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Olgu Sunumu / Case Report

Successfull Treatment of a Child with Advanced Stage Renal Cell Carcinoma

İleri Evre Renal Hücreli Karsinomlu Pediatrik Vakanın Başarılı Tedavisi

Serhan Küpeli[1], Bilgehan Yalçın[1], Münevver Büyükpamukçu[1]

[1]Hacettepe University, Institute of Oncology, Department of Pediatric Oncology, ANKARA

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ABSTRACT

Treatment of renal cell carcinoma (RCC) in children is based on an extensive surgery. Radical nephrectomy with lymph node dissection is sufficient for most of the stage I-II tumors. However, in advanced disease some different management strategies have been defined including immunotherapy. We present a 9-year-old girl with advanced stage RCC, inoperable at the time of diagnosis and successfully treated with interferon-α (IFNα) after operation.

Key Words: Renal cell carcinoma, treatment, interferon alpha, children

ÖZET

Renal hücreli karsinomun çocukluk çağındaki tedavisi esas olarak geniş cerrahi rezeksiyon ile yapılmaktadır. Çoğu evre I-II vaka için radikal nefrektomi ve lenf nodu diseksiyonu yeterli olurken ileri evrelerde immünoterapinin de dahil olduğu farklı tedavi yöntemleri tanımlanmıştır. Burada tanı anında opere edilemeyen, sonrasında interferon alfa ile başarılı bir şekilde tedavi edilen ileri evre renal hücreli karsinomu olan 9 yaşında bir kız sunulmuştur.

Anahtar Kelimeler: Renal hücreli karsinom, tedavi, interferon alfa, çocuklar

INTRODUCTION

Renal cell carcinoma (RCC) in childhood constitutes 2-6% of all renal tumors[1,2]. There are a few case series in literature relating with treatment of this rare entity. Although radical nephrectomy with lymph node dissection is reported as standard treatment for early stages, there is no consensus for treatment of advanced stage disease[3-5]. Here, we report a case of pediatric advanced stage RCC, inoperable at the time of diagnosis, given neoadjuvant chemotherapy and treated with interferon-α (IFNα) after operation. To our knowledge this case is one of a few cases who benefited adjuvant IFNα treatment.

CASE REPORT

A 9-year-old girl was admitted to our hospital with a complaint of painfull swelling on her lower left abdomen. On physical examination there was a solid mass between umbilicus and the left iliac region with irregular borders. Serum biochemistry, complete blood count and urine examination were all normal. Abdominal ultrasonography (US) and computerized tomography (CT) showed a 76x69 mm sized solid mass with calcification, extending from middle and lower poles of the left kidney to the pelvis and multiple enlarged paraaortic lymph nodes. The tumor was considered as inoperable initially because of the proximity to the great vessels. A tru-cut biopsy obtained from the renal mass revealed RCC, clear cell type, Fuhrmann Grade 1-2.

A chemotherapy protocol consisting of cisplatin and dacarbazine, given every 4 weeks and IFNα with a dose of 3 million IU/m^2 5 days in a week were started. After 4 courses of chemotherapy the patient's response was stable disease and a left nephrouretectomy with multiple lymph node excision was performed. Histopathological examination confirmed RCC, clear cell type, Fuhrmann Grade 1-2 and tumoral infiltration in lymph nodes. The patient was considered in stage IIIb according to modified Robson criteria[7]. The same chemotherapy was continued for a total of 10 courses together with IFNα treatment. Cisplatin and dacarbazine chemotherapy was stopped because of mild sensorineural hearing loss. After one year of IFNα administration the schedule was changed to 3 million IU/m^2 2 times/week for one year and once a week for another one year. Treatment was ceased in October 2009. The patient is well without recurrence or metastasis for 5 years from the diagnosis.

Side effects encountered due to cisplatin and dacarbazine treatment were ototoxicity and mild neutropenia which became overt after the 8th chemotherapy course. Renal and liver function tests were normal during the therapy. Related with IFNα administration the patient complainted from flu-like syndrom at the beginning of the treatment. One week after the first administration of the IFNα administration the symptoms like subfebrile fever, headache and myalgia were relieved. Another side effect from IFNα administration was lipodystrophy in areas of injection due to recurrent administration. We did not find any abnormalities in thyroid function tests or lipid profile during the treatment.

DISCUSSION

The incidence of RCC in pediatric age group has been reported to be less than 10 % among the malignant renal tumors and with an equal male/female ratio at different pediatric series[1-4]. Since the differentiation from Wilms' tumor is impossible with imaging studies, sampling of the tumor is necessary for definitive diagnosis[4,6].

The most important prognostic factors for pediatric RCC are tumor stage and extent of surgery[8]. Selle et al.[9] reported event-free survival and overall survival rates of 96% for localized RCC at 5 years, 69% and 75% for regional lymph node-positive, 25% and 33% for distant metastatic RCC, respectively. At the time of diagnosis, surgery was delayed because of the proximity of tumor to the great vessels and four courses of neoadjuvant chemotherapy were given with an intent to facilitate the surgery by decreasing tumor volume. The presented case was classified as stage IIIb because of tumor positive lymph nodes. Although gross-total resection was performed, locally advanced disease has led us to give adjuvant chemo and immunotherapy. Majority of the drugs used in the treatment of RCC are also included in the chemotherapy schemes of pediatric Wilms' tumor[10]. With four courses of chemotherapy combined with immunotherapy a response of stable disease was ensured. The ratio of benefit for these two modalities is difficult to determine although Geller et al. proposed that the outcome for patients with N+M0 pediatric RCC is favorable without adjuvant or any medical therapy[11].

For pediatric RCC, the duration and optimum dose of IFNα as adjuvant therapy were not defined clearly. Pediatric RCC patients treated with IFNα and treatment details is shown in Table 1. Uchiyama et al.[4] suggested a postoperative dose of 3 million IU/m^2 daily for 3-6 months followed by three times a week or every other day for 6-9 months, then two times/week for 1 year, and once a week for 1-2 years. In another study researchers gave IFNα to their 11 patients combined with interleukin-2 in four of them with unknown schedule and they reported no benefit with standard immunotherapy in patients with diffuse disease[10]. Asanuma et al.[12] described 3 patients receiving adjuvant IFNα therapy with beneficial effects. Among the mechanisms of action with immunotherapy by IFNα, immune modulation by

increasing the infiltration of activated dendritic cells and CD8+ T cells in renal tumors and induction of apoptosis or cell cycle arrest have been proposed[13]. Although flu-like symptoms, fatigue, diarrhea, nausea, vomiting, abdominal pain, joint aches, back pain, dizziness, anorexia, increased heart rate, confusion, pancytopenia, increase in liver enzymes and triglycerides, temporary skin rashes, hair loss, depression and suicide have been reported with the use of IFNα none of these side effects except flu-like symptoms at the first week of the treatment occured in our patient.

Table 1. Reported children with RCC treated with interferon alpha

Reference	Age (yr.s)/sex	Stage	Chemotherapy	Radiotherapy	Interferon/ (mo.s)	Outcome
2	3/M	4	ACT-D	No	Yes/?	NED, 14 years
2	14/F	4	5-FU	No	Yes/?	Died, 0.3 years
2	10/F	4	No	No	Yes/?	Died, 1.5 years
4	9/M	3	No	No	Yes/72	NED, 7 years
4	6/M	3	No	No	Yes/36	Lung met., 3 years
5	13/F	3	V+ ACT-D	No	Yes/6	Died, 2 years
5	9/F	3	V	No	Yes/12	NED, 5 years
Present case	9/F	3	Cis+Dac	No	Yes/36	NED, 5 years

V: Vincristin, Cis+Dac: Cisplatin+Dacarbazine, ACT-D: Actinomycin-D, 5-FU: 5-Fluorouracil, NED: No evidence of disease, met: metastasis

Since the patient tolerated IFNα well with a dose of 3 million IU/m^2 five days in a week, we administered it for one year, followed by 3 million IU/m^2 two times/week for another one year and once a week for the last year. Although the complete surgical resection has utmost importance in treatment, based on our experience on the presented case, adjuvant use of IFNα treatment can be considered in patients with locally advanced RCC who are under the risk of recurrence. Being a rare disease, the role of adjuvant therapies in pediatric RCC, including IFNα needs to be investigated in multicentric randomised studies.

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Yazışma Adresi / Address for Correspondence:
Dr. Serhan Küpeli
Hacettepe University,
Institute of Oncology, Department of Pediatric Oncology,
ANKARA
e-mail: serkupeli@yahoo.com

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