مقاله گزارش موردی

پاسخ درمانی به ارلوتينيب در بیماران مبتلا به آدنوکارسینوم پیشرفته ریه

چکیده

معمولاً، در بیمار مشابه به کارسینوم غیر سلول کرچک، ریه، با نظارت اولیه، مابع فراران در پلور و ندول‌های ریوی در طرفه، با داروی خوراکی (Erlotinib (Tarseva; Roche)) درمان شده‌اند. این دارو مهار کننده رسته‌کننده تیروژین کیتار است و از پیام‌های ثانوی سلولی برای رشد سلول‌های سرطانی اپتی‌پاتی جلوگیری می‌کند. بیماران روزی به عدد ۱۵۰ قرص دريافت نمودند.

توصیف نمونه: در بیمار اول پس از دو سال با بیماری دیگر، مثلاً استخوانی و سپس خود ریوی که شده بود، این دارو به نیاز به درمان بیمار نمود. بیمار دوم به مدت ۱۲ ماه پس از شروع درمان داروی ارلوتينيب به بهبود بالینی، بهبود رادیولوژیکی و روزه‌هایی به بهبود روزه‌ها و روزه‌های مرگ‌زا روزه‌های و روزه‌های خود در مدت درمان با Erlotinib بوده‌است.

بحث: با توجه به گزارش‌های متعدد، به نظر می‌رسد مصرف این داروی خوراکی به عنوان خیز اول درمان موارد آدنوکارسینوم ریه در افراد غیر سیگاری ایرانی بسیار مؤثر و کم عارضه است و با افزایش عمر و حفظ کیفیت زندگی بیماران همراه می‌باشد.

کلمات کلیدی: ارلوتينيب، آدنوکارسینوم، سرطان ریه
Dramatic response to erlotinib for advanced lung adenocarcinoma: A case report

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Abstract: We report two non-smoker Iranian patients presenting with massive pleural effusion and multiple lung nodules and diagnosed lung adenocarcinoma. Patients received oral erlotinib 150mg/day. Within three months of medication, both patients showed complete clinical and radiologic response. This response was maintained for 2 years in first patient and continued for 9 months, the time of this report, in the second case. Erlotinib was well tolerated. Nevertheless grade 2-3 rash and grade 1 diarrhea were the only significant toxicities. Both of the patients was able to conduct daily activities throughout their erlotinib therapy.

Conclusion: A subgroup of patients with lung adenocarcinoma who have never been smoker may be good candidates for Therapy with erlotinib as first line.

Keywords: Erlotinib, Adenocarcinoma, Non-smoker, Lung
INTRODUCTION

Lung cancer remains the leading cause of death due to cancer in the world [1]. In Iran, lung cancer is one of the five leading tumors and its incidence has been increasing steadily in both men and women [2]. World wide, Tobacco use account for about 90% of lung cancer [1]. According to a case-control study, 66.5% of all lung cancer cases in Iran are smoker [2]. The Fars Hospital-based Cancer Registry, a major referral center for cancer in southern Iran, has been reported that 32.7% of lung cancer subjects were non-smoker (24.3% of males and 59.6% of females) [3]. So, it seems that the rate of non-smoker lung cancer patients is higher in Iranian population [4]. In the US and Asia, adenocarcinoma is the most frequent histological subtype [5]. Recently non-smoker adenocarcinoma cases have been considered as a distinct diagnostic subgroup with better prognosis than smoker patients. Patients with a never smoking history also have a higher rate of epidermal growth factor receptor (EGFR) mutations, and these mutations have been associated with response to EGFR – thymosine kinase inhibitor (EGFR-TKI) therapy :Gefitinib, erlotinib [5,6]. In a retrospective review of patients treated on phase III trial of carboplatin and paclitaxel with and erlotinib experienced a substantial improvement in overall survival compared with patients who received carbolat and paclitaxel alone; median overall survival were 22.5 versus 10.1 months (HR=0.49; 95% CI: 0.28-0.85) retrospectively [7]. These data have raised the question of whether these patients may benefit from initial Therapy with an EGFR TKI [8,9].

The cancer and Leukemia Group B (CALGB) Phase II trial and the Iressa Pan Asia study (IPASS) Phase III trial represented the model for future drug development in non small cell lung cancer in which a targeted agent is given in a clinically molecularly selected patients populations that has a high likelihood of benefit from the therapy [10]. We report two cases of advanced lung adenocarcinoma successfully treated by EGFR-TKI.

CASE PRESENTATION

Case 1:

Mrs. N.K., 49 year-old homemaker presented with a right side Pleural effusion and some small nodules within the same side of the lung in August 2005. She had an ovarian cyst and mildly elevation in CA-125 levels. Following resection of her benign cyst, level of CA 125 returned to normal but she persistently had nodules within right lung and massive right side pleural effusion. This suggested that the ovary was not to be as the primary site of tumor. Indeed, the histology testing of the plural biopsy suggested that this was the case, reported as metastatic adenocarcinoma; ER and PR was negative in the specimen. There was no obvious primary site elsewhere after physical examination, mammography, abdominal-pelvic CT-Scan and PET – Scan. There was no personal or family history of chronic diseases or malignancy and she was a never – smoker housewife without history of toxic environmental exposure.

From September 2005 she has received 4 cycles of paclitaxel (175 mg/m2) and carboplatin (AUC=6). Despite adding gemcitabin for the next few cycles, she experienced minimal response. We presumed that this was a primary lung adenocarcinoma and as a non-smoker female with lung adenocarcinoma, further treatment choice would be EGFR-TKI. We administered erlotinib for her from October 2005. She showed dramatic response which was seen quite quickly after starting treatment (fig 1,2); but near three years later (October 2008) she experienced an episode of chest pain and further evaluation with bone scan revealed rib and spine metastasis, then she was treated by radiotherapy and zometa.
Case 2:
A 41-year-old never-smoker man presented on January, 2009 with progressive dyspnea for 3 weeks. Chest x ray revealed massive pleural effusion. After temoral of chest tube and relief from pleural effusion, he experienced an acute episode of chest pain. After diagnosis of pulmonary emboli by CT-Angiography, enoxaparin was prescribed. 
After evacuation of the pleural effusion, multiple nodules appeared in the left lung had been appeared. Adenocarcinoma was diagnosed via pleural and lung nodule core needle biopsy. Immunohistochemistry studies were positive for CK7 and negative for CK 20. Mucin was seen in cell block of pleural fluid. Upper GI endoscopy evaluation and barium enema was normal. Ultrasonography of abdomen, pelvis and testicles, CT-Scan of abdomen and pelvis, echocardiography and bone scan were normal. Family history was negative for malignancy and there was no history of exposure to toxic environmental materials. He reported history of proximal lower limb muscle weakness, peribital and skin rashes and symmetrical arthritis which has been diagnosed as rheumatoid arthritis two years earlier and had been treated by prednisolone and chloroquine for 6 month. The treatment was stopped due to severe drug reaction and the diagnosis was changed to dermatomyositis and polymyositis.
From February 2009, he has been treated by erlotinib (150mg/day). After one month of treatment, he revealed complete response. He is on erlotinib and enoxaparin for more than 9 months and until presented report, we observed no nodule on lung CT-Scan up on follow-up (Fig 3 and 4).

**DISCUSSION**

Although tobacco use is the most common etiologic factor for lung cancer; in Iran, it is estimated that approximately 30% of lung cancers occur in patients who have never smoked. There is a unique patient population in Asia who have never been smokers and are suffering from lung adenocarcinoma which is higher among women than men. There is a high response rate to therapy with EGFR-TKI like erlotinib in this group of patients. The two patients who were presented in this report, had most of the characteristics of lung adenocarcinoma in a non-smoker Asian population; and revealed an immediate and rather durable radiographical and clinical response to erlotinib. In the sense, it seems reasonable to use erlotinib as first line systemic therapy in this patient group. Tumor markers, particularly EGFR protein expression, the number of EGFR gene transcripts, and the presence of mutations in the EGFR tyrosine-kinase domain, have also been studied to determines patients who most likely benefit from EGFR-TKI therapy[11]. Rash was the only significant toxicity effect observed in the presented cases, which was tolerable and successfully managed.

Conclusion: A subset of lung adenocarcinoma appears preferentially sensitive to epidermal growth factor receptor tyrosin kinase inhibitors. This patients are non-smoker and could receive first-line therapy with an EGFR TKI.
Figure 2. First case chest CT-Scan, after erlotinib

Figure 3. (a,b): Second case chest CT-Scan before erlotinib

Figure 4. Second case chest CT-Scan after erlotinib

Figure 3. (a,b): Second case chest CT-Scan before erlotinib
REFERENCES


