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Immunoregulatory response associated with persistent inflammation overexpression of PD-L1 and viral RNA detection in chronic suppurative otitis

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Abstract

Objective

Chronic suppurative otitis media (CSOM) is a chronic middle ear inflammatory disease characterized by microbial biofilms, alterations in immune mechanisms, epithelium and tissue destruction. To determine the relationship between PD-L1 expression and viral RNA positivity in patients with CSOM and the potential role of immune checkpoint analysis in terms of chronicity.

Materials and methods

There were fifty participants in this study, which included fifty patients with CSOM and twenty-five healthy controls. 50 of them were patients with CSOM attending the Otorhinolaryngology Department, Diwaniyah General Hospital, and 50 of them were apparently healthy controls without middle ear pathology. Patients were aged between 15 and 75 years of both sexes, and they were diagnosed according to clinical and otoscopic examination. RT-PCR was carried out for the detection of the viral genome of the Respiratory Syncytial Virus (N gene of 113 bp), Rhinovirus (UTR gene of 218 bp) and Adenovirus (310 bp). PD-L1 was measured by immunofluorescence assay with a 4-parameter logistic method (ELI).

Results

Molecular screening for viral RNA by RT-PCR showed that the majority of patients with chronic suppurative otitis media (CSOM) had one or more viral-positive screens. PCR for the detection of RNA from the viruses (SARS-CoV-2, Rhinovirus, and Adenovirus) was performed in 40/50 (80%) patients, and thereafter, 10/50 (20%) and 6/50 (12%) of the patients were found to be positive for the presence of RNA from Rhinovirus and Adenovirus, respectively. The mean serum PD-L1 level was significantly higher in patients compared with controls (0.242 ± 0.13 versus 1.01 ± 0.05 ng/ml; $t = 5.26$; $P < 0.0001$). A positive correlation was found to exist between PD-L1 elevation and viral RNA positivity. PD-L1 expression was remarkably increased in those patients who were positive for viral RNA (1.06 ng/mL) compared to those who were negative (0.58 ng/mL)

Conclusion

The presence of viral RNA and PD-L1 overexpression in CSOM patients suggests an adaptive imbalanced immune response, which results in the silencing of hyperinflammation and microbial tolerance. These results suggest a major contribution of the PD-1/PD-L1 pathway to the chronic nature of otitis media.

Keywords: Corona Virus, Rhinovirus, Chronic Suppurative Otitis Media, Immune Checkpoint, RT-PCR

Paper Type: Research Paper.

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Introduction

Chronic suppurative otitis media (CSOM) is a long-lasting infection of the middle ear mucosa that causes the tympanic membrane to break, ear drainage, and swelling. Bacterial agents, particularly *Staphylococcus aureus* and *Pseudomonas aeruginosa*, continue to be the most

predominant causative agents and they support biofilm-mediated persistence which can complicate antimicrobial therapy (Hiremath et al., 2019). However, molecular studies have shed more light on the involvement of the virus. Reverse transcriptase polymerase chain reaction (RT-PCR) analysis in CSOM patients showed the presence of RNA from the virus in 80% of samples for viral RNAs from the family Coronaviridae (SARS-CoV-2), in 20% for viruses of the family Paramyxoviridae (Rhinovirus), and in 12%, for viruses of the family Herpesviridae (Adenovirus) in blood samples, suggesting the presence of viral components in the system or of residual RNAemia. Such findings support the possibility of the coexistence of viral antigens associated with bacterial infection in chronic otitis media (Muñoz-Cobo et al., 2011; Durmaz et al., 2021; Frazier et al., 2022). Persistence of viral RNA in the blood after acute infection has been found in several post-infectious conditions (Mijwel et al., 2023; Al-Kaif et al., 2024). In the middle ear, viral - bacterial synergy may involve disruption of epithelial barriers and subsequent biofilm development, as well as enhanced mucosal injury (Marom et al., 2012; Jotic et al., 2025). These accumulations of interactions maintain chronic inflammation and exhaustion of the immune system. The mechanism known as programmed death-1 (PD-1)/programmed death-ligand 1 (PD-L1) has a central role in the regulation of the immune response during chronic inflammataroy stress. The expression of PD-L1 is stimulated by cytokines, such as interferon-gamma and TNF-alpha, through the JAK/STAT and NF-kappa B protein signaling pathways (Zhao et al., 2020). The upregulation of this suppresses effector T-cell activation and release of cytokines, which contribute to immune exhaustion and the persistence of pathogens (Jubel et al., 2020; Gao et al., 2022). In CSOM serum PD-L1 was significantly increased in patients (1.01± 0.05) in comparison to controls (0.242± 0.13; $P < 0.0001$) confirm immune checkpoint activation (Ancın et al., 2022). This systemic increase probably indicates chronic antigenic stimulation by EBV in this case: both by the bacterial biofilms from the viruses and by the remains of the viruses. Moreover, soluble PD-L1 released from epithelial and stromal tissues might contribute to the systemic suppression of the immune system (Pan et al., 2016; Mair et al., 2020). Altogether, these results suggest that viral persistence and PD-L1 overexpression have a synergistic role in maintaining inflammatory activity and impairing microbial clearance. Considering this relationship is important in sympathetic our understanding of the immunopathogenesis of CSOM and possible checkpoint-targeted therapies to restore host defense balance. This work aimed to determine the correlation between PD-L1 expression and viral RNA positivity in patients with CSOM and the potential role of the immune response.

Materials and methods

Study design: This study was carried out in the form of a case-control observational study to understand the relationship between viral detection and PD-L1 overexpression among Individuals suffering from CSOM. The case-control design was used because of its ability to directly compare immune and molecular parameters in diseased and healthy populations and reduce the effects of confounders by proper matching of age, sex, and number (Kaye et al., 2005).

Study population: A total of 100 subjects were included. 50 of them were patients with CSOM attending the Otorhinolaryngology Department, Diwaniyah General Hospital, and 50 of them were apparently healthy controls without middle ear pathology. Patients were aged between 15 and 75 years of both sexes, and they were diagnosed according to clinical and otoscopic examination (Qureishi et al., 2014). Exclusion criteria included acute otitis media, autoimmune diseases, immunodeficiency disorders, and the use of immunosuppressive medication to prevent any type of immune bias (Yuan et al., 2022).

Ethical considerations: Ethical approval was obtained from the College of Medicine of the University of Babylon & the Babylon Health Directorate. The ethical standards of the Declaration of Helsinki (2013 revision) were followed ensuring informed consent, confidentiality, and safety of participants (WMA, 2013).

Study period and setting: Samples were collected between September 2024 to March 2025 from Diwaniyah General Hospital. Laboratory procedures, including microbiological, molecular and immunological procedure, were conducted in the target department of Microbiology, College of Medicine, University of Babylon, and partially at the University of Al-Qadisiyah laboratories equipped for advanced molecular analysis (Juhn et al., 2008).

Blood samples: From each subject, 5 mL of venous blood were aseptically collected. Three milliliters were placed into plain tubes to obtain serum by centrifugation (3000 rpm for 10 min) and stored at -20^{o}C for immunological test. The remaining 2 mL was transferred to Eppendorf (Edinburgh, UK) tubes in an ice bath and stored at -80^{o}C for viral and molecular analyses (Brook, 2003; Torretta et al., 2022).

Detection of virus RNA with molecules: Viral RNA was extracted from 200ul of serum by following the manufacturer's instructions and using the Geneaid viral nucleic acid extraction kit II (Taiwan). Reverse transcription was done with All-in-One 5X RT Master Mix (abm, Canada). Amplification targeted: SARS-CoV-2 N gene (113 bp), Rhinovirus UTR gene (218 bp), and Adenovirus hexon gene (301 bp). PCR conditions were optimized based on the protocols of Wu et al. (2020) and Bwire et al. (2021) using 35 cycles of amplification (95 C denaturation, 60-72 C annealing and 72 C extension). Ethidium bromide-stained agarose gel electrophoresis was used

to observe the PCR results, and a UV transilluminator (Quantum, France) was used to record the bands.

Measurement of serum PD-L1: Serum levels of PD-L1 protein were measured by sandwich-ELS (Elabscience, China). Anti-human PD-L1 antibody-coated microplate were also prepared. After incubation with standards and samples biotinylated detection antibody, HRP-avidin conjugate were added sequentially, followed by the inclusion of a stop solution and TMB substrate. The Beckman microplate reader (Germany) was used to detect absorbance at 450 nm. PD-L1 concentrations used a standard calibration curve and all procedures were performed as described by Mair et al. (2020) and Pan et al. (2016).

Statistical analysis: Data analysis was performed with the help of a software program (SPSS v."25", IBM, USA). Results were re-expressed as means ± SE. The means across groups were compared using the independent samples t-test, and the associations between PD-L1 levels and viral RNA positivity were examined using Pearson's correlation. At $P < 0.05$, statistical significance was observed (George & Mallery, 2018).

Results

Viral RNA detection: Molecular screening for viral RNA by RT-PCR showed that the majority of patients with chronic suppurative otitis media (CSOM) had one or more viral positive screens. As depicted in Table 1, SARS-CoV-2 RNA for the N gene fragment (113 bp) was identified in 40 out of 50 patients (80%). Furthermore, Rhinovirus RNA specific to the untranslated region (218 bp), and Adenovirus RNA (301 bp) specific to the *exon* gene were found in 10 patients (20%) and 6 patients (12%), respectively. The amplicons amplified by both assays were electrophoretically analyzed to ensure the specificity of the assays and revealed the presence of bands at the anticipated molecular sizes for each virus. No amplification was reported in the healthy control group, suggesting that cross-contamination does not occur and proving that the assay is reliable. These results highlight a high viral load in CSOM patients, that will be characterized by SARS-CoV-2 positivity followed by late typing and adenoviruses. The effective co-viremic positivity achieved 84%, which was indicative of a strong correlation, remarkably for the combination of incompatible viral material and persistent inflammation.

Serum PD-L1 concentrations: The findings indicated a noteworthy distinction in the level of PD-L1 between CSOM patients and healthy controls by serum analysis. Table 2 showed that the mean concentration value of PD-L1 in patients was 1.01 ± 0.05 ng/mL, which was significantly greater than that of the controls (0.242 ±0.13 ng/mL). An extremely significant difference was shown by statistical analysis using the independent t-test ($t=5.26$, $P < 0.0001$). Patients showed a significant shift of PD-L1 values towards high values, with more than 90% of

the values being above the upper limit of values in the control samples. These findings provide evidence of a clear expression of the PD-1/PD-L1 immune checkpoint axis in chronic infection, which may be a host compensatory response to curb sustained inflammation.

Table 1. Detection of viral RNA among CSOM patients and controls by RT-PCR

Virus Type	Target Gene	Amplicon Size (bp)	Positive Cases (n = 50)	Positivity Rate (%)	Control (n = 25)
SARS-CoV-2	*N gene*	113	40	80.0	0
Rhinovirus	*UTR*	218	10	20.0	0
Adenovirus	*Hexon*	301	6	12.0	0
Total viral positivity	-	-	**42***	**84.0**	**0**

*Total includes co-detections where more than one viral RNA was found in the same sample.

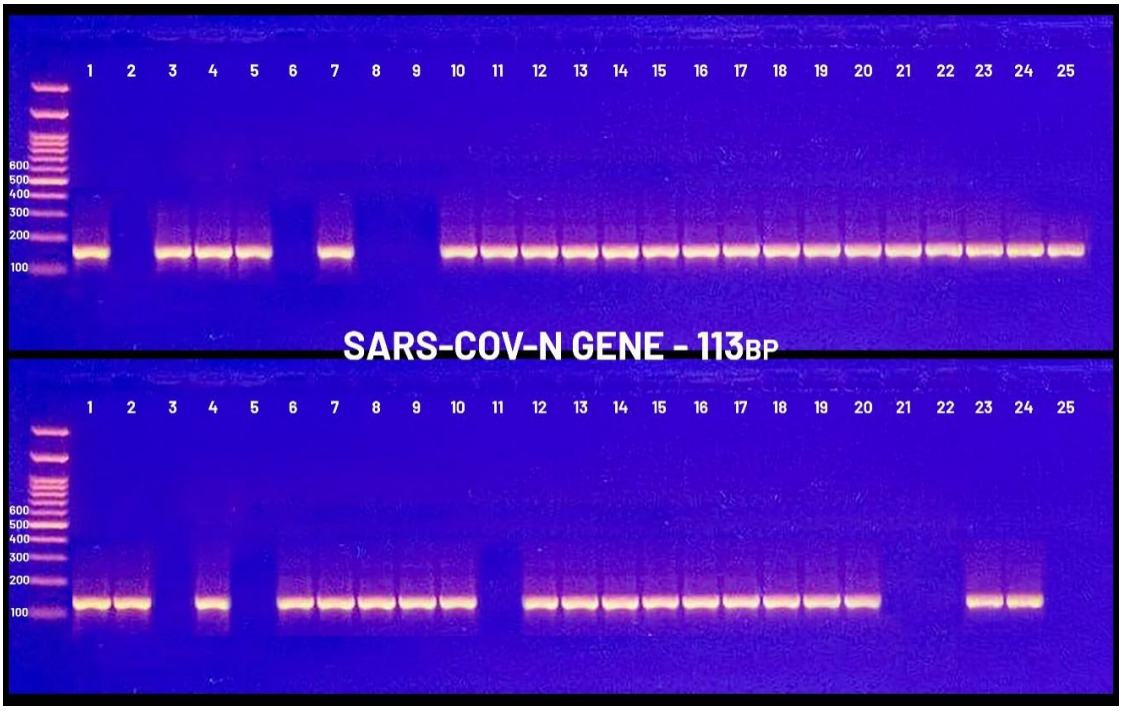

Figure 1. RT-PCR targeting the SARS-CoV-N gene (113 bp). A molecular size marker with a range of 100-1500 bp was used to segregate the PCR results on a 2% agarose gel. Clear bands at the 113 bp position in multiple lanes indicate positive amplification for the SARS-CoV-N gene, with 40 samples showing positivity, 10 samples lacked visible bands and were considered negative

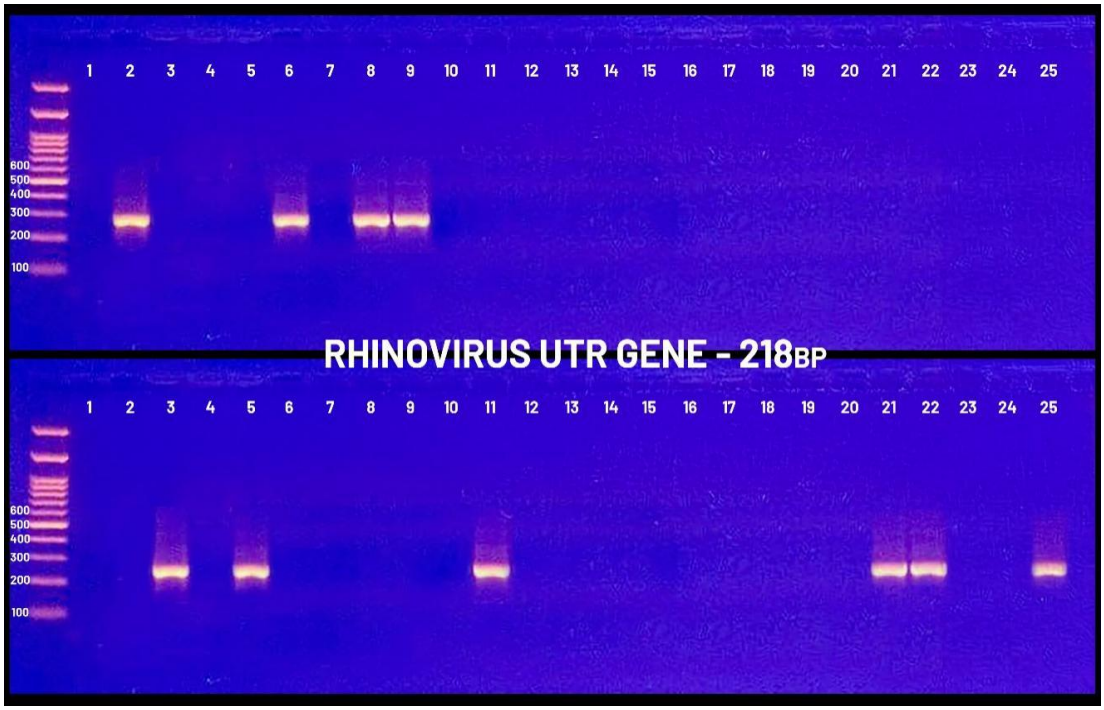

Figure 2. RT-PCR targeting the Rhinovirus UTR gene (218 bp). Using a molecular size marker between 100 and 1500 bp, the amplified products were separated on a 2% agarose gel. Distinct bands at the 218 bp position were considered positive for Rhinovirus RNA. 10 samples showed clear amplification bands at the expected size, whereas 40 samples were negative

Correlation of viral RNA and PD-L1 expressions: PD-L1 upregulation correlated with viral persistence; serum levels in patients positive and negative for viral RNA from whole blood were compared. As shown in Table 3, PD-L1 expression was remarkably increased in those patients who were positive for viral RNA (1.06 ng/mL) compared to those who were negative (0.58 ng/mL). A substantial positive link was statistically shown by the correlation analysis that was included ($r = 0.71 P < 0.001$) between the detection of the viruses and the concentration of PD-L1. These results indicate that persistent viral Ags contribute directly to the long-term activation of PD-L1 expression providing a positive feedback loop to maintain immune tolerance, thus slowing the clearance of infection.

Table 2. Serum PD-L1 Concentrations among CSOM Patients and Healthy Controls

Group	No. of Subjects (n)	Mean±SE PD-L1 (ng/mL)	t-Value	P-Value
CSOM Patients	50	1.01± 0.05	5.26	<0.0001
Controls	25	0.242± 0.13	-	-

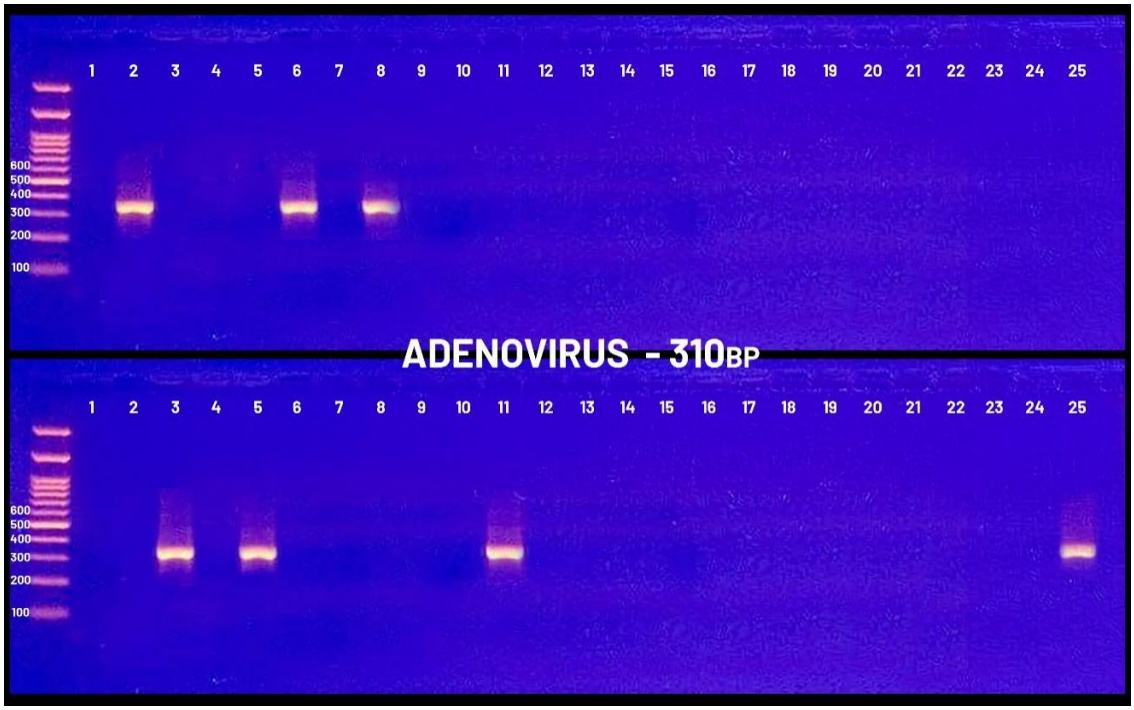

Figure 3. RT-PCR targeting the adenovirus gene (310 bp). A molecular size marker spanning from 100 to 1500 bp was used to segregate the PCR results on a 2% agarose gel. Bands observed at the 310 bp position were considered positive. six samples showed positive amplification at the expected size, while 44 samples were negative

Table 3. Correlation between Viral RNA Positivity and Serum PD-L1 Levels in CSOM Patients

Viral Detection Status	No. of Patients (n)	Mean PD-L1 (ng/mL)	Correlation (r)	Significance (P)
Viral RNA Positive	42	1.06	0.71	<0.001
Viral RNA Negative	8	0.58	-	-

Comparative virulence of various viruses: Results of additional comparative PD-L1 abundance analysis according to the particular virus types are shown in Table 4. Patients who were positive for SARS-CoV-2 RNA had the highest mean PD-L1 value (1.08 ± 0.04 ng/mL), which was followed by Rhinovirus-positive patients (0.87 ±0.06 ng/mL) and Adenovirus-positive cases (0.82 ±0.08 ng/mL). In contrast, although the differences between viral groups were not statistically significant because of the small study populations in the subgroups, the overall trend was consistent with higher PD-L1 concentrations in all virus-positive patients compared with those who did not have detectable virus. This signal supports the hypothesis that viral persistence of any kind plays a role in maintenance of PD-L1 activation.

Table 4. Comparative Analysis of PD-L1 Levels among SARS-CoV-2, Rhinovirus, and Adenovirus-Positive CSOM Patients

Virus Detected	Positive Cases (n)	Mean ±SE PD-L1 (ng/mL)	Range (Min-Max)
SARS-CoV-2	40	1.08±0.04	0.94-1.15
Rhinovirus	10	0.87±0.06	0.75-0.98
Adenovirus	6	0.82±0.08	0.70-0.94

Molecular and immunological results: The more important molecular and immunological results are summarized in Table 5. Collectively, the findings confirm high rate of viral RNA detection in association with (marked) PD-L1 elevation in CSOM patients. The epidemiochore potential of SARS-CoV-2, Rhinovirus and Adenovirus together with the induction of PD-L1 implies a mechanistic relationship between viral persistence and immuno checkpoint activation. These findings indicate with high likelihood that PD-L1 overexpression was a critical immunoregulatory response that, while limiting tissue damage, may also at the same time allow for long-term microbial survival and chronicization of otitis media.

Table 5. Summary of molecular and immunological findings in CSOM patients

Parameter	Finding	Explanation
SARS-CoV-2 RNA positivity	80%	Indicates persistent viral components in chronic inflammation
Rhinovirus RNA positivity	20%	Suggests concurrent viral colonization
Adenovirus RNA positivity	12%	May act as secondary viral co-factor
Mean PD-L1 in CSOM	1.01 ± 0.05 ng/mL	Significant immune checkpoint activation
Mean PD-L1 in controls	0.242 ± 0.13 ng/mL	Normal baseline immune regulation
PD-L1 correlation with viral RNA	$r = 0.71$, $P < 0.001$	Strong direct relationship

Discussion

The current study revealed high virality (primarily SARS-CoV-2) and high PD-L1 overexpression in patients with chronic suppurative otitis media (CSOM). These findings highlight the increasing awareness that chronic otitis media is not caused bacteria only but may involve the persistence of the virus which is the reason for the ongoing immune modulation. The finding of the presence of the RNA of coronavirus (SAR19) in 80% of patients with CSOM strengthens the hypothesis that the components of the virus circulate in the body for long periods after the defeat of the acute respiratory infection, so that they entering the work of the main mechanism of selecting and increasing the local defense reactions. Similar findings were made by Zhou *et al*. who found persistent SARS-CoV-2 RNA fragments in mucosal biopsies months after infection indicating incomplete viral clearance also in immunocompetent patients (Goh et al., 2022). Rhinovirus and Adenovirus were also found, albeit at lower hit frequencies, as has

been shown in the studies by Harris *et al*. provided in which they report that these respiratory viruses persist in epithelial reservoirs and this, in turn, has an impact on bacterial colonization. Viral persistence can alter the epithelial barrier, increase bacterial adhesion, and cytokine secretion, especially of IL-6, IL-8 and interferon-regulated mediators, a pro-inflammatory state characteristic of a CSOM (Serban et al., 2021). The finding of more than the one type of virus in this study supports the idea of polymicrobial synergy where viral remnants act to stabilize and protect bacterial biofilms as well as inhibit immune clearance (Heikkinen & Chonmaitree, 2000). The significantly higher levels of PD-L1 among CSOM patients than controls suggest activation of immune check point pathways. Consistent with these results, PD-L1 ligation to PD-1 expressed on T cell targets inhibits effector responses, inhibits cytokine production, and induces exhausted states of T cells. This has been found to occur in other chronic infections such as hepatitis B, tuberculosis, and chronic sinusitis, where PD-L1 expression is associated with pathogen persistence (Chang et al., 2014). The present results were consistent with Schönrich et al., (2019) who demonstrated that under chronic viral infection, the excessive up-regulation of PD-L1 plays a role in anergy and clearance impairment by consistent antigenic stimulation. A strong positive correlation was found between viral RNA positivity and serum PD-L1 levels suggesting the presence of the virus directly stimulates the activation of the immune checkpoint processes. Since interferon-y mediated induction of PD-L1 transcription has been reported to occur through the JAK/STAT1 and IRF1 pathways in chronic respiratory infections (Moon et al., 2017), this may represent a mediating mechanism in this area. Hence, PD-L1 was sustained by the antigen characteristics of persistent viruses as an immune evasion mechanism that involves a balance of host defense and tissue tolerance. In CSOM this mechanism probably prevents excessive tissue destruction but at the same time promotes microbial survival and disease chronicity. Inter-group comparative analysis demonstrated the highest PD-L1 levels in the SARS-CoV-2 positive cases followed by Rhinovirus and Adenovirus. This gradient may reflect the differences in viral tropism, viral replication kinetics and viral immunogenicity. In particular, it has been demonstrated that severe acute respiratory syndrome coronavirus (SARS)-coV-2 potently upregulates PD-L1 on epithelial and myeloid cells through activation of NF-kB and type I interferon signaling (Huang et al., 2023). Rhinovirus and Adenovirus, although less potent inducers, by toll-like receptor- mediated pathway can still induce PD-L1 resulting in a sustained inhibitory environment. Collectively, these results led us to suggest that CSOM with up-regulated optical PD-L1 was a sign of chronic immune adaptation. The high levels of soluble PD-L1 that we find could also be the result of proteolytic shedding of the membrane protein PD-L1 or alternative splicing, both of which have been described in chronic inflammatory conditions (Niu et al., 2022). Besides the expression of PD-L1 on local mucosal tissues, circulating soluble PD-

L1 can further bind PD-1 and subject the body to systemic immunosuppression. The clinical implications of this activation of the immune checkpoint are two-fold. First, PD-L1 expression might be important as a biomarker of chronicity or viral persistence in otitis media. Second, modulation of this pathway would hold potential for therapeutic opportunities. Several publications have proposed that checkpoint blockade can help to restore T-cell function and support the clearance of pathogens in chronic infections (Wykes and Lewin, 2018). However, in diseases such as CSOM, where inflammation was anatomically well circumscribed and recurrent, systemic blockade may pose a risk of adverse immunogenic effects; therefore, more localized immunomodulation may be a safe strategy (Abbasifard et al., 2025). current findings make a mechanistic connection between the persistence of the virus and the PD-L1 related immune control in chronic otitis media. The combination of viral RNAemia and high PD-L1 was the hallmark of the operation of such an immunological feedback loop whereby the persistence of antigenic stimulation kept the immune system inhibited and both viral and bacterial pathogens alive.

Conclusion: The current study showed a link between viral RNA presence and PD-L1 overexpression in a group of patients suffering chronic suppurative otitis media (CSOM). The striking elevation of serum levels of PD-L1 in affected patients would point to persistent stimulation of the immune checkpoint. The good correlation between the positivity of viral RNA and expression of PD-L1 further endorses the concept of viral persistence as permanent stimulus of immunoregulatory signaling.

Author Contributions

I.N.K. and M.A.K.A. contributed to the conceptualization and design of the study. They were responsible for methodology development, data collection, formal analysis, data curation, and drafting the original and revised versions of the manuscript. S.H.A. contributed to supervision and visualization. All authors reviewed and approved the final version of the manuscript.

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Ethical approval

This study was approved by the Ethical Approval Committee of the College of Education, University of Babylon, Iraq (Reference No. 318, dated 7/4/2024). All procedures were conducted in accordance with ethical standards, and informed consent was obtained from all participants. The study was performed with scientific integrity and without fabrication, falsification, plagiarism, or any form of scientific misconduct.

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Conflict of interest

The authors declare that they have no competing interests related to this study.

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پاسخ تنظیمی ایمنی مرتبط با التهاب پایدار: بیش‌بیان PD-L1 و شناسایی RNA ویروسی در اوتیت چرکی مزمن

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چکیده

هدف: اوتیت میانی چرکی مزمن (CSOM) یک بیماری التهابی مزمن گوش میانی است که با تشکیل بیوفیلم‌های میکروبی، تغییر در مکانیسم‌های ایمنی، تخریب اپی‌تلیوم و آسیب بافتی مشخص می‌شود. هدف از این مطالعه تعیین ارتباط بین بیان PD-L1 و مثبت بودن RNA ویروسی در بیماران مبتلا به CSOM و بررسی نقش بالقوه تحلیل نقاط وارسی ایمنی (immune checkpoint) در تداوم بیماری بود.

مواد و روش‌ها: در این مطالعه، پنجاه شرکت‌کننده مورد بررسی قرار گرفتند که شامل پنجاه بیمار مبتلا به CSOM و بیست‌وپنج فرد سالم به‌عنوان گروه کنترل بودند. از میان شرکت‌کنندگان، ۵۰ نفر بیمار مبتلا به CSOM مراجعه‌کننده به بخش گوش، حلق و بینی بیمارستان عمومی دیوانیه و ۵۰ نفر افراد ظاهراً سالم بدون آسیب‌شناسی گوش میانی بودند. بیماران در بازه سنی ۱۵ تا ۷۵ سال از هر دو جنس قرار داشتند و بر اساس معاینات بالینی و اتوسکوپیک تشخیص داده شدند. برای شناسایی ژنوم ویروسی شامل ویروس سنسیشیال تنفسی (ژن N به طول ۱۱۳ جفت‌باز)، رینوویروس (ژن UTR به طول ۲۱۸ جفت‌باز) و آدنوویروس (۳۱۰ جفت‌باز)، آزمون RT-PCR انجام شد. سطح PD-L1 با استفاده از آزمون ایمونوفلورسانس و به روش لجستیک چهارپارامتری (ELI) اندازه‌گیری گردید.

نتایج: غربالگری مولکولی RNA ویروسی به روش RT-PCR نشان داد که اغلب بیماران مبتلا به اوتیت میانی چرکی مزمن دارای یک یا چند نتیجه مثبت از نظر ویروسی بودند. PCR برای شناسایی RNA ویروس‌ها (SARS-CoV-2، رینوویروس و آدنوویروس) در ۴۰ نفر از ۵۰ بیمار (٪۸۰) انجام شد و متعاقب آن، در ۱۰ نفر (٪۲۰) RNA رینوویروس و در ۶ نفر (٪۱۲) RNA آدنوویروس شناسایی گردید. میانگین سطح سرمی PD-L1 در بیماران به‌طور معنی‌داری بالاتر از گروه کنترل بود (۰/۱۳ ± ۰/۲۴۲ در برابر ۰/۰۵ ± ۱/۰۱ نانوگرم/میلی‌لیتر؛ $t = ۵/۲۶$؛ $P <۰/۰۰۰۱$). همچنین، همبستگی مثبت معنی‌داری بین افزایش PD-L1 و مثبت بودن RNA ویروسی مشاهده شد. بیان PD-L1 در بیمارانی که از نظر RNA ویروسی مثبت بودند (۱/۰۶ نانوگرم/میلی‌لیتر) به‌طور قابل‌توجهی بیشتر از بیمارانی بود که نتیجه منفی داشتند (۰/۵۸ نانوگرم/میلی‌لیتر).

نتیجه‌گیری: وجود RNA ویروسی و بیش‌بیان PD-L1 در بیماران مبتلا به CSOM بیانگر یک پاسخ ایمنی تطابقی نامتوازن است که منجر به مهار التهاب بیش‌ازحد و افزایش تحمل میکروبی می‌شود. این یافته‌ها نشان می‌دهد که مسیر PD-1/PD-L1 نقش مهمی در ماهیت مزمن اوتیت میانی ایفا می‌کند.

کلمات کلیدی: اوتیت میانی چرکی مزمن، رینوویروس، نقطه وارسی ایمنی، ویروس کرونا، RT-PCR

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