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Surgical removal of bone and muscle metastases of renal cancer

Fifteen men and six women with renal cancer underwent surgical removal of metastatic lesions in bone (19 patients) or muscle (two patients). The operation was carried out 2 years before nephrectomy/renal resection in two patients, on the same occasion in four, and 1–196 months after in 15. Surgical interventions of various kinds were undertaken, resulting in the loss of a lower limb in seven patients and an upper limb in one.
The observed 5-year survival was 4 out of 10. Six patients were alive at follow-up, five of them without evidence of disease. Eight of the remaining 15 patients died of an unrelated disease (five without evidence of tumor); the other seven patients died of metastatic tumor disease. Local recurrence was diagnosed, and removed, in two patients. The results compare favourably with reports on surgically removed pulmonary metastases of renal cancer and seem to justify an aggressive attitude towards solitary bone and muscle metastases of renal cancer.

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Considerable improvements have been made in the non-surgical treatment of some metastatic cancers during recent years, but this is not the case in metastatic renal cancer. The effect of cytostatics, hormones and radiotherapy is mainly palliative (Rodriguez & Johnson 1978, Child et al. 1982, Fosså et al. 1982). Surgical therapy may, however, be beneficial in certain cases of metastasis of renal cancer and long survival has repeatedly been reported. This applies particularly to surgically removed lung and brain metastases (Barney & Churchill 1939, Störtebecker 1951, Kulski 1978, O'Dea et al. 1978). Only a few cases of operation for metastasis in the musculoskeletal system have been published (Chisholm 1975, Tolia & Whitmore 1975, Grabstald 1976). As we have operated on 21 patients with renal cancer metastasis in bone or muscle, we decided to review and report our results.

Patients and methods

Twenty-one patients with bone or muscle metastasis of renal cancer underwent surgical treatment at the Department of Orthopaedic Surgery, Sahlgren Hospital, Gothenburg, Sweden, between 1968 and 1981 (Table 1). Fifteen patients were male and six female. The mean age at nephrectomy was 59 years, 54 (46–69) for the males, and 71 (54–79) for the females. Eleven patients were referred from other hospitals.

The renal tumor

The primary tumor was located in the left kidney in 15 patients and in the right in five. One patient, a 79-year-old woman (Case 1), had bilateral tumors.

All patients underwent nephrectomy, except a 50-year-old man (Case 2); he had bilateral fibromuscular dysplasia of the renal arteries and underwent a partial nephrectomy with the removal of a tumor which measured 4.5 cm in diameter. Case 1 who had bilateral cancers was subjected to nephrectomy on one side and partial nephrectomy on the other with a 4-week interval. The nephrectomy was perifascial in 19 patients and intrafascial in two. It included adrenalectomy in 12 patients and lymphadenectomy in five.

The metastases

In two patients, the metastasis was located in the thigh musculature. In the other 19 patients, it af-

Table 1. Operative procedures for metastases in 21 patients

Case	Sex	Age[1]	Time[2]	Location of bone or muscle metastasis	Operation for bone or muscle metastasis (primary site)	Operation for metastasis elsewhere (months after operation for renal tumor)
1	F	79	−3, −2 −3, −2	Distal left femur (pathologic fracture)	1. Incisional biopsy 2. Hip joint disarticulation	
2	M	50	−5 −2	Left sternoclavicular joint	1. Incisional biopsy 2. Extirpation of clavicle + resection of sternum and first rib	
3	M	49	0	Right ilium	Hemipelvectomy	
4	M	47	0	Proximal right femur	1. Curettage + filling with acrylic cement and internal fixation (AO)	1. Craniotomy (+110) 2. Craniotomy (+111)
			+73	Local recurrence	2. Resection of femur + long-stem Moore prosthesis with acrylic cement spacer	
			+80	Local recurrence	3. Hemipelvectomy	
5	M	58	−1 0	Left ilium and adjacent spine	1. Incisional biopsy 2. Extended hemipelvectomy	
6	F	72	0	Proximal left femur	Resection of femur + long-stem Moore prosthesis with acrylic cement spacer	
7	M	51	+1	Distal left femur and left ilium	Thigh amputation + resection of iliac wing	1. Resection of right second rib (+15) 2. Resection of left sternoclavicular joint and left first rib (+20)
8	F	73	+1	Left humerus (pathologic fracture)	1. Bore biopsy 2. Interscapulothoracic amputation	
9	M	49	+1	Left ilium	Resection of iliac wing	Decompressive laminectomy (+4)
10	M	68	+1	Right scapula	Resection of scapula and adjacent clavicle	Osteosynthesis of pathologic fracture of right femoral neck (+12)
11	F	71	−1	Proximal left femur (Pathologic fracture)	1. Tumor evacuation + filling with acrylic cement and osteosynthesis (Ender)	
			+3		2. Hemipelvectomy	
12	F	54	+12	Left sternoclavicular joint	1. Resection of clavicle, sternum, and first rib	Internal fixation of right humerus as prophylaxis against pathologic fracture (+25)
			+18	Local soft tissue recurrence	2. Excision	
13	M	56	+15	First lumbar vertebra	Complete vertebrectomy + bone transplantation	
14	M	69	+17	Proximal right femur	Resection of femur + osteosynthesis (AO)	
15	M	48	+18	Left ilium	Extended hemipelvectomy	
16	F	76	+25	Neck of left femur (pathologic fracture)	Femoral head and neck replacement (Christiansen)	
17	M	55	+33	Left thigh muscles	Extirpation of hamstrings and adductor magnus	
18	M	54	+37	Left side of L1–L3	Partial removal of L1–L3 + bone transplantation	Thoracotomy (+13)
19	M	58	+45	Proximal right femur	Resection of femur + long-stem Moore prosthesis with acrylic cement spacer	
20	M	55	+54	Proximal right femur	Resection of femur + long-stem Moore prosthesis with acrylic cement spacer	Craniotomy (+12)
21	M	46	+196	Left thigh muscle	Resection of vastus medialis and vastus intermedius	

[1] Age at operation for renal tumor.
[2] Time interval to operation for metastasis.

fected different parts of the skeleton: the shoulder girdle or humerus in four patients, the vertebral column in two, the ilium and adjacent spine in one, and the pelvic girdle and/or femur in 12. The skeletal or muscle metastasis was located in the left half of the body in 14 patients, the right in six, and the middle in one (L1). Of the 19 patients with unilateral renal tumor and metastasis not located in the middle of the body, 13 had the metastasis on the same side as the primary tumor.

In 12 patients, symptoms from the metastasis, i.e. local swelling and pain, with or without pathologic fracture, were the first signs of renal cancer. In the other nine patients, clinical investigation was initiated as a result of symptoms from the urinary tract or because of symptoms such as fatigue and weight loss; in these patients, there was a free interval of mean 4 (5–194) months after nephrectomy until symptoms of metastasis appeared. These symptoms were palpable tumor or pain, with or without pathologic fracture. Before the appearance of bone metastasis, one patient (Case 18) had undergone surgery for a lung metastasis and another, (Case 20), for two brain metastases (Table 1).

Clinical investigations included intravenous urography, renal angiography, radiography of the lungs, and scintigraphy of the skeleton and the liver. (Computed tomography had not yet been introduced at our hospital.) In most patients, angiography of the lesion was carried out in addition to plain radiography. Five patients underwent biopsy before the definitive operation, one of them (Case 11) in conjunction with osteosynthesis of a pathologic fracture.

Treatment

The removal of bone or muscle metastasis was carried out 2–3 months before the nephrectomy/renal resection in two patients, on the same occasion in four, and after 31 (1–196) months in 15.

The operation (Table 1) required the loss of a lower limb in seven patients and an upper limb in one. In Case 4, curettage of a femoral metastasis was carried out during the same session as the nephrectomy. The bone cavity was filled with acrylic cement and prophylactic fixation was achieved using an angulated metal plate and (A0) screws. The patient did not develop signs of recurrence until 6 years later, whereupon resection of the femur was performed; hemipelvectomy, not accepted at first, was carried out 7 months later. Case 11, who sustained a pathologic femur fracture, was first treated by partial tumor evacuation, filling with acrylic cement, and osteosynthesis (Ender nails). A hemipelvectomy was performed 4 months later with a view to removing all residual tumor tissue in the limb.

In two patients, an extended hemipelvectomy was performed. In Case 15, the surgical specimen included a substantial portion of the sacrum and in Case 5, also parts of L4 and L5 (Figure 1). In the latter patient, the resultant large posterior defect was substituted by a long thick myocutaneous flap from the ipsilateral thigh in accordance with a method described elsewhere (Stener 1984).

In four patients (Cases 4, 6, 19, 20), the proximal part of the femur was removed along with the metastasis. The defect was then replaced by a long-stem

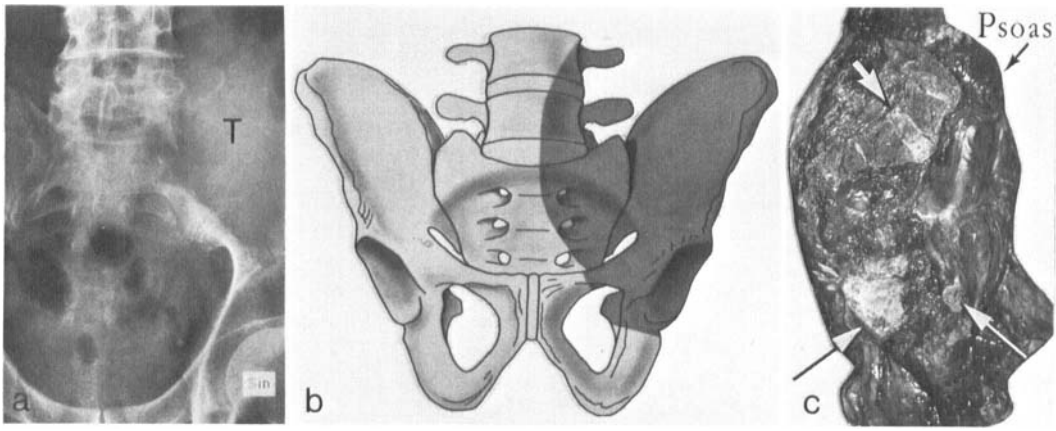

Figure 1. Case 5.
(a) Metastasis of renal cancer (T) has destroyed the left iliac wing and adjacent parts of the spine.
(b) A hemipelvectomy was performed which was extended posteriorly but reduced anteriorly (dark areas).
(c) Medial aspect of the spinopelvic part of the surgical specimen. Left top arrow indicates the lumbosacral disk, left bottom arrow the transected area of the ischium, and right bottom arrow the transected area of the pubis.

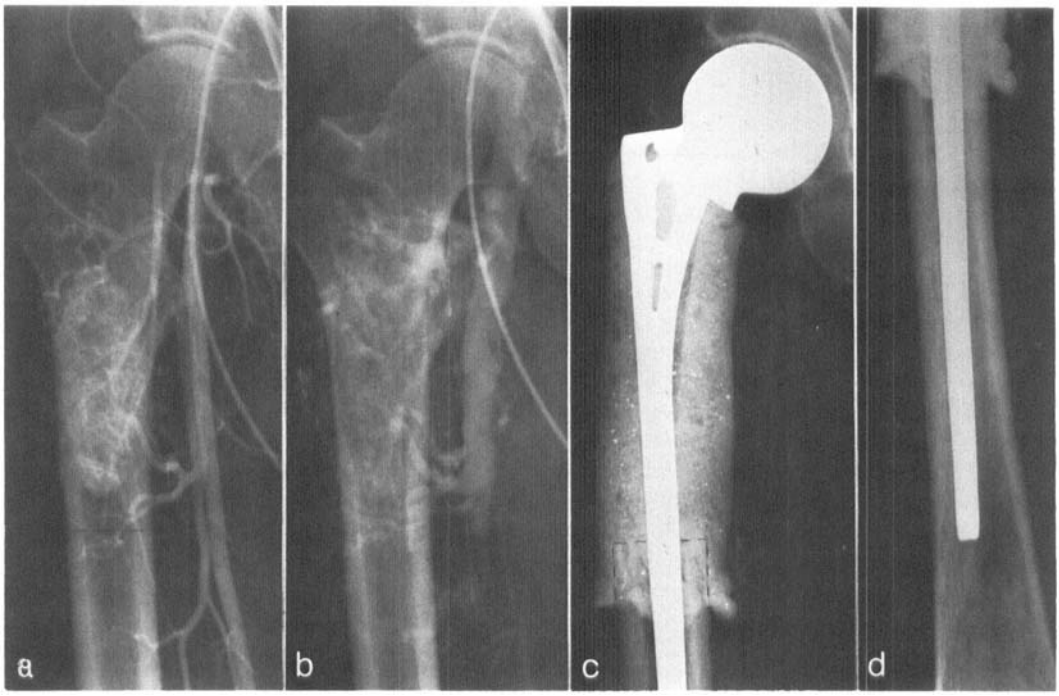

Figure 2. Case 19.
(a and b) Angiography. Highly vascular metastasis of renal cancer in the proximal femur (a), with pronounced arteriovenous shunting (b).
(c and d) After resection of the proximal femur, the defect has been replaced by a long-stem Moore prosthesis and acrylic cement. Level of resection indicated in a and c.

Moore prosthesis with acrylic cement used as a spacer as described previously (Stener & Gunterberg 1983) (Figure 2).

In Case 13, the whole first lumbar vertebra, including parts of the adjacent vertebrae, was removed, after which the spine was reconstructed using a method described previously (Stener 1977) (Figure 3).

Five patients (Cases 4, 7, 9, 10, 12) underwent surgery for metastasis elsewhere in the body after the primary site of bone metastasis had been treated (Table 1). In two of these patients (Cases 4, 7), the metastases were removed; in the others, palliative operations were carried out.

Combinations of cytostatic drugs, given to two patients (Cases 12, 15) for short periods, had no obvious effect; neither had hormones, given for extended periods in three patients (Cases 4, 7, 12). Palliative radiotherapy was often given in the terminal stage of metastatic tumor.

Follow-up

Information was obtained from patient records, autopsy protocols, and death certificates. Examinations that had been performed (often repeatedly) were radiography of the lungs, intravenous urography of the remaining kidney, radiography and scintigraphy of the skeleton, as well as evaluation of function. Postmortem examination had been carried out in 8 of the 15 patients who had died.

Histopathologic methods

All blocks from surgical specimens and autopsies were collected, and new 5-μm sections were stained with H&E and according to the Weigert van Giesen method. The tumors were graded according to the principles described by Skinner et al. (1971).

Results

The mean diameter of the renal tumors was 6.6 (3.0–10.5) cm as estimated by the pathologists (Table 2). Tumor thrombus was not found in the vena cava or main renal vein at nephrectomy in any of the patients.

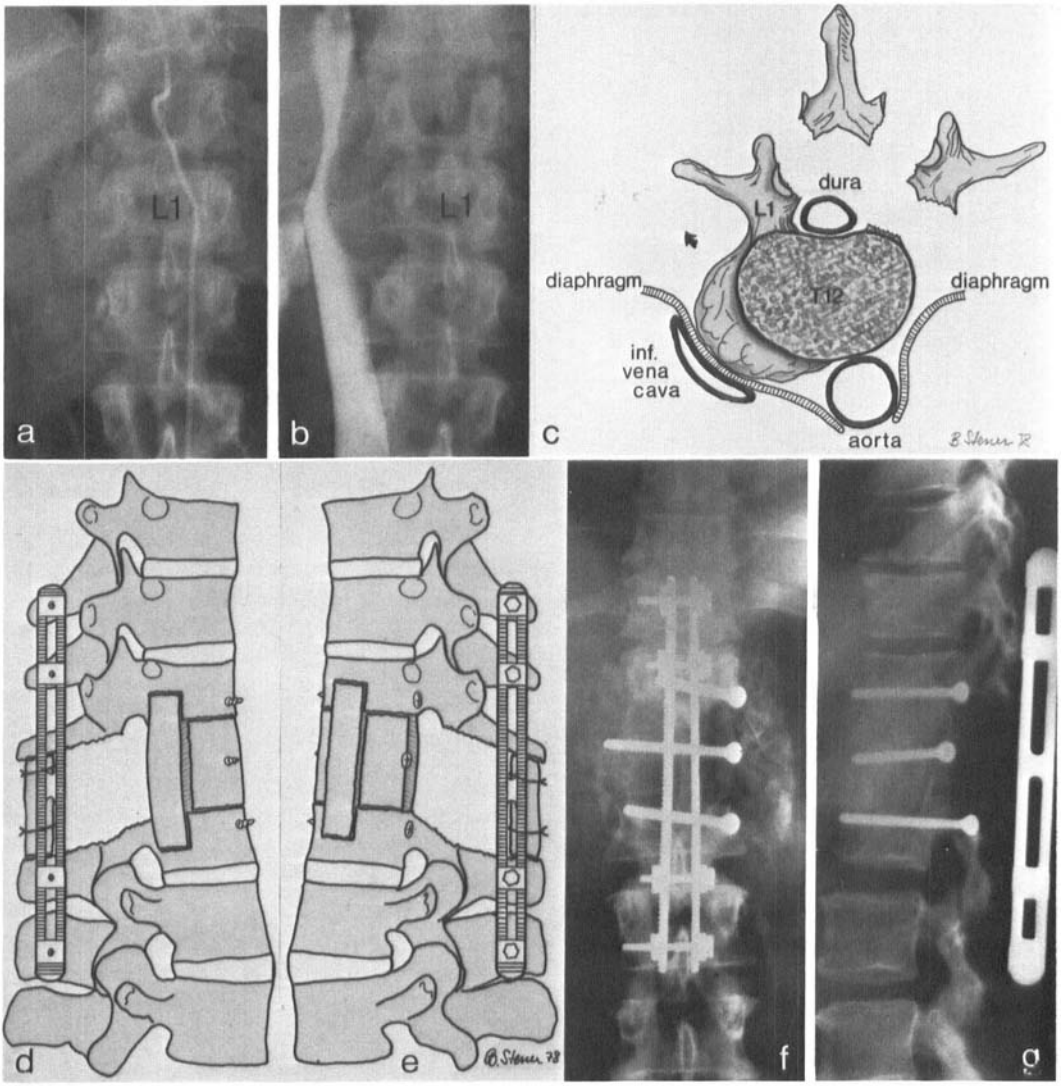

Figure 3. Case 13. Metastasis of renal cancer in L1.
As revealed by late phase of aortography (a) the tumor has expanded outside the vertebra on the right side making an impression in the inferior vena cava (b).
The right crus of the diaphragm, located between the tumor and the vena cava (c), facilitated removal of the whole of L1, including the adjacent discs and parts of T12 and L2, without damaging the vein. The lamina and the left pedicle were free from tumor and could be removed separately to allow extraction of the specimen, as indicated by an arrow, without damaging the dural sac with its contents.
The spine was reconstructed using three corticocancellous blocks of iliac bone (d and e). The largest graft, formed as a match-box, was placed obliquely in grooves made inferiorly in the body of T12 and superiorly in the body of L2; it was inserted posteriorly on the right side (d) and came out anteriorly on the left side (e). The three grafts were fixed with three screws inserted posteriorly on the left side (b). Meurig-Williams plates were used for posterior fixation.
Pieces of cancellous iliac bone were placed outside the inserted grafts as visible on radiographs taken 4 weeks after operation (f and g). The result, a block-vertebra, permitted ambulation after 4 months.

Eighteen tumors (in 17 patients) were clear-cell carcinomas, six of them Grade 2 and 12 Grade 3; both tumors in Case 1 were Grade 2. Four tumors were undifferentiated with spindle cell areas (Grade 4); they also exhibited small areas of clear-cell carcinoma. The appearance of the metastasis was identical to that of the primary tumor in all cases. One of

Table 2. Relation between size and grade of the primary tumor, location of metastases, and survival

Patient	Primary tumor		Location of surgically treated metastases	Survival time after first surgical removal of bone or muscle metastasis (months)	State at follow-up
	Size (cm)	Grade			
1	5; 5.5	2; 2	Femur	18	Alive, NED
2	4.5	2	Sternoclavicular joint	149	Dead (unrelated disease, NED)
3	4.5	4	Ilium	2	Dead (autopsy: widespread metastases, including lymph nodes)
4	6	3	Femur, brain	112	Dead (unrelated disease, NED)
5	4.5	3	Ilium and adjacent spine	11	Dead (RED: skeletal and pulmonary metastases)
6	5	3	Femur	14	Dead (autopsy: unrelated disease; NED)
7	3	2	Femur, ilium, ribs, sternum	86	Dead (autopsy: unrelated disease; two vertebral metastases)
8	8	2	Humerus	13	Dead (autopsy: unrelated disease; NED)
9	6	3	Ilium	22	Dead (autopsy: vertebral and adrenal metastases)
10	8	3	Scapula	21	Alive (RED: skeletal metastases)
11	5	3	Femur	48	Alive, NED
12	10	4	Sternoclavicular joint	13	Dead (RED: skeletal and pulmonary metastases)
13	8	3	Vertebra (L1)	15	Dead (RED: metastases to lungs and one vertebra)
14	5	3	Femur	28	Dead (autopsy: unrelated disease; RED: one vertebral metastasis)
15	10.5	2	Ilium	16	Dead (RED: pulmonary metastases)
16	8	3	Femur	10	Dead (RED: pulmonary and skeletal metastases)
17	8	4	Thigh muscles	93	Alive, NED
18	8	3	Lung, vertebrae (L1–L3)	1	Dead (autopsy: unrelated disease; NED)
19	6	3	Femur	10	Alive, NED
20	8	4	Brain, femur	13	Dead (autopsy: unrelated disease; widespread metastases, including lymph nodes)
21	8.5	3	Thigh muscle	45	Alive, NED

NED = no evidence of tumor disease.
RED = radiologic evidence of tumor disease.

the muscle metastases was a clear-cell carcinoma (Grade 3) and the other an undifferentiated, partly spindle cell carcinoma (Grade 4). A single regional lymph node metastasis was recorded at nephrectomy in one patient (Case 3); he had an undifferentiated renal carcinoma (Grade 4).

The operations for bone and muscle metastases were uneventful in all patients. There was only one early postoperative death: a 57-year-old man (Case 18) died 3 weeks after resection of the spine. The cause of death was sepsis following bilateral aspiration pneumonia. Post-mortem examination revealed no metastases.

In 10 patients, the follow-up time after the first surgical removal of bone or muscle metastasis was at least 5 years. Four of these patients (Cases 2, 4, 7, 17) lived for 12, 9, 7, and >8 years after the operation (Table 2). Case 2, a 50-year-old man, who survived longest (12 years), underwent partial nephrectomy for a clear-cell carcinoma 2 months after the removal of a solitary bone metastasis. He died of arteriosclerotic heart disease without clinical evidence of tumor. Cases 4 and 7 died of bronchopneumonia, the former without evidence of disease, the latter with two vertebral metastases (disclosed at autopsy). Case 17 was still alive and without evidence of disease at the follow-up. The observed 5-year survival was thus four out of ten. Of the six patients (Cases 3, 5, 9, 14, 15, 18) who did not survive 5 years, two died of unrelated disease one of them without autopsy evidence of further metastasis.

In 11 patients, the follow-up time after the operation for metastasis was less than 5 years. Four of these patients (Cases 1, 11, 19, 21) were alive and without evidence of disease after 2, 4, 1 and 4 years, respectively. In Case 21, 16 years had elapsed between the nephrectomy and the operation for metastasis; with the addition of 4 years, he had thus lived for more than 20 years after the removal of the primary tumor. Case 10 was alive after 21 months but with radiographic evidence of other skeletal metastases. Six patients died after 10–15 months. Three of them (Cases 12, 13, 16) died of generalized disease. Case 20 also had widespread metastases, but the main cause of death was infarction of the brain. Case 6 died of arteriosclerotic heart disease, and Case 8 of cerebral hemorrhage; both these patients were free of tumor as verified by autopsy.

Of the seven patients who lost a lower limb, five (Cases 4, 5, 7, 11, 15) were fitted with a prosthesis, even those who underwent an extended hemipelvectomy; they learned to walk with or without (Case 7) support. Case 1 who underwent a hip joint disarticulation because of a pathologic fracture of the left femur was paralyzed in the left arm after hemiplegia 10 years previously and, after trial, she was found unsuitable for the use of a prosthesis. She was grateful, however, to have undergone removal of her left lower limb which was useless: it was painful, fractured without hope of healing, and paralyzed. Case 3 who underwent a hemipelvectomy for an apparently solitary metastasis in the right ilium died after 2 months from generalized disease before he had adjusted to wearing a prosthesis. He was relieved, however, of the severe pain he suffered before operation. Case 8 who lost an upper limb (interscapulothoracic amputation) received a cosmetic prosthesis with a movable elbow joint. All four patients (Cases 4, 6, 19, 20) in whom the defect after a proximal femur resection was replaced by a long-stem Moore prosthesis and acrylic cement had a satisfactory ambulatory function, three of them using support in one hand and one (Case 19) in both hands. Case 13 who underwent a complete vertebrectomy (Figure 3) was relieved of pain and regained good ambulatory function without support; his well-being lasted until symptoms of generalized disease appeared. The loss of function was negligible in the two patients (Cases 17, 21) who underwent removal of various thigh muscles, in the three patients (Cases 2, 7, 12) who lost a sternoclavicular joint, and in the two patients (Cases 7, 9) who underwent resection of an iliac wing. Case 10 had poor active motion of his right shoulder after resection of not only the scapula and clavicle but also adjacent parts of the trapezius and deltoid muscles. Case 14 had the inconvenience of

shortness in one lower limb after a 7-cm femoral resection. Case 16 who sustained a pathologic femoral neck fracture at the age of 78 years received palliation from a replacement of the femoral head and neck by an endoprosthesis. Case 18 had unimpaired motor function in the lower limbs after partial removal of the upper three lumbar vertebrae, but unfortunately he died 3 weeks after operation.

Discussion

Several of the 21 patients operated on for bone or muscle metastasis of renal cancer had a good long-term survival. Moreover, eight of the 15 patients who were dead at the follow-up had died of unrelated disease (five without evidence of tumor). In five of these eight patients, the cause of death was cardiac or cerebral lesions due to arteriosclerosis, which is not surprising considering the fairly high mean age of the 21 patients: 59 years at the time of nephrectomy.

The survival of our patients with bone or muscle metastasis seems to be at least as good as that of renal cancer patients operated on for pulmonary metastases. Five-year survival rates of 31 and 40 per cent have been reported following surgical removal of solitary pulmonary metastases (Wilkins et al. 1961 and Choksi et al. 1972, respectively). The survival of the two patients with muscle metastases, 45 and 93 months, seems remarkable, especially since the tumor in the latter patient was Grade 4. Moreover, these patients still have no evidence of further metastases. The satisfactory rehabilitation of the amputated patients who were fitted with a prosthesis (six of eight) seems to justify the removal of a solitary bone metastasis of renal cancer even when ablative surgery is necessary.

Local recurrence was diagnosed, and removed, in two patients (Cases 4, 12). None of the other patients showed any clinical signs of local recurrence, nor did autopsy (eight patients) reveal any remaining tumor where a metastasis had been removed. Case 4 who had a local recurrence twice would probably have escaped both if the proximal femur had been resected initially (instead of curettage) and replaced by a long-stem Moore prosthesis and acrylic cement. However, this type of operation had not yet been conceived when the metastasis was diagnosed. The second recurrence would have been avoided if the patient had accepted hemipelvectomy as treatment for the first recurrence.

The method of replacing the defect after a proximal femur resection by a long-stem Moore prosthesis and acrylic cement has been practised at our orthopedic institution for almost 10 years. The fear that the cement, used as a spacer between the neck of the prosthesis and the femur, would fracture and break up under load seems to be unfounded. It has not happened in any of the 11 patients operated on so far. The mean observation time is more than 8 years for the three youngest patients (aged 19, 23, and 33); they underwent the operation for a benign but locally aggressive bone tumor (Stener & Gunterberg 1983). We believe that this method, which is simple and inexpensive, is especially useful for patients suffering a solitary metastatic lesion in the upper femur. These patients, usually elderly, do not load the limb too heavily and their life expectancy is not many years.

Most unfortunately, the 56-year-old man who was relieved of pain and regained good ambulatory function after a complete vertebrectomy developed pulmonary metastases. Another patient, a 33-year-old woman with a giant-cell tumor in T11, in whom the same method was used for spinal reconstruction after a complete vertebrectomy (Stener 1977), still has a very good function after more than 8 years. Her reconstructed spine has successfully stood the test of a completed pregnancy: 3.5 years after operation she gave birth to a child (Stener 1984).

The renal carcinomas of other series of patients with skeletal metastases have generally been reported as being of the clear-cell type (Freid 1946). In the present study, most tumors (18/22) were of this type, and metastatic spread to other organs than the skeleton was uncommon. One patient (Case 4) had brain metastases (removed), one (Case 18) a solitary

lung metastasis (removed), and four (Cases 5, 13, 15, 16) radiologic evidence of lung metastases. Of the six autopsied patients with a Grade 2 or 3 clear-cell carcinoma, only one had metastatic spread outside the skeleton; this was Case 9 who, besides vertebral metastases, had a metastatic nodule in his remaining adrenal gland. The two other autopsied patients (Cases 3, 20), who had Grade 4 tumor, both had metastatic spread outside the skeleton.

Fifteen of the 20 unilateral primary tumors affected the left kidney, whereas no side predominates in large series. The localization of the metastasis to the same side of the body as the primary tumor in most patients could possibly be due to an easier hematogenous spread of tumor cells to more closely situated parts of the body. It has been suggested that the paravertebral venous plexus of Batson plays a role in the spread of renal cancer metastases to the skeleton (Batson 1940, Arkless 1965). Hematogenous rather than lymphogenous dissemination in the present series is supported by the finding of lymph node metastasis at nephrectomy in only one patient. This figure should be compared with a lymph node involvement in 5–33 per cent of the patients with renal cancer reported in the literature (Chisholm 1975).

Our results allow the conclusion that it is justifiable in many cases to remove a solitary metastasis of renal cancer affecting the musculoskeletal system. Such operations may be indicated for palliation and can also result in long, disease-free survival.

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