The Role Of Single-Cell RNA Sequencing In Cardiac Tumor - A Case Report

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Research Article

Keywords: Single-cell RNA sequencing, Cardiac tumor, Case report

Posted Date: February 24th, 2022

DOI: <https://doi.org/10.21203/rs.3.rs-1364662/v1>

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Abstract

Background: The benign cardiac tumor is a common disease. We often completely removed it by operation. However, the characteristic of the tumor is not studied deeply. Here, we used the technique of single-cell RNA sequencing to analyze cell composition and growth patterns in a giant cardiac tumor.

Case presentation: A 65-year-old woman presented to our hospital with 5 day of chest tightness, dyspnea, lower abdominal distension. Echocardiography revealed a mass in the right atrium. An emergency operation was carried out to prevent tumor shedding. The single-cell RNA sequencing was applied to analysis the nature of the tumor.

Conclusion: Single-cell RNA sequencing is a good manner to analyze the growth pattern and search for therapeutic targets. Based on the result of single-cell RNA sequencing, it is helpful to reduce the recurrence of the tumor and benefit the quality of life of patients.

Background

A cardiac tumor is a common disease. Treatment for the cardiac tumor is generally surgical resection, and show a good prognosis in benign tumor than a malignant one [1]. However, we often do not analyze the cell components and the cause of growth for tumors. Therefore, for a malignant tumor, surgical resection is not enough to obtain a satisfactory survival due to the lack of precision-targeted drugs. Recently, the technique of single-cell RNA sequencing is widely used [2]. It is helpful to understand the potential mechanism of the growth of the tumor. Herein, we report the application of single-cell sequencing in a giant cardiac tumor.

Case Presentation

A 65-year-old (62kg) female patient was admitted to our department in 2021. Her previous history was no special, but hypertension for 10 years. A mass in the right atrium was demonstrated on echocardiography. More seriously, the other mass was stuck in the tricuspid valve orifice. To prevent pulmonary embolism caused by tumor shedding, an emergency operation was carried out.

Two masses were excised under cardiopulmonary bypass. The base of the larger tumor was located in the right atrial wall and filled the right atrium (Figure 1, A). The base of the smaller tumor was located above the tricuspid valve annulus, and the tumor crossed the tricuspid valve and penetrated deep into the right ventricle (Figure 1, B). The size was $3.0 \times 7.0 \times 7.0 \text{ cm}^3$ and $2.0 \times 4.0 \times 6.0 \text{ cm}^3$, respectively (Figure 2, A). This patient recovered uneventfully, with no evidence of recurrence after 9 months of follow-up.

The tumor was rich in cellular myxoma with chondroid metaplasia and sarcomatoid differentiation (Figure 2, B). Immunohistochemistry shown that Vimentin (+), Filami-1 (FIL-1) (+), Cluster of differentiation 99 (CD99) (+), Cluster of differentiation 34 (CD34) (+), Neuron specific enolase (NSE) (+),

Casein kinase (CK) (-), S100 (-), Epithelial membrane antigen (EMA) (-), Cluster of differentiation 117 (CD117) (-), Specific AT sequence binding protein-2 (SATB-2) (-), proliferation index of Ki67 was 40%.

To identify the features of tumor growth, we determined the cell composition and growth pattern of the tumor via single-cell RNA sequencing. Comparing with the public data in published studies [2], we found that the major cell components of this tumor were chondrocytes, mesenchymal stromal cells, and smooth muscle cells. After filtering, Gene Ontology (GO) analysis of 36 hub genes are involved in the multicellular organismal process, anatomical structure development, cellular response to stimulus, and cell differentiation, et al. Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment showed that cyclic Guanosine monophosphate-cyclic - guanosine monophosphate (cGMP-PKG) signaling pathway, transcriptional misregulation in cancer, and p53 signaling pathway are related to the growth of the tumor. Protein-protein interaction of these genes was also analyzed (Figure 3).

Discussion And Conclusions

According to the classification of cardiac tumors from WHO in 2015 [3], myxomas and papillary fibroelastomas are the most common benign cardiac tumors, and are typically endocavitary. In our case, this tumor is classified into myxomas, although chondroid and sarcomatoid components were detected via immunohistochemistry. Surgery is the first choice of therapy for myxomas with a satisfactory long-term survival rate [1].

During the operation, we suspect that the tumor is malignant from its appearance. We chose two methods to detect its characteristics, one is pathological examination, the other is single-cell RNA sequencing. Luckily, the pathologic test revealed that the property of this tumor is benign. Meanwhile, the single-cell RNA sequencing is completed. From its results, we get much more information about this tumor. First, the components mainly include chondrocytes, smooth muscle cells, fibroblasts, mesenchymal stromal cells, osteoblasts. It echoes the result of the pathological examination. We do confirm that the tumor is benign by double confirmation. Secondly, through KEGG enrichment and protein-protein interaction of hub genes, we speculated that the causes of tumor growth were related to three signaling pathways, whose role in tumor has been studied widely [4-6].

Although it is a benign tumor in our case, benign or malignant tumor is a postoperative diagnosis that must keep in mind to select a proper treatment strategy. Currently, treatment and prognosis in malignant cardiac tumor are not satisfied⁷. Thus, it is necessary to improve the treatment plan, especially in postoperative strategy. We do believe that single-cell RNA sequencing is a good manner to analyze the growth pattern and search for therapeutic targets. Based on the result of single-cell RNA sequencing, seeking out a precision-targeted drug is helpful to reduce the recurrence of a malignant tumor and benefit the quality of life of patients.

Abbreviations

FIL: Filamin; CD: Cluster of differentiation; NSE: Neuron specific enolase; CK: Casein kinase; EMA: Epithelial membrane antigen; SATB: Specific AT sequence binding protein; cGMP-PKG: cyclic Guanosine monophosphate-cyclic - guanosine monophosphate

Declarations

Acknowledgments

We sincerely thank Jialei Zheng, Lili Zhai, and Mingfang Zhang for their assistance in this work.

Authors' contributions

Xian-jie Qi -Writing, Statistics and Draft. Chao Shi - Writing and Draft. Wei Ting -Data analysis. Sheng-qiang Zhang -Data analysis. Jin-jin Meng -Statistics. Yi-yao Jiang -Design, Reviewing. The authors read and approved the final manuscript.

Funding

This work was supported by grants from the National Natural Science Foundation of China (81800214), Excellent Young Talents Fund Program of Higher Education Institutions of Anhui Province (gxyqZD2016167), Key Research and Development Projects of Anhui Province (1804h08020280), Graduate scientific research innovation program of Bengbu Medical College (Byycx21077).

Availability of data and materials

Not applicable.

Ethics approval and consent to participate

Not applicable.

Consent for publication

The patient provided written, informed consent.

Competing interests

The authors declare that they have no competing interests

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Figures

Figure 1

A The larger tumor was located in the right atrial wall and filled the right atrium.

B The base of the smaller tumor was located above the tricuspid valve annulus.

Figure 2

A Photograph shows a macroscopic view of the tumor, which were $3.0 \times 7.0 \times 7.0 \text{ cm}^3$ and $2.0 \times 4.0 \times 6.0 \text{ cm}^3$, respectively.

B Immunohistochemistry detected tumor was rich in cellular myxoma with chondroid metaplasia and sarcomatoid differentiation.

Figure 3

A Cell subgroups and cell numbers.

B Dimension Reduction Clustering grouping display between heart tumor and normal heart.

C Cell type diagram.

D Heat map of cell type identification correlation.

E Protein-protein interaction of 36 hub genes.