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Case report

Immunotherapy "Shock" with vitiligo due to nivolumab administration as third line therapy in lung adenocarcinoma

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ABSTRACT

Non-small cell lung cancer is still diagnosed at late stage due to the lack of early symptoms and methods of diagnostic prevention. In the past ten years several targeted therapies have been introduced or explored. Tyrosine kinase inhibitors and immunotherapy are currently considered the most effective and safe therapies in comparison to the non-specific cytotoxic agents. Regarding tyrosine kinase inhibitors the adverse effects have been fully explored, however; on the other hand for immunotherapy there are still several issues to be clarified. We report a rare case of a patient with lung cancer adenocarcinoma who developed vitiligo throughout his body after nivolumab administration.

1. Introduction

Lung cancer is still diagnosed at a late stage due to the fact that there are no early symptoms. Usually most of the patients have a persistent cough which they attribute to their smoking habit. Most patients visit their doctor if they observe hemoptysis or their cough changes character. Unfortunately until now we do not have an effective prevention algorithm. During the last decade tyrosine kinase inhibitors (TKIs) and immunotherapy (nivolumab and pembrolizumab) have entered our everyday clinical practice. The TKIs are based on the expression of the epidermal growth factor receptor (EGFR) and anaplastic lymphoma kinase (ALK) [1–3]. On the other hand in order to administer immunotherapy (pembrolizumab) as first line we need programmed death-ligand 1 (PD-L1) expression > 50% and for second line PD-L1 > 2% (pembrolizumab) [4]. Regarding nivolumab we can administer as second line indifferent of the PD-L1 expression as second line [5,6]. Current guidelines indicate that additional molecular pathways such as; proto-oncogene B-Raf and v-Raf murine sarcoma viral oncogene homolog B (BRAF) and Proto-oncogene tyrosine-protein kinase ROS-1 (ROS-1) have to be investigated upon diagnosis for adenocarcinoma and in squamous cell carcinoma, however; for now these two additional pathways are not obligatory for squamous cell carcinoma as it is with PD-L1 expression [7–10]. In the case of EGFR positive patients and disease relapse we can investigate for the T790M mutation and administer osimertinib [11], while in the case of ALK positive patients upon disease relapse we can use ceritinib [12]. In any case tissue biopsy is the best material to investigate mutations and again re-biopsy should be performed when necessary [13–15].

2. Case

A 65 year old patient was diagnosed with convex probe endobronchial ultrasound endoscopy (EBUS) from a right lower lobe mass (Figs. 1–3). Positron emission computed tomography (PET-CT) revealed

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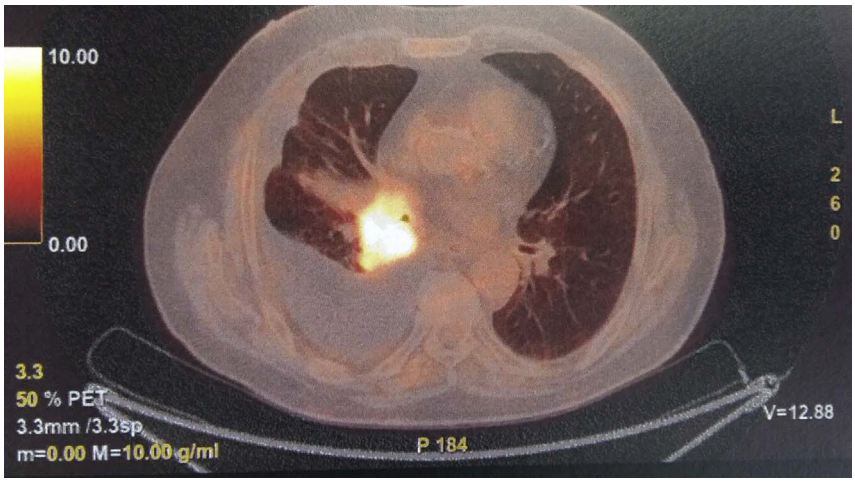

Fig. 1. PET-CT slice presenting the mass in the right lower lobe with pleural effusion.

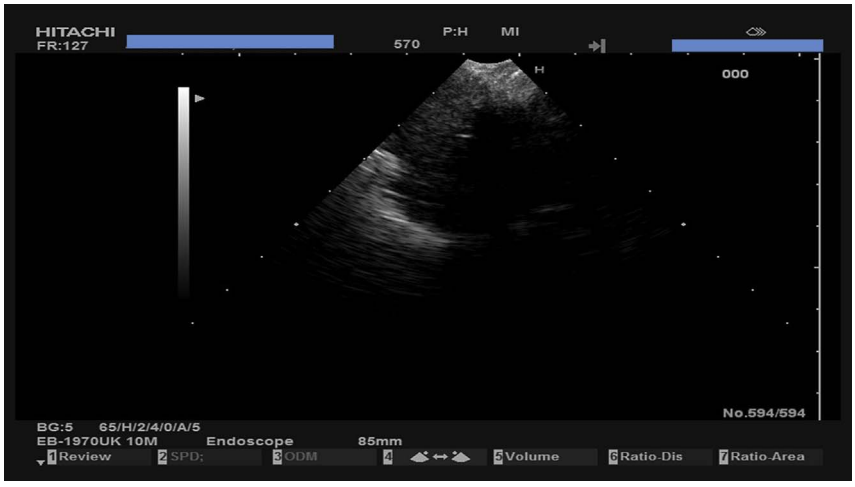

Fig. 2. Figure from the ultrasound source EUB-6500HV presenting the mass during the biopsy procedure (figure by Paul Zarogoulidis).

Fig. 3. Biopsy sample from the mass with a 22G Mediglobe® needle (first biopsy 3 to follow during the procedure).

bone metastasis and the patient was investigated for epidermal growth factor (EGFR) expression and anaplastic lymphoma konase (ALK) expression. Both unfortunately were not identified and therefore a chemotherapy doublet of carbo AUC-6 and pemetrexed was administered. The patient received 6 cycles in total and remained under observation for 4 months where disease relapse was observed in the primary lesion and it was decided to receive carbo AUC-6 and gemcitabine. He received in total 6 cycles and remained under observation for 3 months where disease relapse was observed with liver metastasis. Programmed death-ligand 1 (PD-L1), along with proto-oncogene B-Raf and v-Raf murine sarcoma viral oncogene homolog B (BRAF) and Proto-oncogene tyrosine-protein kinase ROS-1 (ROS-1) were investigated. PD-L1 was observed to be 10% with Dako PD-L1 IHC 22C3 pharmDx kit, while BRAF and ROS-1 expression were negative. Based on these findings and the performance status of the patient (PS-1), it was decided that he received nivolumab. After 4 days from the administration skin scabs were observed. During the next 30 days vitiligo was observed throughout the body of the patient after healing of the skin scabs

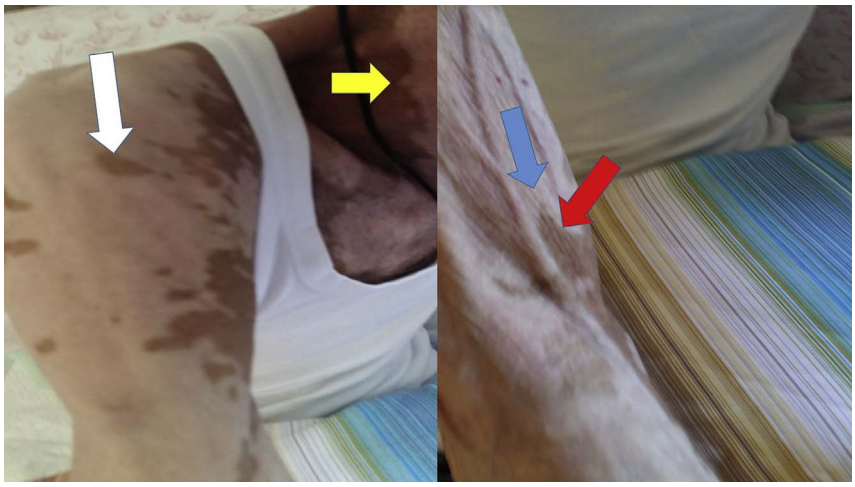

Fig. 4. Patient after 6 cycles of nivolumab; white arrow: area with melatonine, yellow arrow: area with melatonine, red arrow: area with melatonine (right hand), blue arrow: area with vitiligo (right hand). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

(Fig. 4). The patient did not receive any more nivolumab administration, and he receives methylprednisolone 16mg daily and he will be under close follow up for the next 30 days, where a decision will be made based on his clinical status whether he will continue or change his treatment.

3. Discussion

Non-specific cytotoxic agents have severe side effects and in some cases life threatening [16]. Therefore alternative treatments such as; targeted therapies were welcomed. Tkis are considered targeted treatments with mild side effects most commonly observed are a diarrhea, skin rash and in very rare cases pneumonitis. In the case of adverse effects the dose has to be decreased, however; there have been cases where the drug admnistration had to be stopped [17,18]. Immunotherapy on the other hand if it is administered based on the percentage of PD-L1 expression, then it could be considered again as a targeted treatment [6]. Immunotherapy treatment is an efficient alternative to those patients that cannot receive tki treatment and their performance status does not allow non-specific cytotoxic agents. However; for immunotherapy to be a successful therapy the immunological status plays a crucial role. Several factors are responsible for the adverse effects of immunotherapy, these could be summarised to the virus or vaccines that a patient had be exposed and to whether or not there is an underlying or undiagnosed systematic disease [19,20]. To our knowledge the patient that we presented did have a systematic underlying disease and the development of vitiligo was due to the nivolumab administration. The PD-L1, BRAF and ROS-1 molecular pathways were investigated later on his treatment period due to the fact that they were not in the treatment guidelines as they are now. Vitiligo has been previously reported in patients with melanoma receiving immunotherapy [21].

Conflict of interest

None to Declare.

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