

Levels of IL-6, IL-8, IL-10 and IL-17A in serum and IL-8 in bronchoalveolar lavage fluid are elevated in haematological patients with invasive pulmonary aspergillosis

Background and Objectives

Infections with *Aspergillus fumigatus* and other moulds have been shown to induce elevated levels of several immunologic markers. However, diagnostic potential of these markers for invasive pulmonary aspergillosis (IPA) has not been sufficiently evaluated yet.

Objectives:

- 1) To determine concentrations of cytokines in bronchoalveolar lavage fluid (BALF) and serum/plasma: Interleukin (IL)-4/-6/-8/-10/-15/-17A/-22, soluble IL-2 receptor (sIL-2R), tumor necrosis factor α (TNF α), interferon γ (IFN γ), "regulated on activation, normal T cell expressed and secreted" (RANTES)
- 2) To determine statistically significant differences in cytokine concentrations in probable/proven IPA vs. no evidence of IPA

Study Design and Methods

Prospective recruitment of the cohort and sample collection (04/2014-09/2016). Cases were graded for IPA according to the 2008 revised EORTC/MSG criteria (probable/proven, possible and no evidence of IPA, respectively). Retrospective measurement of the cytokine concentrations (09/2016-10/2016).

Locations: Patient recruitment: Department of Internal Medicine, University Hospital of Graz, Graz, Styria, Austria. **Immunoassays:** Centre for Medical Research, Medical University of Graz, Graz, Styria, Austria.

Inclusion criteria: Adult patients with a haematological malignancy as underlying disease, suspected pulmonary infection, who underwent routine bronchoscopy.

Samples: Serum/plasma samples were collected at the same day according to bronchoscopy and stored at -80°C until cytokine measurement.

Cytokine concentrations were determined with a personalized ProcartaPlex[®] 11plex immunoassay (eBioscience, Vienna, Austria).

Statistical methods: Mann-Whitney-U-Test, Receiver Operating Characteristics (ROC) curve analysis and area under the curve (AUC) calculations

Results

87 patients were recruited, most frequent underlying diseases were: Acute myeloid leukemia (40,2%), non-hodgkin lymphoma (23%), acute lymphoblastic leukemia (9%). After exclusion of 28 cases with possible IPA, 59 cases were included in the analysis (23 men, 36 women, age range 27-82 years; 2 proven IPA, 7 probable IPA, 50 cases with no evidence of IPA).

IL-6, IL-8, IL-10, IL-17A were significantly elevated in serum/plasma, IL-8 was significantly elevated in BALF in probable/proven IPA (n=9) vs. no evidence of IPA (n=50) (table 1 and 2).

Conclusion

Serum concentrations of IL-6, IL-8, IL-10 and IL-17A as well as BALF levels of IL-8 were significantly higher in patients with probable/proven IPA compared to those without evidence of IPA. Our study indicates that these biomarkers may have diagnostic potential for diagnosing IPA among haematological malignancy patients. Further investigations are needed.

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Table 2: Diagnostic performance of cytokine levels in BALF and serum/plasma (probable/proven IPA (n=9) vs. no evidence of IPA (n=50), significant differences (p<0.05) are highlighted). AUC: Area under the curve; CI: Confidence interval

¹Medical University of Graz, Department of Internal Medicine, Division of Pulmonology, Graz, Austria; ²Medical University of Graz, Department of Internal Medicine, Section of Infectious Diseases and Tropical Medicine, Graz, Austria; ³Medical University of Graz, Clinical Institute of Medical and Chemical Laboratory Diagnostics, Graz, Austria; ⁴Medical University of Graz, Department of Internal Medicine, Division of Haematology, Graz, Austria; ⁵Medical University of Graz, Centre for Medical Research, Graz, Austria; ⁶University of California, Department of Medicine, Division of Infectious Diseases, San Diego, USA

Table 1: Minimum (Min) and maximum (Max) measured concentrations [pg/mL] of significantly elevated cytokine concentrations (probable/proven IPA (n=9) vs. no evidence of IPA (n=50)) as well as median concentration and interquartile range (IQR) in serum/plasma and BALF, respectively.

		Probable/proven IPA				No evidence of IPA			
	Marker [pg/mL]	Min	Max	Median	IQR	Min	Max	Median	IQR
Serum/Plasma	IL-10	0.2	358.7	8.5	50.3	0.0	220.2	1.8	3.4
	IL-17A	0.0	3.7	0.5	2.6	0.0	2.7	0.0	0.2
	IL-6	3.7	3049.4	301.9	1686.7	0.0	3044.7	21.8	75.1
	IL-8	14.3	2300.4	361.6	1052.6	0.0	490.5	17.9	87.5
BALF	IL-8	263.7	5705.8	2062.5	2232.4	80.6	5672.7	533.1	1189.1

More information and figures will be available at our paper poster presentation!

	Serum/Plasma			BALF		
Marker	AUC	95% CI	p-value	AUC	95% CI	p-value
IFN γ	0.571	0.347-0.795	0.500	0.489	0.248-0.730	0.918
IL-10	0.736	0.540-0.931	0.025	0.570	0.366-0.773	0.508
IL-15	0.648	0.447-0.849	0.161	0.460	0.308-0.611	0.702
IL-17A	0.733	0.527-0.940	0.027	0.584	0.369-0.799	0.425
sIL-2R	0.567	0.331-0.802	0.527	0.460	0.286-0.634	0.702
IL-22	0.660	0.445-0.875	0.129	0.515	0.337-0.694	0.885
IL-4	0.510	0.311-0.709	0.924	0.394	0.157-0.632	0.315
IL-6	0.711	0.484-0.938	0.045	0.685	0.515-0.855	0.078
IL-8	0.769	0.584-0.954	0.011	0.760	0.608-0.913	0.013
RANTES	0.593	0.390-0.796	0.376	0.532	0.314-0.749	0.764
TNF α	0.619	0.348-0.890	0.259	0.645	0.473-0.817	0.169

