Original Article

High frequency of GATA2 variants in patients with pulmonary fungal disease without immunocompromised risk factors: a retrospective study

Yongxun Zhuansun[1#], Peng He[2#], Yumo Du[1], Lin Lin[1], Rui Chen[1], Jianguo Li[1]

[1]Department of Respirology, Sun Yat-sen Memorial Hospital, Sun Yat-sen University, Guangzhou, China; [2]Department of Intensive Care Medicine, The Fifth Affiliated Hospital of Guangzhou Medical University, Guangzhou, China

Contributions: (I) Conception and design: Y Zhuansun, P He, J Li; (II) Administrative support: Y Du, L Lin, R Chen; (III) Provision of study materials or patients: Y Zhuansun, R Chen, J Li; (IV) Collection and assembly of data: P He, Y Du, L Lin; (V) Data analysis and interpretation: Y Du, L Lin, R Chen; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

[#]These authors contributed equally to this work.

Correspondence to: Jianguo Li, PhD. Department of Respirology, Sun Yat-sen Memorial Hospital, Sun Yat-sen University, No. 107 Yanjiang West Road, Guangzhou 510120, China. Email: lijguo@mail.sysu.edu.cn.

Background: The global incidence of pulmonary fungal diseases is on the rise. Individuals harboring underlying immunocompromised conditions such as human immunodeficiency virus (HIV)/acquired immune deficiency syndrome (AIDS), malignant tumors, or those who have undergone organ transplantation, among others, are particularly susceptible to fungal infections. However, in clinical practice, certain patients diagnosed with pulmonary fungal infections exhibit no discernible risk factors for immunosuppression. GATA2, a pivotal transcription factor governing hematopoiesis, is implicated in GATA2 deficiency, predisposing individuals to fungal infections. This study aims to scrutinize GATA2 variants in adult patients afflicted with pulmonary fungal infections devoid of recognized risk factors for immunosuppression.

Methods: A cohort of adult patients (aged 18–65 years old, n=22) diagnosed with pulmonary fungal diseases lacking underlying immunosuppression risk factors, treated at Sun Yat-sen Memorial Hospital from January 2016 to December 2021, underwent Sanger sequencing of the *GATA2* gene.

Results: Among the 22 patients devoid of immunocompromised risk factors and diagnosed with pulmonary fungal diseases, 17 patients (77.3%) exhibited single nucleotide variants (SNVs) within the exons of the *GATA2* gene. Notably, exon 3 variants were present in 7 cases (41.2%), exon 4 variants in 10 cases (58.8%), and exon 5 variants in 11 cases (64.7%), emerging as the most prevalent exonic variants within GATA2. Among the 17 patients harboring GATA2 SNVs, a total of 28 SNVs were identified. Of these, eight variants (NM_001145661.2:c.33G>A, NM_001145661.2:c.523C>T, NM_001145661.2:c.77A>G, NM_001145661.2:c.545C>T, NM_001145661.2:c.7G>A, NM_001145661.2:c.1406A>G, NM_001145661.2:c.977A>G, NM_001145661.2:c.742A>C) were identified as missense mutations with the potential to alter the structure and function of the GATA2 protein on the basis of multiple in silico predictive programs interpretation. One nonsense mutation (NM_001145661.2:c.664A>T) was classified as "likely pathogenic" according to 2015 American College of Medical Genetics and Genomics (ACMG) guidelines.

Conclusions: GATA2 variants are prevalent among patients afflicted with pulmonary fungal infections in the absence of traditional immunosuppressive risk factors. Further investigations are warranted to elucidate the impact of GATA2 variants on the expression and functionality of the GATA2 protein.

Keywords: GATA2; pulmonary fungal diseases; single nucleotide variants (SNVs)

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Introduction

Pulmonary fungal diseases impose significant morbidity and mortality among individuals with established immunocompromised states (1). These conditions, leading to immunosuppression, encompass a spectrum including human immunodeficiency virus (HIV)/acquired immune deficiency syndrome (AIDS), solid organ transplantation, malignant neoplasms, hematologic malignancies, chemotherapy or immunosuppressive therapy, prolonged glucocorticoids use, among others (2). Nonetheless, within clinical contexts, a subset of patients diagnosed with pulmonary fungal infections lacks the customary risk factors associated with immunosuppression. It is postulated that such patients may harbor underlying immune deficiencies.

Single nucleotide variants (SNVs) arise from alterations in individual nucleotides within the DNA sequence and represent the predominant form of GATA2 mutations. These mutations can precipitate structural or functional changes in the GATA2 protein, consequently resulting in GATA2 deficiency.

GATA2 serves as a transcription factor pivotal for regulating hematopoiesis and lymphatic angiogenesis. Deficiency in GATA2 may manifest as various clinical entities, including MonoMAC syndrome [characterized by susceptibility to nontuberculous mycobacterial (NTM), viral, and fungal infections], DCML (dendritic cell, monocyte, B and natural killer lymphoid) deficiency, myelodysplastic syndrome (MDS), acute myeloid leukemia (AML), and Emberger syndrome (featuring lymphedema and MDS or leukemia) (3,4). Notably, opportunistic pathogens infections, such as NTM infections, in individuals lacking recognized risk factors for immunosuppression may indicate an underlying genetic predisposition to immunodeficiencies (5). However, reports concerning GATA2 mutations in pulmonary fungal diseases remain sparse.

In this study, we sought to elucidate the presence of GATA2 variants in adult patients diagnosed with pulmonary fungal infections in the absence of recognized risk factors for immunosuppression. Such investigations are crucial for identifying potential underlying immune defects attributable to GATA2 mutations in this life-threatening condition. We present this article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-583/rc).

Highlight box

Key findings

- Immune deficiencies caused by GATA2 mutations should be regarded as an underlying etiology of pulmonary fungal infections.

What is known and what is new?

- A subset of patients diagnosed with pulmonary fungal infections lacks the customary risk factors associated with immunosuppression.
- GATA2 variants are prevalent among patients afflicted with pulmonary fungal infections in the absence of traditional immunosuppressive risk factors.

What is the implication, and what should change now?

- GATA2 mutations should be tested in patients with pulmonary fungal disease without immunocompromised risk factors.

Methods

Study design

This study employed a retrospective design. Medical records and clinical data of patients diagnosed with pulmonary fungal diseases at Sun Yat-sen Memorial Hospital between January 2016 and December 2021 were retrospectively retrieved from the medical record information system. Twenty-two patients, aged 18–65 years, lacking underlying risk factors for immunosuppression, and from whom samples (including peripheral blood or pathological paraffin sections of lung tissue) could be obtained for Sanger sequencing, were included for the analysis of GATA2 variants (*Figure 1*).

Inclusion and exclusion criteria

Inclusion criteria: patients diagnosed with pulmonary fungal disease and aged 18–65 years were included. Exclusion criteria: patients with risk factors for immunosuppression were excluded. These risk factors included: HIV infection, solid malignant tumors, hematologic malignancy, solid organ transplantation, autoimmune disease, interstitial lung disease, diabetes, history of major surgeries, long-term intensive care unit (ICU) hospitalization, application of chemotherapy or immunosuppressants, long-term use of glucocorticoids, long-term mechanical ventilation or indwelling catheters, long-term broad-spectrum antibiotic application, and total parenteral nutrition.

Sample preparation

Peripheral blood DNA and RNA extraction was performed

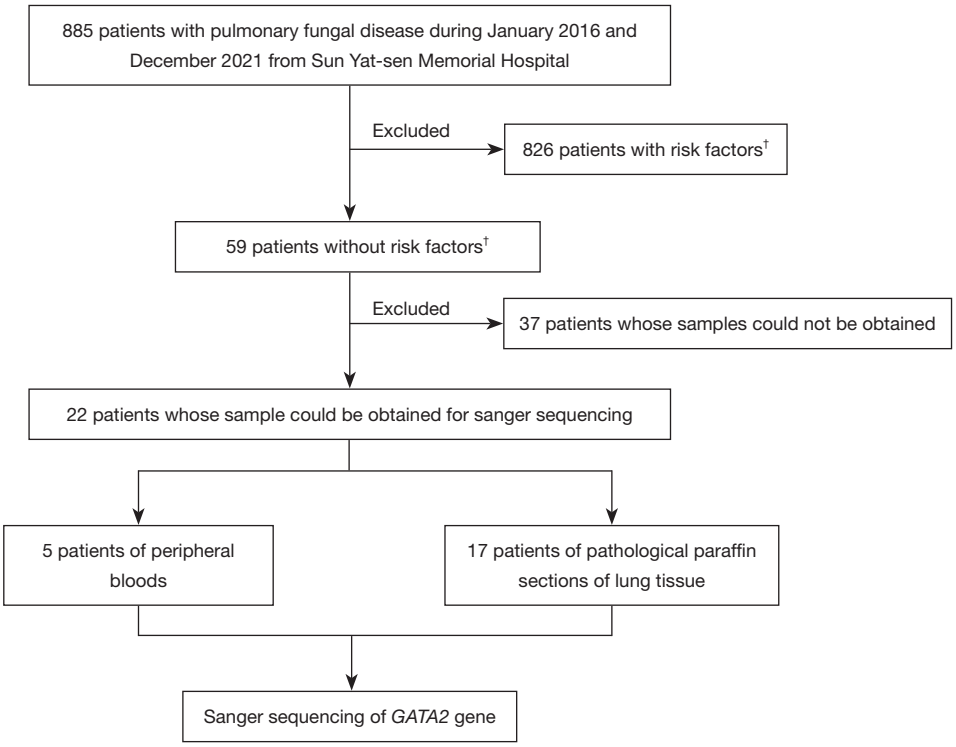

Figure 1 Flow diagram illustrating participant screening process. †, risk factors for immunosuppression.

using the E.Z.N.A.™ DNA/RNA isolation kit (OMEGA, California, USA) following the manufacturer's standard procedure. Additionally, DNA extraction from pathological paraffin sections of lung tissue was carried out using centrifugation.

Sanger sequencing

Primer design and synthesis

Eight pairs of polymerase chain reaction (PCR) primers were designed to target the eight exons of the *GATA2* gene. These primers were synthesized by Guangzhou IGE Biotechnology Ltd. (Guangzhou, China). The sequences of the PCR primers are provided in *Table 1*.

PCR, electrophoresis, and sequencing

Following PCR amplification of DNA extracted from peripheral blood or pathological paraffin sections of lung tissue, the PCR product was applied onto a 2.0% agarose gel. After 20 minutes of electrophoresis, the target strip was excised from the gel, and DNA recovery was performed using the iPurePCR recovery kit (Guangzhou IGE Biotechnology Ltd.). Subsequently, the recovered DNA was precipitated with ethanol and subjected to detection using a 3730xl sequencer (ABI, Massachusetts, USA).

Sequence analysis

Sequencing data from the sample were aligned to the reference sequence NM_00114566.2 of the *GATA2* gene obtained from National Center for Biotechnology Information (NCBI). Variant analysis of the *GATA2* gene exons was conducted using the Sequencher 5.4.5 software (Gene Codes Corporation, Michigan, USA). Additionally, VarCards (http://www.genemed.tech/varcards) which include multiple in silico predictive programs was utilized to predict the potential effects of GATA2 variants on the structure and function of the GATA2 protein. Pathogenic classification of GATA2 variants was based on American College of Medical Genetics and Genomics (ACMG) standards and guidelines for the interpretation of sequence variants [2015] (6).

Statistical analysis

For asymmetrically distributed quantitative variables, statistical description was performed using the median and

Table 1 PCR primer sequence

Exons of *GATA2* gene	Forward primer	Reverse primer	Fragment size (bp)
Exon 1	AGGGATGTGTGCGTGTCC	GCAAACGGACCAAGCGAT	800
Exon 2	CCCCAGTACTCGGCACC	AGCAGTAACTAACCACCAACTGC	748
Exon 3	GGTCTGGGTAGGTAACTGCG	AAAGCACACCAAAGCAGTCG	763
Exon 4	ATGTGCACGGGTGTGTGATT	GGACAGACCCTACAGGGAAC	734
Exon 5	TCCGGTGGGGTTCCTTCTAT	AAATGCTCCCCTCTTCCACG	895
Exon 6	CACCCTACCCTCGGCAAAG	AGAGAGACGACCCCAACTGA	638
Exon 7	TGTAGCTCTTGCAATCCCGTT	GCCAAGCCAAGCTGGATATT	477
Exon 8	GGGTCTCGGACTAGGGAAGTG	AGCGGTGGGGAACATTCACAG	783

PCR, polymerase chain reaction.

interquartile range. Frequency was utilized for the statistical description of qualitative variables, and the Chi-squared test (χ^2) was employed for comparing frequencies between groups. A P value of <0.05 was considered statistically significant. IBM SPSS statistics 26.0 (IBM Corp., Armonk, NY, USA) was used for statistical analysis.

Ethical statement

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of Sun Yat-sen Memorial Hospital (ID SYSKY-2023-085-01) and informed consent was obtained from all individual participants.

Results

Demographic and clinical data of patients with pulmonary fungal disease without immunocompromised risk factors

Table 2 presents the demographic and clinical data identified in patients diagnosed with pulmonary fungal diseases without associated immunocompromised risk factors. Among the 22 patients included in the study, 13 (59.1%) were male. The median age of the cohort was 49.5 years (interquartile range, 41.3–58 years). Regarding the specific fungal pathogens detected, 15 (68.2%) patients were infected with cryptococcus, 4 (18.2%) with aspergillus, 1 (4.5%) with fusarium, and 2 (9.1%) cases were classified as unspecified. In terms of blood cell count results, 2 (9.1%) patients had lymphocytopenia. Two (9.1%) patients had neutropenia, and 1 (4.5%) patient had leukopenia. The family history of these patients was noncontributory.

GATA2 variants in patients with pulmonary fungal disease without immunocompromised risk factors

Twenty-two patients diagnosed with pulmonary fungal disease without underlying immunocompromised risk factors underwent Sanger sequencing of the *GATA2* gene. Peripheral blood samples were available for sequencing from five patients, while pathological paraffin sections of lung tissue were obtained from 17 patients. The GATA2 variants detected in these patients are summarized in *Table 3*. Seventeen patients (77.3%) exhibited SNVs within the exons of the *GATA2* gene. Among these 17 patients with GATA2 variants, exon 3 variants were present in 7 cases (41.2%), exon 4 variants in 10 cases (58.8%), and exon 5 variants in 11 cases (64.7%), emerging as the most prevalent exonic variants within GATA2. A total of 28 SNVs were detected among the 17 patients with GATA2 SNVs. Upon analysis of missense variants of the *GATA2* gene using VarCards, eight variants (NM_001145661.2:c.33G>A, NM_001145661.2:c.523C>T, NM_001145661.2:c.77A>G, NM_001145661.2:c.545C>T, NM_001145661.2:c.7G>A, NM_001145661.2:c.1406A>G, NM_001145661.2:c.977A>G, NM_001145661.2:c.742A>C) were identified as missense mutations with the potential to alter the structure and function of the GATA2 protein on the basis of multiple in silico predictive programs interpretation. One nonsense mutation (NM_001145661.2:c.664A>T) was classified as "likely pathogenic" according to 2015 ACMG guidelines. The remaining variants were categorized as "benign", "likely

Table 2 Demographic and clinical data of patients with pulmonary fungal disease without immunocompromised risk factors

Case	Sex	Age (years)	Pathogen	No. of episodes of fungal infection	Extrapulmonary infection	Features of GATA2 deficiency†	Family history of similar features
1	M	42	Fungus (unspecific classification)	Five	None	None	None
2	F	61	*Cryptococcus*	One	None	None	None
3	F	20	Fungus (unspecific classification)	One	None	None	None
4	M	32	*Cryptococcus*	One	None	None	None
5	F	50	*Fusarium*	One	None	None	None
6	F	51	*Cryptococcus*	Three	None	Leukopenia	None
7	M	46	*Cryptococcus*	One	None	None	None
8	M	47	*Aspergillus*	One	None	Neutropenia	None
9	F	58	*Aspergillus*	One	None	Lymphocytopenia	None
10	F	33	*Aspergillus*	One	None	None	None
11	F	62	*Aspergillus*	One	None	None	None
12	M	58	*Cryptococcus*	One	None	None	None
13	M	53	*Cryptococcus*	One	None	None	None
14	M	43	*Cryptococcus*	One	None	None	None
15	M	48	*Cryptococcus*	One	None	Neutropenia	None
16	M	39	*Cryptococcus*	One	None	None	None
17	F	60	*Cryptococcus*	One	None	Lymphocytopenia	None
18	M	59	*Cryptococcus*	One	None	None	None
19	F	56	*Cryptococcus*	One	None	None	None
20	M	58	*Cryptococcus*	One	None	None	None
21	M	24	*Cryptococcus*	One	None	None	None
22	M	49	*Cryptococcus*	One	None	None	None

†, other clinical features that would be consistent with GATA2 deficiency. No., number; M, male; F, female.

Table 3 *GATA2* variants of patients with pulmonary fungal disease without immunocompromised risk factors

Case	Sample	*GATA2* variants	Exons	Codons	Prediction‡	Pathogenic classification†
1	Peripheral blood	c.1-836A>C	3			Uncertain significance
		c.15C>G	4	p.Pro5Pro		Benign
		c.490G>A	5	p.Ala164Thr		Benign
2	Peripheral blood	c.1-836A>C	3			Uncertain significance
		c.1-744G>T	3			Uncertain significance
		c.15C>G	4	p.Pro5Pro		Benign

Table 3 (*continued*)

Table 3 (*continued*)

Case	Sample	*GATA2* variants	Exons	Codons	Prediction[‡]	Pathogenic classification[†]
3	Peripheral blood	c.1-836A>C	3			Uncertain significance
		c.15C>G	4	p.Pro5Pro		Benign
		c.490G>A	5	p.Ala164Thr		Benign
4	Peripheral blood	c.1-836A>C	3			Uncertain significance
		c.15C>G	4	p.Pro5Pro		Benign
		c.490G>A	5	p.Ala164Thr		Benign
5	Peripheral blood	c.15C>G	4	p.Pro5Pro		Benign
		c.490G>A	5	p.Ala164Thr		Benign
6	Lung tissue[§]	c.1219A>G	8	p.Ser407Gly		Uncertain significance
7	Lung tissue[§]	c.15C>G	4	p.Pro5Pro		Benign
		c.490G>A	5	p.Ala164Thr		Benign
8	Lung tissue[§]	c.33G>A	4	p.Met11Ile	Damaging	Uncertain significance
		c.225G>A	4	p.Ala75Ala		likely benign
		c.490G>A	5	p.Ala164Thr		Benign
9	Lung tissue[§]	c.1-5880C>T	1			Uncertain significance
		c.1-14C>T	4			Uncertain significance
		c.15C>G	4	p.Pro5Pro		Benign
		c.77A>G	4	p.His26Arg	Damaging	Uncertain significance
10	Lung tissue[§]	c.1-836A>C	3			Uncertain significance
		c.15C>G	4	p.Pro5Pro		Uncertain significance
		c.490G>A	5	p.Ala164Thr		Benign
		c.545C>T	5	p.Ser182Phe	Damaging	Uncertain significance
		c.561C>T	5	p.Thr187Thr		Likely benign
11	Lung tissue[§]	c.7G>A	4	p.Val3Met	Damaging	Uncertain significance
		c.15C>G	4	p.Pro5Pro		Benign
		c.419T>C	5	p.Val140Ala		Uncertain significance
		c.490G>A	5	p.Ala164Thr		Benign
		c.523C>T	5	p.Pro175Ser	Damaging	Uncertain significance
12	Lung tissue[§]	c.1-347TCdel	2			Uncertain significance
		c.1406A>G	8	p.His469Arg	Damaging	Uncertain significance
13	Lung tissue[§]	c.1083C>T	7	p.Arg361Arg		Likely benign
14	Lung tissue[§]	c.1-6115C>T	1			Uncertain significance
		c.490G>A	5	p.Ala164Thr		Benign
		c.579A>G	5	p.Pro193Pro		Likely benign

Table 3 (*continued*)

Table 3 (*continued*)

Case	Sample	*GATA2* variants	Exons	Codons	Prediction‡	Pathogenic classification†
15	Lung tissue§	c.1-1381G>A	2			Uncertain significance
		c.1-1351A>G	2			Uncertain significance
		c.1-836A>G	3			Uncertain significance
		c.322G>A	5	p.Ala108Thr		Uncertain significance
16	Lung tissue§	c.1-836A>C	3			Uncertain significance
		c.977A>G	6	p.Asn326Ser	Damaging	Uncertain significance
17	Lung tissue§	c.490G>A	5	p.Ala164Thr		Benign
		c.576T>C	5	p.Ser192Ser		Likely benign
		c.664A>T	5	p.Lys222Tre	LOF	Likely pathogenic
		c.742A>C	5	p.Thr248Pro	Damaging	Uncertain significance

†, pathogenic classification according to 2015 ACMG Standards and Guidelines for the Interpretation of Sequence Variants: (I) pathogenic, (II) likely pathogenic, (III) uncertain significance, (IV) likely benign, (V) benign; ‡, the prediction of the effect of GATA2 variants on the expression or function of GATA2 transcription factor on the basis of multiple in silico predictive programs; §, sample from pathological paraffin sections of lung tissue. Pro, proline; Ala, alanine; Thr, threonine; Ser, serine; Gly, glycine; Met, methionine; Ile, isoleucine; His, histidine; Arg, arginyl; Phe, phenylalanine; Val, valine; Asn, asparagine; Lys, lysyl; Tre, termination codon; LOF, loss-of-function.

Table 4 The frequency of GATA2 SNVs of patients with pulmonary fungal disease without immunocompromised risk factors compared with ExAC database

SNV	Cases† (n=22)	ExAC_all‡	P
c.15C>G	0.40909	0.69432	0.005
c.490G>A	0.45455	0.20562	0.008
c.523C>T	0.04545	0.00001	<0.001

†, the frequency of GATA2 SNV in patients with pulmonary fungal disease without immunocompromised risk factors; ‡, the frequency of GATA2 SNV reported in ExAC database. SNV, single nucleotide variant; ExAC, Exome Aggregation Consortium.

benign", or "uncertain significance" based on 2015 ACMG guidelines.

Frequency of GATA2 SNVs in patients with pulmonary fungal disease without immunocompromised risk factors compared with Exome Aggregation Consortium (ExAC) database

Among the 28 SNVs identified in patients with pulmonary fungal disease without immunocompromised risk factors, three were previously reported in the ExAC database. As depicted in *Table 4*, the frequency of variants NM_001145661.2:c.490G>A and NM_001145661.2:c.523C>T in patients without immunocompromised risk factors was significantly higher than the reported incidence rate in the ExAC database (P<0.05). Conversely, the frequency of variant NM_001145661.2:c.15C>G in patients without immunocompromised risk factors was significantly lower than the reported incidence rate in ExAC database (P<0.05).

Discussion

GATA2, a vital transcription factor governing hematopoiesis, plays a pivotal role in immune function. Mutations in the *GATA2* gene can result in GATA2 deficiency, predisposing individuals to susceptibility to opportunistic pathogens infections, including fungi. In this study, we observed that 77.3% of patients diagnosed with pulmonary fungal infections without traditional immunosuppressive risk factors harbored at least one SNVs within the exons of the *GATA2* gene. Notably, variants within exon 3, exon 4, and exon 5 were the most frequently

identified regions. Among these variants, eight variants (NM_001145661.2:c.33G>A, NM_001145661.2:c.523C>T, NM_001145661.2:c.77A>G, NM_001145661.2:c.545C>T, NM_001145661.2:c.7G>A, NM_001145661.2:c.1406A>G, NM_001145661.2:c.977A>G, NM_001145661.2:c.742A>C) were identified as missense mutations, capable of inducing mRNA or protein changes. One nonsense mutation (NM_001145661.2:c.664A>T) was classified as "likely pathogenic" based on 2015 ACMG guidelines.

In 2011, a group of diseases caused by genetic mutations of the *GATA2* gene was identified and termed GATA2 deficiency (7-10). Several studies have since reported on the association between GATA2 SNVs and the onset of fungal infections. For instance, Egenlauf *et al.* documented a case of disseminated infection with the black yeast-like fungus *Arthrocladium fulminans* in a patient harboring a heterozygous intronic GATA2 mutation (11). Another study reported a heterozygous missense mutation in GATA2 (c.1114G >A, p.A372T) associated with disseminated infections caused by *Aspergillus flavus*, *A. fumigatus*, *Candida glabrata*, and *M. avium* (12). Additionally, a case of *pneumocystis jiroveci* pneumonia was attributed to a c.1078T>A mutation of the *GATA2* gene (13). Mendes-de-Almeida *et al.* reported GATA2 SNVs in 10 out of 22 patients with non-tuberculous mycobacterial or fungal infections without known immunodeficiencies (14). Furthermore, a patient with a GATA2 c.1009C>T mutation was documented to have multiple opportunistic infections, including *P. jirovecii* pneumonia, invasive pulmonary aspergillosis, and disseminated NTM infection (15). A survey of 79 French and Belgian patients with GATA2 deficiency revealed severe infectious diseases caused by mycobacteria, fungus, and human papilloma virus (16).

The *GATA2* gene, located on human chromosome 3q21.3, comprises eight exons. Among these, exons 5, 6, and 7, encoding two zinc finger domains, which located between 294–344 and 349–398 amino acids on the GATA2 protein, are frequently implicated in SNVs. SNVs within these zinc finger regions can lead to haploinsufficiency by compromising the function of the GATA2 protein (17). In this study, we identified two variants NM_001145661.2:c.1083C>T (p.Arg361Arg) and NM_001145661.2:c.977A>G (p.Asn326Ser) which located in the two zinc finger domains. However, mutations without the zinc finger domains also could cause GATA2 deficiency (18). One nonsense mutation NM_001145661.2:c.664A>T (p.Lys222Tre) identified in this cohort which lead to early termination of translation at the 222 amino acid within GATA2 protein, could cause loss of two zinc finger domains and was categorized as "likely pathogenic".

Notably, reported GATA2 mutations are classified into five categories by the ClinGen/ClinVar database: "pathogenic", "likely pathogenic", "uncertain significance", "likely benign", and "benign". In this study, we identified one "likely pathogenic" nonsense mutation based on 2015 ACMG guidelines and eight missense mutations potentially to alter the functionality of GATA2 protein on the basis of multiple in silico predictive programs in patients with pulmonary fungal infections lacking immunosuppressive risk factors. However, further functional studies are warranted to elucidate the clinical significance of these variants.

Allele frequency in population databases such as ExAC was used for pathogenicity classification according to 2015 ACMG guidelines. Allele frequency of >5% in ExAC is a "stand-alone" evidence for benign variants. Two variants (NM_001145661.2:c.15C>G and NM_001145661.2:c.490G>A) were classified as "benign" based on this criteria. The higher frequency of NM_001145661.2:c.490G>A and NM_001145661.2:c.523C>T and lower frequency of NM_001145661.2:c.15C>G found in this cohort compared with ExAC may reflect the difference of allele frequency between different population with different genetic background. The allele frequency difference with the population databases should not be considered as evidence of "pathogenic" or "protective" effect of variants according to 2015 ACMG guidelines.

Despite the valuable insights gained from this study, several limitations should be acknowledged. This study had a small sample size and was retrospective in nature, which may limit the generalizability of the findings. Other than that, the possibility of selection bias cannot be discounted, as the study population was derived from patients treated at a single medical institution. Moreover, the use of Sanger sequencing for mutation detection may have restricted the identification of certain types of GATA2 mutations. Specifically, non-coding regions of the *GATA2* gene were not included in the sequencing analysis, potentially resulting in the oversight of important mutations such as gene deletions, regulatory mutations in non-coding regions, and frameshift mutations. Future studies employing advanced sequencing techniques and larger sample sizes are warranted to comprehensively evaluate the role of GATA2 mutations in pulmonary fungal infections.

Conclusions

In conclusion, this study reveals a notable prevalence of GATA2 variants among patients diagnosed with pulmonary fungal infections lacking traditional immunosuppressive risk factors. However, to fully comprehend the implications of these variants on the expression and functionality of the GATA2 protein, further investigations are imperative.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-583/rc

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-583/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of Sun Yat-sen Memorial Hospital (ID SYSKY-2023-085-01) and informed consent was obtained from all individual participants.

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