MUSCLE AND SMALL INTESTINAL METASTASIS OF RENAL CELL CARCINOMA MARKEDLY RESPONSIVE TO INTERFERON-α THERAPY : A CASE REPORT

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Skeletal muscle and small intestine are rare sites of metastasis in renal cell carcinoma. Therefore very few reports of interferon-alpha (IFN-α) therapy exist for these types of metastasis. Here, a case of metastatic renal cell carcinoma to muscle and jejunum is reported. After IFN-α therapy for 9 weeks, muscle metastasis completely disappeared and intestinal lesions were markedly reduced. However, subsequent patient compliance for this therapy was poor, resulting in death after relapse of the RCC.

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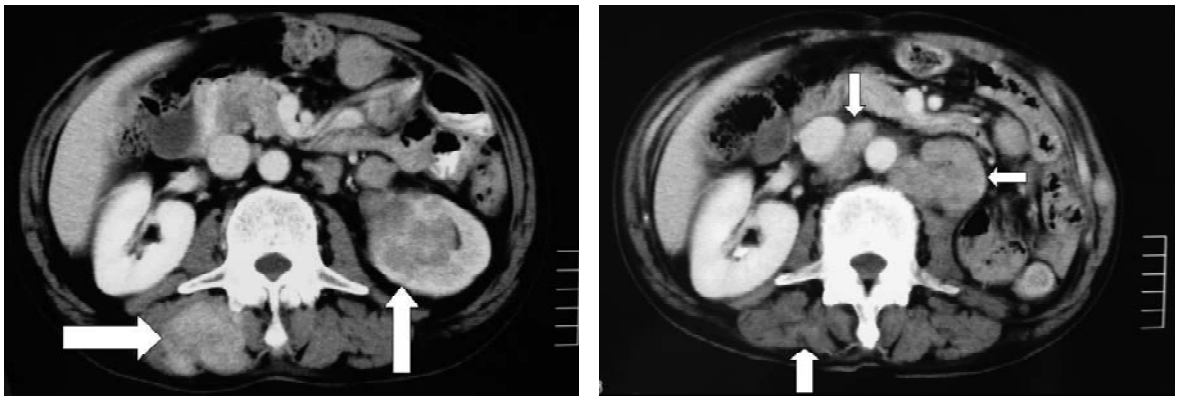
Key words : Renal cell carcinoma, Metastasis, Small intestine, Muscle, Interferon

CASE REPORT

A 53-year-old male had undergone partial duodenectomy and Billroth I type of reconstruction due to duodenal ulcer at the age of 29. He presented to the hospital with general fatigue. Laboratory data indicated a hemoglobin level of 6.2 g/dl. However, all other data were within normal limits. Enhanced computed tomography (CT) indicated a left renal tumor and high density mass in the right longissimus thoracis muscle (Fig 1a). The tumor in the muscle was greater than 15 cm in sagittal section. Subsequent right hemiplegia was observed. Magnetic resonance imaging (MRI) indicated a 40 mm mass in the left frontal lobe of the brain. Initially tumorectomy of the brain was performed, and then three weeks later a retroperitoneoscopic nephrectomy was performed. Pathological examination indicated Stage pT3aN1M1, unclassified RCC, partly including clear cell RCC (Fig 2a, 2b).

Muscle metastasis rapidly continued to worsen. CT scans (obtained before nephrectomy, 6 weeks after the initial examination) showed many new lesions in other skeletal muscles. Postoperatively, severe anemia continued. Gastrointestinal fiberscopy demonstrated multiple polypoid tumors in the jejunum. Biopsy of the tumor was performed (Fig 3a). Pathologically, the brain tumor, the dorsal muscle and small intestinal tumors were all poorly differentiated (Fig 2c – 2e). Therefore, it was difficult to diagnose the primary tumor site. Clinically, the conclusion was metastasis of a primary RCC because features of a poorly differentiated tumor and clear cell cancer were seen in a single tumor in the kidney, the respective poorly differentiated tumors were morphologically similar, and since no other organs exhibited clinical malignancy.

From 1 week after nephrectomy, systemic immunotherapy (6×10^6 units of IFN-α) was administered 3 days a week. After 6 weeks of this therapy, both muscle and intestinal lesions were markedly reduced (Fig 3b). There were no noticeable adverse reactions due to



a b

Fig. 1. a) Abdominal CT indicating a left renal tumor and an enhanced mass within the right longissimus thoracis muscle (arrows). b) CT scan obtained on the second admission Muscle metastasis completely absent, but bulky lymph nodes present after discontinuation of IFN-α.

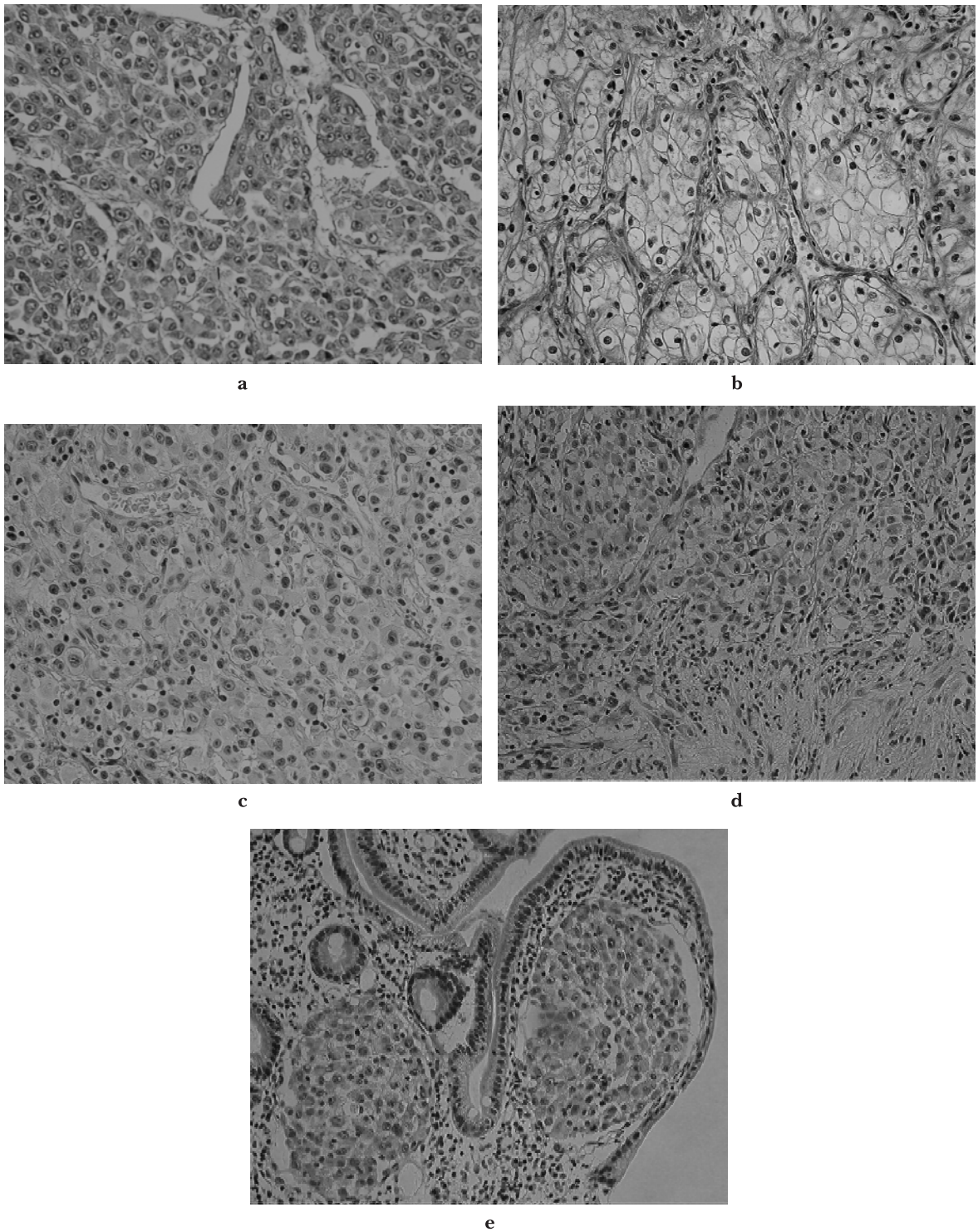


Fig. 2. a) Microscopic findings for unclassified region of the left kidney (HE stain ×200). b) clear cell RCC of the left kidney (HE stain ×200). c) Brain metastasis (HE stain ×200). d) Muscle metastasis (HE stain × 200). e) Jejunal metastasis (HE stain × 100). In each metastatic site, large to medium-sized cylindroid tumor cells with prominent nucleoli are present.

interferon. Oral intake became possible and the patient was able to be discharged, with the intention of continuing immunotherapy as an outpatient. However, patient compliance was poor from this stage, with no attendance for outpatient care. Eventually, interferon therapy was discontinued 9 weeks after starting. Seven weeks after discharge, the patient presented again to the hospital with paraplegia. Although there were no metastatic lesions in the brain and muscle, multiple lymph node, bone and lung metastases had developed, and intestinal metastasis had relapsed (Fig 1b).

We sought to restart interferon therapy, but this could not be continued because of consciousness disturbance and general debility due to uncontrollable hypercalcemia. The patient died 3 weeks after this second hospital admission.

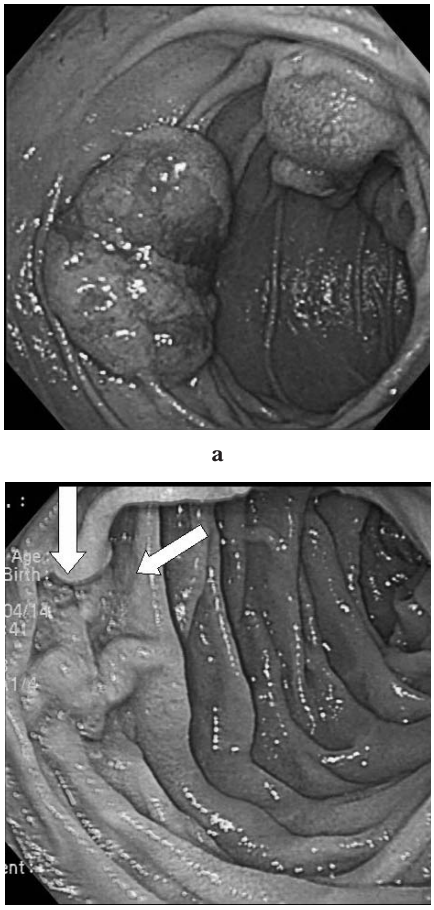


Fig. 3. a) Multiple polypoid tumors in the jejunum. b) Following 6 weeks of IFN-a therapy, tumor sizes decreased markedly. An ulcer has developed at the site originally occupied by tumor (arrows).

DISCUSSION

Incidence of metastatic RCC in the small intestine is 14.6% in autopsy cases[1]. Clinically, however, it is difficult to identify, because of the challenge of diagnosing lesions of the small intestine. Most of these cases are discovered after presenting with symptoms such as nausea, abdominal pain and bleeding[2]. Surgical resection of the small intestine is sometimes performed, but the prognosis is very poor as other metastasis exists in most cases[3].

Most studies of interferon therapy for renal cell carcinoma have shown an overall response rate of 10% to 15%[4,5]. In this case, the prognosis was considered very poor from clinical predictors, such as low Performance Status, multiple metastasis and low hemoglobin[6]. Since there was no abdominal pain or findings of ileus, and given that there were numerous metastases in skeletal muscle, we selected interferon α as systemic therapy, rather than choosing a local therapy option such as resection of the small intestine or resection of intramuscular metastatic sites. The fact that treatment with interferon resulted in shrinkage of the tumor and that relapse occurred after its discontinuation suggests that it was likely to ameliorate further metastatic spread. To our knowledge, this is the first case reported for interferon being effective as treatment for small intestinal metastasis, in which fiberscopy was employed to assess the therapeutic benefit.

As mentioned previously, clinically-evident metastasis to the small intestine is infrequent, and when it is discovered, surgery is often the treatment of choice because of ileus or other considerations[2]. Therefore, one may well conclude that there would be no reports of interferon therapy for small intestinal metastasis. Recently, great advances have been made in enteroscopy[7,8]. This technique offers improvement in the ability to diagnose small intestinal tumors, as compared with conventional means, and reports have also appeared of its use in the discovery of small intestinal metastases of other cancers[9]. The wider dissemination of such a new technique may increase our knowledge about small intestinal metastasis of renal cell carcinoma.

Muscle metastasis of renal cell carcinoma is rare, occurring at rates of 0 to 0.6% in autopsy cases[1]. Palpation, CT scan and MRI are useful in diagnosis. If a solitary muscle metastasis is detected, operative management should be considered.

The medical literature contains only scant reports on the use of interferon to treat intramuscular metastasis, and its effectiveness remains uncertain[10]. In our patient, a response of CR was obtained for the muscle metastasis after treatment for 9 weeks, and no relapse was observed after discontinuation of treatment. In contrast, differences in the efficacy of interferon according to the metastasis site were evident, with enlargement of the small intestinal and lymph node lesions after discontinuation of treatment, and the new appearance of lung and bone metastases. Investigations into the efficacy of interferon for rare sites of metastasis remain inadequate, suggesting a need to investigate more cases.

CONCLUSIONS

This case demonstrates the unpredictable nature of RCC, which can both rapidly spread to many locations within the body, and occasionally respond to immunotherapeutic agents dramatically. Clinically-evident metastasis to the small intestine is rare, and thoroughgoing investigations of the gastrointestinal tract are therefore essential in patients with progressive renal cell carcinoma who present with such symptoms as anemia.

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和文抄録

インターフェロン α が著効した腎癌骨格筋・小腸転移の 1 例

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腎癌では骨格筋転移や小腸転移は稀であり，これらの転移に対するインターフェロン α による療法の報告は非常に少ない．われわれは腎癌骨格筋・空腸転移の 1 例を経験した．9 週間のインターフェロン α 療法により筋肉転移は完全に消失し，空腸転移も著明に縮小した．しかしながら治療の自己中断により病変の再燃を認め，癌死の転帰をとった．

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