

CASE REPORT



Efficacy Of Lorlatinib In Combination With Alectinib In Patients With Anaplastic Kinase-Positive Small Cell Lung Cancer With Moderate Lung Disease: A Case Report.

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Abstract:

We evaluated a Comorian girl aged 3 years 6 months with neuroregression and seizures. The child was third born to second-degree consanguineous parents by lower-segment cesarean section due to cephalopelvic disproportion. Birth weight was 3.1 kg with uneventful perinatal history. There was maternal history of normal healthy live birth in the first pregnancy and spontaneous miscarriages in second and fourth pregnancies in early trimesters. The fourth pregnancy was associated with Down syndrome. The mother was given antenatal progesterone for excess bleeding in the first trimester.

Keywords: Infantile Sandhof disease, ventricular septal defect, hexosaminidase, hyperneuropathy, cherry red staining,

Introduction

By revealing genetic defects in anaplastic kinase (ALK)-positive non-small cell lymphoma Lung Cancer (NSCLC), High Potency ALK Tyrosine Kinase Inhibitors (ALK-TKIs) are developed for therapy.

obstacle to achieving a high level of influence in the central nervous system (CNS) [1]. Because of its effectiveness, lorlatinib is a common treatment option for patients ALK-positive non-small cell lung cancer with one or more ALK-TKIs No success.

A 57-year-old Japanese man complained of tinnitus and was presented to the otolaryngology department of our hospital. A contrast-enhanced computed tomography (CT) scan showed a tumor in the upper lobe of the left lung, approximately 40 mm in the long axis.

The hilar and mediastinal lymph nodes were also enlarged. Suspected primary lung cancer, the patient was referred to the Department of Otolaryngology and Respiratory Medicine on the day of admission confirmed.

The results of the 18F-FDG PET/CT and other findings led to the diagnosis of lung adenocarcinoma [cT2bN2M1c (PUL, OSS); stage IVB]. We recommended rebiopsy considering the possibility of a genetic mutation, but the patient refused the examination because of strong coughing during the

first bronchoscopy and progressive symptoms of hoarseness. The patient strongly desired an early treatment, so we initiated first-line therapy with cisplatin (75 mg/m²) and pemetrexed (500 mg/m²) 3 weeks after the first visit.

U pacienta sa však vyvinula renálna dysfunkcia 2. stupňa [kreatinín, 1,83 mg/dl; odhadovaná rýchlosť glomerulárnej filtrácie (eGFR) a vidíme, že ide o čiastočnú odpoveď, ale opacita skla a infiltrácia sa naďalej šíri oboma smermi. V tomto čase sa pacient sťažoval na aktívnu dýchavičnosť a perkutánnu saturáciu kyslíkom. Je asi 82 % vo vnútornom ovzduší. Analýza plynov ukazuje, že parciálny tlak kyslíka je 58,2 torr, čo naznačuje zlyhanie dýchania. Testy funkcie pľúc ukázali obštrukčné poškodenie dýchacích ciest s vitálnou kapacitou (VC) 2,11 l a %VC 57,1 %.

Discussion and conclusions

In the search for advanced lung cancer treatment, driver genes have been identified, and several molecular-targeted drugs have been developed and reported to exhibit remarkable antitumor effects. For ALK-positive NSCLC, alectinib was more effective than crizotinib in phase III trials (ALEX study) and is, therefore, widely used for first-line treatment. Lorlatinib and ceritinib are effective against alectinib-resistant lung cancer and have been used in second-

line treatments, based on the status of the resistance gene. Lorlatinib, which is derived from crizotinib, is structurally optimized to inhibit mutations conferring resistance, including G1202R, and those with a high rate of migration to the CNS. In the CROWN trial, the intracranial response among patients with measurable brain metastases at baseline was 82%, with a complete intracranial response rate of 71%. In the global ALEX, ALTA-1L, and eXalt3 trials, the corresponding complete intracranial response rates with alectinib, brigatinib, and ensartinib were 38%, 28%, and 27%, respectively. Moreover, in the CROWN trial, lorlatinib significantly decreased the cumulative incidence of CNS progression, which suggests that the prolonged progression-free survival seen with lorlatinib may be partly due to the prevention of CNS metastases. In the CROWN trial, progression-free survival was significantly longer among patients with ALK-positive NSCLC who received first-line lorlatinib than among those who received crizotinib. In untreated patients, lorlatinib may eliminate rare preexisting subclones harboring ALK resistance mutations or prevent the emergence of such resistant subclones.

We evaluated a Comorian girl aged 3 years 6 months with neuroregression and seizures. The child was third born to second-degree consanguineous parents by lower-segment cesarean section due to cephalopelvic disproportion. Birth weight was 3.1 kg with uneventful perinatal history. There was maternal history of normal healthy live birth in the first pregnancy and spontaneous miscarriages in second and fourth pregnancies in early trimesters. The fourth pregnancy was associated with Down syndrome. The mother was given antenatal progesterone for excess bleeding in the first trimester.

History and physical examinations pointed toward the diagnosis of GM2 gangliosidosis (Tay–Sachs disease, SD, AB variant). In view of cherry-red spots and coarse facies, GM1 gangliosidosis was also considered. No significant abnormality was noted in complete blood count, electrolytes, or renal and liver function tests. Ultrasonography of abdomen did not reveal any hydronephrosis or other anatomic abnormalities. Computerized tomography scan of brain without contrast was suggestive of mild bilateral symmetric hyperdensity of thalami (Fig. 3). Electroencephalogram (EEG) showed slowing of delta frequencies associated with drowsiness. Video-fluoroscopic assessment for swallowing function was suggestive of aspiration on both fluoroscopic runs. Magnetic gain weight till 5 months of age, after which there was fattening of the growth curve and

failure to thrive. At 6 months, she had developmental arrest followed by progressive neuroregression. She also had severe startle response since 8 months of age. Ten, she started having generalized recurrent seizures from 9 months onward. The epileptic episodes were mostly focal with secondary generalization, with the most severe event reported as having frequency of ten seizure episodes within 2 hours time period despite anticonvulsant therapy. She had also macrocephaly with coarse facial features, persistent laryngomalacia, and hyperacusis. There was no muscle atrophy. Central hypotonia, peripheral hypertonia, and a positive Babinski reflex were elicited. Organomegaly was absent. Ophthalmological examination showed bilateral macular cherry-red spots and an inability to fixate the eyes. At 12 months, she developed gastroesophageal reflux disease (GERD) as well as reactive airway disease. Gastrostomy tube feeding was also commenced. She had frequent episodes of hospitalizations due to repeated aspiration pneumonia, reactive airway diseases, and other central nervous system complications. History and physical examinations pointed .