control carcinoma harboring the EML4–ALK rearrangement.

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REFERENCES


To the Editor:

Malignant granular cell tumors (GCTs) are extremely rare. We read that De Luca et al1 reported a giant malignant GCT of posterior mediastinum. In this letter, we would like to share our experience of a case with malignant pulmonary GCT and explore the underlying mechanisms by next generation sequencing.

A 63-year-old woman presented with chronic cough for several months. An enhanced chest computed tomography indicated a large solitary mass in the lower lobe of left lung, approximately 14 × 10 × 9 cm in size (Fig. 1). Physical examination, laboratory evaluation, and other radiological tests revealed no significant abnormalities, with the exception of high expression of NSE (67.41 μg/liter, range, 0–16.3 μg/liter). A bronchoscopic biopsy was performed from the basal stem of left lower lobe, and the diagnosis of GCT was considered given that the immunohistochemistry staining of S-100 (+), Vimentin (+), and HMB45 (−). Because GCTs are not sensitive to chemotherapy or radiotherapy, a complete left pneumonectomy together with systemic lymphadenectomy was therefore performed. Pleural metastasis was found during the operation, and therefore, GCT of this patient was malignant. The diagnosis of pulmonary GCT was identified again by postoperative immunohistochemistry staining (Fig. 2). A gene mutation profiling was performed by next generation sequencing (OncoScreen TM 295 genes, Burning Rock Dx, Guangzhou, China; Supplemental Table, Supplemental Digital Content, http://links.lww.com/JTO/A862). The results detected seven mutations on five genes. No copy number variation or fusion/translocation events

Next Generation Sequencing Un Covers Potential Genetic Driver Mutations of Malignant Pulmonary Granular Cell Tumor

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FIGURE 3. EML4–ALK fusion gene in all four examinations (immunohistochemistry/fluorescence in situ hybridization/reverse transcriptase-polymerase chain reaction/next generation sequencer).
Overall, the sequencing results indicate that the abnormalities of ASXL1-mediated, Notch2-mediated, and PARP4-mediated pathways are possibly involved in the disease initiation and progression of MGCT. Targeted therapeutics against PARP family (veliparib and niraparib) or NOTCH family (demcizumab) might be the promising medications; however, the clinical efficacy needs to be further evaluated.

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FIGURE 2. The immunohistochemistry staining results. The tumor is positive for S-100 and CD68, which are the specific markers of granular cell tumors.

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FIGURE 3. Gene mutation analysis results and TCGA data. The mutations of AR, Notch2, Notch4, ASXL1, and PARP4 detected in this sample overlaid as black arrows on the mutation distribution diagrams of these genes from the TCGA project.