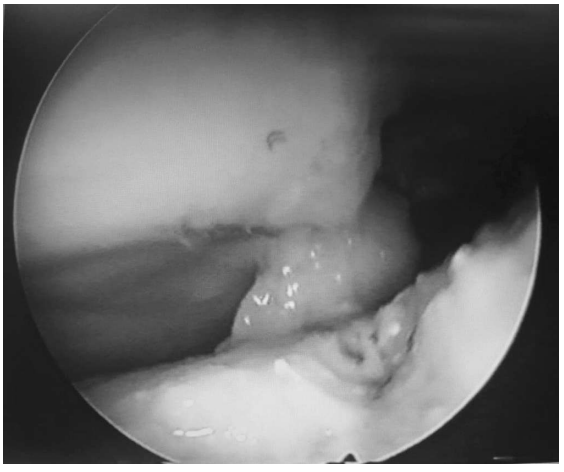


Fig. 8. Arthroscopy showing a swollen synovium in the suprapatellar pouch.

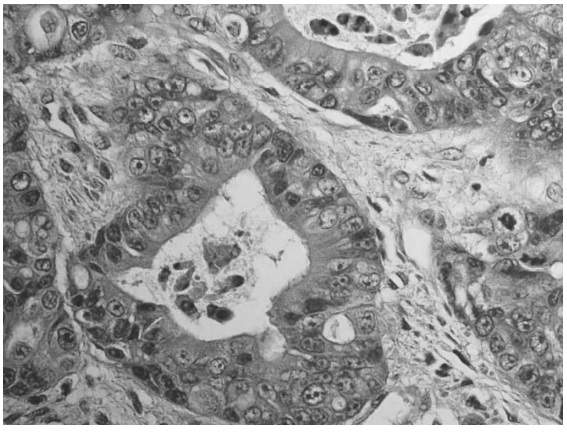
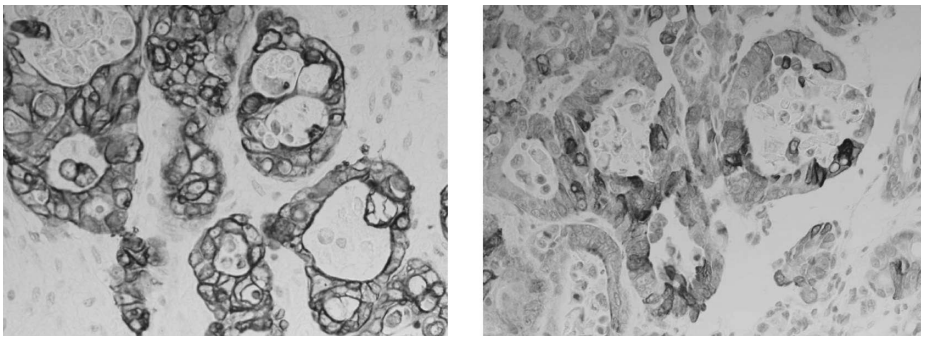


Fig. 9. Atypical cells forming glands in the synovial membrane (hematoxylin-eosin stain; original magnification, ×400)

orthopedics in May 2008. Examination of the left knee revealed tenderness and swelling with reduced mobility (range of motion: 0-100 degrees) (Fig. 3). Laboratory examination demonstrated mild inflammation, with a white blood cell count of 9,000/μl (normal: 4,500-8,500/μl); a C-reactive protein level



(a) (b)

Fig. 10. Cytokeratins 7 and 20 were detected in neoplastic cells. (original magnification, ×400) (a) Cytokeratin 7; (b) Cytokeratin 20

of 1.6 mg/dl (normal: 0.0–0.3 mg/dl), and an erythrocyte sedimentation rate of 92 mm (normal: 4–20 mm). Levels of tumor markers were elevated: carcinoembryonic antigen was 846 ng/ml (normal values: 0.0–5.8 ng/ml), and CA19-9 was 2,112 U/ml (normal: 0.0–37 U/ml). The joint effusion was hemorrhagic, and joint fluid cultures were negative for bacteria. Cytologic examination of the synovial fluid was not performed.

Plain radiographs and CT scans showed degenerative changes in the medial part of the knee (Fig. 4, 5). Magnetic resonance imaging (MRI) revealed hydrarthrosis and a tumor within the suprapatellar pouch. However, abnormal lesions were not identified in the bone marrow (Fig. 6). A whole-body Tc-99m bone scan showed increased uptake in the left knee (Fig. 7).

Conservative treatment with corticosteroid injections and physiotherapy was not effective. Diagnostic arthroscopy with multiple synovial biopsies was performed in July 2008. Macroscopically, the synovium was swollen and white (Fig. 8), and pathological examination indicated metastatic adenocarcinoma (Fig. 9). Immunohistochemical studies showed cytokeratins 7 and 20 (Fig. 10).

Despite additional systemic chemotherapy and local analgesic radiation, the patient's condition rapidly deteriorated, and he died 2 months after the diagnosis had been established.

DISCUSSION

Synovial metastasis was first reported by Karten and Bartfeld in 1962[1], and only 47 cases have been reported to date[1–41]. Characteristics of the 48 cases, including the present case, are summarized in Table 1. The patients were 20 females and 28 males with a mean age of 61 years (range, 13–96 years). In these 48 cases, the knee was the most frequently affected joint (28 cases), followed by the shoulder (5 cases), the ankle, and the sternoclavicular joint (4 case). Metastases were more frequent in the lower extremities[40]. The most frequent sites of primary tumors were the lungs (14 cases) and the colon (10 cases), followed by the stomach, the kidney, and the skin (3 cases). Several authors have emphasized the importance of careful examination of the lungs, because they are the most common source of synovial metastasis when the primary tumor is unknown[36]. The most common histopathological type was adenocarcinoma (24 cases), followed by squamous cell carcinoma (6 cases) and malignant melanoma (3 cases).

In most reviewed cases, plain radiographs usually appeared normal or showed minimal degenerative changes, except for cases with evident bone invasion. Both MRI and CT were helpful for evaluating periarticular soft tissue and the spread of disease. In many cases, technetium-99m bone scans showed increased uptake within the affected areas. Joint fluid was generally bloodstained and tended to rapidly reappear after aspiration[40].

Table 1. Characteristics of the 48 cases

Case	Age	Sex	Joint	Histological type	Origin	Year	Author	Reference
1	59	M	Finger	Squamous cell carcinoma	Lung	1962	Karten I	1
2	66	M	Knee	Squamous cell carcinoma	Lung	1965	Benedeck TG	2
3	13	F	Knee	Lymphoma	Unknown	1973	Emkey RD	3
4	63	M	Knee	Squamous cell carcinoma	Lung	1974	Gall EP	4
5	70	F	Knee	Adenocarcinoma	Stomach	1974	Roques C-F	5
6	62	F	Knee	Adenocarcinoma	Colon	1975	Goldenberg DL	6
7	53	F	Knee	Adenocarcinoma	Breast	1975	Moutsopoulos HM	7
8	51	F	Hip	Adenocarcinoma	Colon (sigmoid colon)	1976	Graham DF	8
9	67	M	Ankle	Transitional cell carcinoma	Bladder	1977	Bevan DA	9
10	53	M	Shoulder	Adenocarcinoma	Kidney	1977	Fremland A	10
11	51	F	Hip	Not known	Lung	1978	Meals RA	11
12	61	F	Knee	Adenocarcinoma	Lung	1979	Fam AG	12
13	68	M	Knee	Adenocarcinoma	Lung	1980	Fam AG	13
14	77	F	Shoulder	Adenocarcinoma	Lung	1980	Fam AG	13
15	69	M	Sternoclavicular	Clear cell carcinomaa	Lung	1980	Murray GC	14
16	54	F	Sternoclavicular	Lymphoma	Unknown	1980	Adunsky A	15
17	71	F	Knee	Rhabdomyosarcoma	Soft-tissue	1981	Weinblatt ME	16
18	73	M	Knee	Malignant melanoma	Cutaneous	1982	Speerstra F	17
19	29	F	Knee	Malignant melanoma	Cutaneous	1982	Shenberger KN	18
20	55	M	Sternoclavicular	Squamous cell carcinoma	Tongue	1983	Rozboril MB	19
21	62	M	Elbow	Squamous cell carcinoma	Lung	1983	Philipson JD	20
22	83	F	Knee	Adenocarcinoma	Colon	1984	Newton.P	21
23	52	M	Knee	Adenocarcinoma	Lung	1984	Newton.P	21
24	19	F	Sternoclavicular	Hodgkin's disease		1984	Newton.P	21
25	60	M	Knee	Adenocarcinoma	Pancreas	1984	Kaklamanis PH	22
26	22	F	Knee	Ewing's sarcoma	Bone	1984	McGirr EE	23
27	59	F	Ankle	Chordoma	Sacrococcyx	1986	Agoada D	24
28	76	M	Knee	Adenocarcinoma	Colon	1987	Evans PD	25
29	96	F	Shoulder	Adenocarcinoma	Unknown	1988	Benhamou CL	26
30	61	M	Ankle	Adenocarcinoma	Lung	1989	Lario BA	27
31	75	M	Knee	Adenocarcinoma	Stomach	1990	Kolstad k	28
32	58	F	Hip	Renal cell carcinoma	Kidney	1992	Chakravarty KK	29
33	57	M	Ankle	Renal cell carcinoma	Kidney	1992	Chakravarty KK	29
34	59	M	Temporomandibular	Adenocarcinoma	Colon	1993	MacAfee KA	30
35	58	F	Knee	Ductal adenocarcinoma	Breast	1995	Munn RK	31
36	47	M	Knee	Small cell carcinoma	Lung	1996	Thompson KS	32
37	71	M	Knee	Mixed-cell nodular lymphoma		1996	Thompson KS	32
38	60	M	Shoulder	Adenocarcinoma	Lung	1998	Morbidi M	33
39	63	M	Knee	Malignant melanoma	Cutaneous	1999	Tandogan RN	34
40	59	M	Knee	Not known	Colon	2000	Zissiadis Y	35
41	64	M	Knee	Adenocarcinoma	Lung	2002	Younes M	36
42	71	M	Knee	Squamous cell carcinoma	Ureter	2002	Younes M	36
43	83	M	Knee	Adenocarcinoma	Colon	2002	Beckers C	37
44	67	M	Temporomandibular	Adenocarcinoma	Stomach	2004	Smolka W	38
45	70	F	Knee	Adenocarcinoma	Colon (rectum)	2005	Devis P	39
46	74	F	Shoulder	Adenocarcinoma	Colon	2007	Capovilla M	40
47	72	M	Knee	Adenocarcinoma	Colon	2008	Currall VA	41
48	65	M	Knee	Adenocarcinoma	Stomach?	2008	present case	

The diagnosis of synovial metastasis can be established with cytologic examination of the synovial fluid or with histopathologic examination of the synovium[40]. Cytologic evaluation appeared to have a low sensitivity but was easy to perform and produced results rapidly[40]. Several authors have suggested performing an additional synovial biopsy, because the absence of malignant cells in the synovial fluid does not rule out metastasis[40]. Immunohistochemical studies might be helpful for identifying the primary tumor, especially in patients without a history of malignancy. In the present case immunohistochemical studies of the synovium showed that cytokeratins 7 and 20 were expressed by neoplastic cells. This finding suggests that the stomach can be regarded as the origin of the metastasis, even though the gastric biopsy was not performed.

The differential diagnosis of monoarthritis inflammatory disease (such as gout and chondrocalcinosis) usually includes avascular osteonecrosis, septic arthritis, synovial sarcoma, pigmented villonodular synovitis, and metastasis to bone surrounding the joint space (such as the patella). The mechanism of the bone metastasis is not clearly understood, but 2 possible processes have been considered: direct invasion of the synovium from a periarticular bone metastasis and metastasis via the hematogenous route. The former has been considered most likely, because in almost every case some changes are found on X-ray films or bone scans[41]. However, in the present case the spread via a hematogenous route seems more likely, because gastrointestinal tumors do not usually metastasize to the bone and because abnormal lesions could not be identified in the bone marrow with MRI. Furthermore, the specificity of bone scan analysis seems to be low, and increased uptake near the joint cannot be considered evidence of metastasis to bone.

Because disease metastatic to a joint appears to be extremely aggressive and presents at the time of diagnosis as a widely disseminated disease with an average survival of less than 5 months, palliative treatments, such as systemic chemotherapy, local analgesic radiation therapy, and surgical procedures (synovectomy, external or internal fixation), are often performed. In general, synovitis is resistant to nonsteroidal anti-inflammatory drugs. Only after the primitive tumor has been resected and no other metastasis has been found can curative treatments, such as joint resection with prosthesis, be performed[40].

In an elderly patient with a malignancy and chronic arthritis, the possibility of joint metastasis should be considered. Early cytological or pathological examinations are important because they allow better treatment and care.

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