

Multisystem Inflammatory Syndrome in Adult after First Dose of mRNA Vaccine

Appendix

Additional Methods

After discharge, we measured a panel of 67 cytokines and chemokines from the patient and 3 healthy controls using Bio-plex Pro Human Chemokine assays (Bio-Rad, <https://www.bio-rad.com>) (Appendix Table, Appendix Figure 2) to investigate abnormal responses induced by coronavirus disease. The patient's BCA-1/CXCL13, HGF, IL-5, IL-6, IL-8/CXCL8, IL-13, IL-15, IL-16, IP-10/CXCL10, MIF, MPIF-1/CCL23, PDGF-BB, and VEGF levels were elevated before steroid administration compared to healthy controls and became almost normal during the recovery period.

Among the cytokines known to be elevated in the cytokine storm, IL-1, IL-2, IL-6, IL-7, IL-12, IL-17, IL-18 TNF- α , MCSF, G-CSF, CXCL-10/IP-10, CCL-3, CCL-5, IFN- γ , and MCP-1, only IL-6 and CXCL-10/IP-10 were elevated in the acute phase (1). We believe that the elevation of IL-5, IL-16, MIF, and VEGF are also characteristic of this case. IL-5, IL-16, and MIF have been reported to be elevated in myocardial injury (2–4), and MIF and VEGF have been suggested to be associated with vasculitis (5,6), which may be related to the pathogenesis of this case.

References

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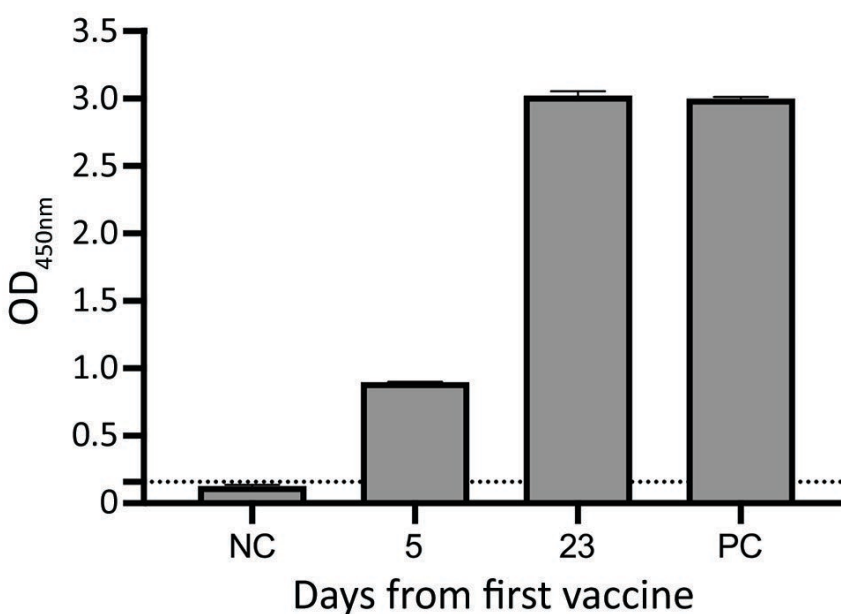
Appendix Table. Profile of 67 cytokines and chemokines from a patient with multisystem inflammatory syndrome in an adult and 3 healthy persons who had received 2 doses of mRNA vaccine for coronavirus disease

| Cytokines and chemokines | Patient | | | | | Controls | | |
|--------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| | Day 5 | Day 6 | Day 9 | Day 23 | Day 44 | N1 | N2 | N3 |
| BCA-1/CXCL13 | 91.93 | 93.02 | 33.63 | 27.79 | 33.04 | 26.81 | 27.16 | 24.96 |
| HGF | 860.57 | 916.26 | 513.33 | 420.42 | 462.91 | 328.58 | 242.75 | 187.56 |
| IL-5 | 45.35 | 48.35 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| IL-6 | 99.29 | 79.43 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| IL-8/CXCL8 | 23.01 | 21.97 | 10.25 | 12.13 | 14.56 | 9.03 | 10.68 | 7.85 |
| IL-13 | 1.73 | 1.93 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| IL-15 | 573.25 | 551.10 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| IL-16 | 251.27 | 192.02 | 86.50 | 108.90 | 121.02 | 91.20 | 81.37 | 73.20 |
| IP-10/CXCL10 | 923.37 | 836.39 | 103.41 | 92.82 | 152.13 | 197.93 | 97.95 | 150.18 |
| MIF | 21,666.34 | 45,596.47 | 17,066.50 | 24,660.14 | 2,433.82 | 1,568.66 | 1,421.55 | 2,559.85 |
| MPIF-1/CCL23 | 917.16 | 1,077.75 | 317.36 | 249.18 | 185.88 | 168.91 | 67.99 | 291.75 |
| PDGF-BB | 7,437.96 | 5,179.37 | 3,261.03 | 2,455.29 | 2,895.53 | 4,077.71 | 1,628.17 | 2,180.10 |
| VEGF | 227.94 | 271.61 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| b-NGF | 30.04 | 30.13 | 6.32 | 7.72 | 3.19 | 0.00 | 0.00 | 0.00 |
| GCP-2/CXCL6 | 160.60 | 127.54 | 234.13 | 194.95 | 373.96 | 29.53 | 27.86 | 37.87 |
| G-CSF | 808.20 | 572.19 | 1,101.25 | 1,189.84 | 3,463.18 | 116.85 | 166.68 | 122.80 |
| Gro-b/CXCL2 | 613.63 | 558.26 | 874.69 | 747.56 | 1,276.49 | 199.66 | 315.38 | 296.14 |
| IFN- α 2 | 9.54 | 7.06 | 4.75 | 5.93 | 8.34 | 0.00 | 0.00 | 0.00 |
| IL-1 α | 38.68 | 31.24 | 22.65 | 25.09 | 21.90 | 2.01 | 2.01 | 0.19 |
| IL-1 α | 869.98 | 878.00 | 130.95 | 172.08 | 309.16 | 44.71 | 0.00 | 0.00 |
| IL-2 α | 118.62 | 116.42 | 79.87 | 80.98 | 108.86 | 50.41 | 40.80 | 46.40 |
| IL-12(p40) | 180.16 | 128.66 | 124.88 | 113.61 | 181.62 | 65.73 | 35.30 | 35.30 |
| IL-17 | 12.88 | 8.42 | 2.49 | 4.62 | 9.87 | 0.00 | 0.00 | 0.00 |
| IL-18 | 113.03 | 93.66 | 53.68 | 56.97 | 60.35 | 20.16 | 35.33 | 19.20 |
| I-TAC/CXCL11 | 128.64 | 130.71 | 258.81 | 158.94 | 79.01 | 22.94 | 17.68 | 30.81 |
| M-CSF | 39.22 | 29.75 | 26.71 | 27.35 | 22.10 | 7.17 | 11.19 | 10.18 |
| MIP-1 α /CCL3 | 267.53 | 194.33 | 378.72 | 435.93 | 1554.19 | 4.76 | 7.27 | 4.76 |
| MIP-1 δ /CCL15 | 5,363.92 | 5,592.40 | 3,610.77 | 3,456.25 | 4,886.33 | 2,536.68 | 2,686.14 | 1,751.91 |
| 6Ckine/CCL21 | 26,044.85 | 39,882.28 | 17,327.50 | 19,974.72 | 59,927.96 | 23,972.90 | 25,506.51 | 21,218.49 |
| ENA-78/CXCL5 | 1,212.70 | 977.62 | 942.50 | 695.23 | 3,312.40 | 825.19 | 776.21 | 764.77 |

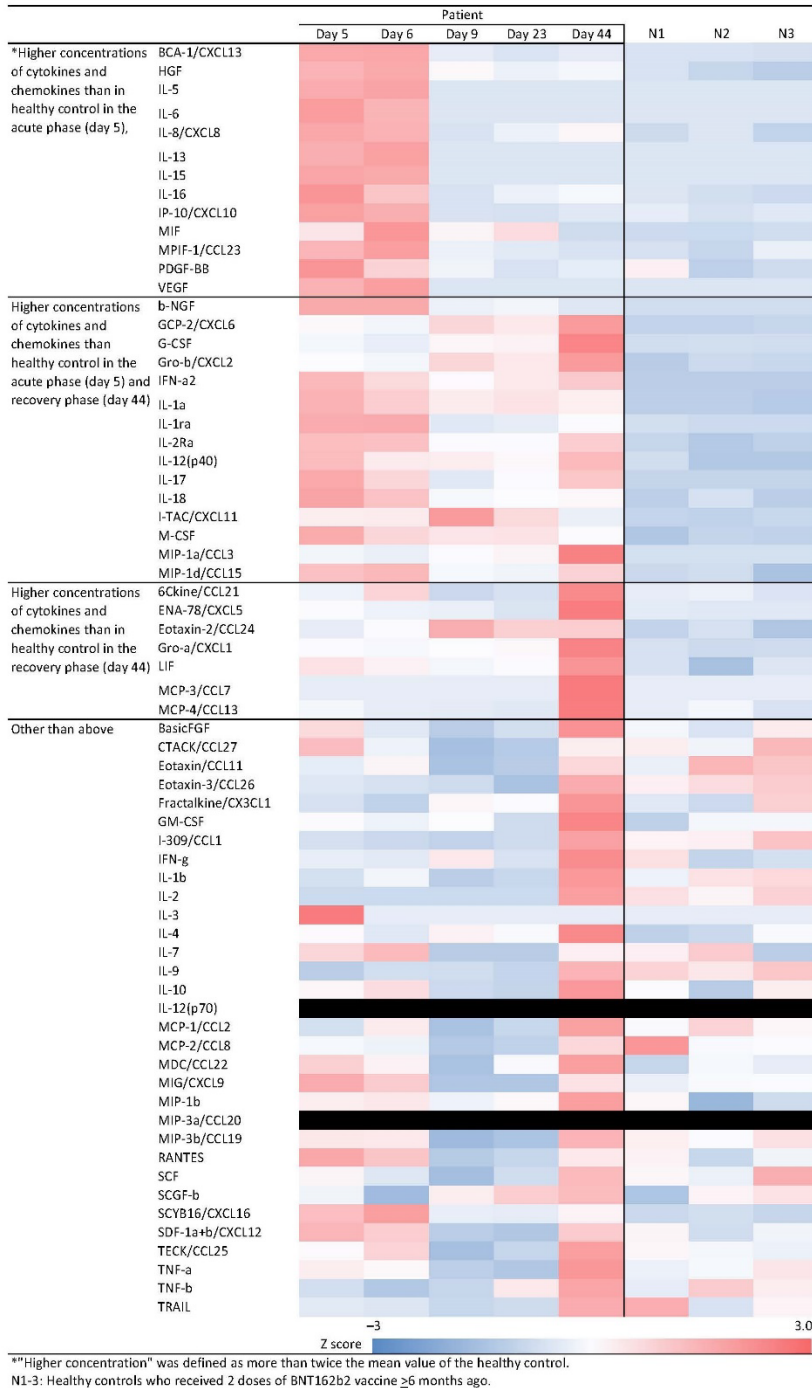
| Cytokines and chemokines | Patient | | | | | Controls | | |
|--------------------------|------------|------------|------------|------------|------------|------------|------------|------------|
| | Day 5 | Day 6 | Day 9 | Day 23 | Day 44 | N1 | N2 | N3 |
| Eotaxin-2/CCL24 | 610.70 | 733.43 | 1160.59 | 968.08 | 976.64 | 428.15 | 526.03 | 332.06 |
| Gro-a/CXCL1 | 365.64 | 347.95 | 376.18 | 393.44 | 921.62 | 218.10 | 174.88 | 182.84 |
| LIF | 77.01 | 70.30 | 61.98 | 66.18 | 112.24 | 50.08 | 30.82 | 52.39 |
| MCP-3/CCL7 | 0.00 | 0.00 | 0.00 | 0.00 | 42.59 | 0.00 | 0.00 | 0.00 |
| MCP-4/CCL13 | 66.89 | 60.32 | 59.43 | 57.52 | 134.17 | 60.58 | 66.21 | 53.50 |
| BasicFGF | 51.09 | 40.12 | 33.58 | 37.90 | 64.48 | 43.51 | 38.95 | 47.77 |
| CTACK/CCL27 | 1103.94 | 746.55 | 438.94 | 502.99 | 873.03 | 878.66 | 759.24 | 1123.30 |
| Eotaxin/CCL11 | 47.07 | 53.18 | 34.86 | 37.49 | 59.50 | 47.78 | 67.31 | 63.64 |
| Eotaxin-3/CCL26 | 83.57 | 81.38 | 79.49 | 70.25 | 113.99 | 94.96 | 100.01 | 104.82 |
| Fractalkine/CX3CL1 | 126.98 | 112.19 | 154.47 | 149.99 | 222.58 | 133.50 | 119.69 | 181.95 |
| GM-CSF | 25.22 | 24.23 | 25.16 | 22.18 | 33.92 | 21.10 | 24.61 | 24.70 |
| I-309/CCL1 | 32.89 | 30.92 | 29.11 | 31.80 | 61.86 | 43.29 | 44.17 | 54.29 |
| IFN-g | 27.31 | 26.81 | 30.19 | 26.10 | 37.50 | 30.88 | 24.68 | 25.84 |
| IL-1b | 6.29 | 6.76 | 5.89 | 6.09 | 8.62 | 6.68 | 7.35 | 7.51 |
| IL-2 | 0.00 | 0.00 | 0.00 | 0.00 | 14.05 | 7.31 | 5.32 | 8.90 |
| IL-3 | 0.01 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| IL-4 | 81.83 | 75.30 | 83.59 | 80.30 | 107.60 | 68.40 | 70.87 | 80.52 |
| IL-7 | 9.74 | 12.49 | 0.00 | 0.00 | 7.35 | 7.35 | 10.87 | 0.07 |
| IL-9 | 208.11 | 228.20 | 226.58 | 216.36 | 327.58 | 297.72 | 281.09 | 311.00 |
| IL-10 | 8.16 | 8.79 | 6.89 | 6.72 | 10.54 | 8.03 | 6.42 | 8.40 |
| IL-12(p70) | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| MCP-1/CCL2 | 53.91 | 64.66 | 46.43 | 52.05 | 79.06 | 60.63 | 69.33 | 62.39 |
| MCP-2/CCL8 | 53.48 | 50.60 | 26.42 | 31.40 | 71.61 | 101.63 | 54.37 | 55.22 |
| MDC/CCL22 | 792.45 | 701.66 | 474.66 | 665.63 | 928.56 | 541.04 | 662.62 | 620.09 |
| MIG/CXCL9 | 56.05 | 47.46 | 16.67 | 16.96 | 41.42 | 30.58 | 34.09 | 34.39 |
| MIP-1b | 224.02 | 225.72 | 217.14 | 221.23 | 244.88 | 221.81 | 196.70 | 209.23 |
| MIP-3a/CCL20 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| MIP-3b/CCL19 | 138.39 | 135.39 | 0.00 | 15.78 | 204.26 | 127.83 | 107.47 | 147.32 |
| RANTES | 9,363.29 | 8,820.77 | 6,618.98 | 6,886.85 | 8,146.81 | 7,986.42 | 6,914.73 | 7,588.66 |
| SCF | 75.83 | 64.30 | 46.75 | 59.98 | 95.11 | 75.33 | 68.48 | 99.40 |
| SCGF-b | 141,179.79 | 108,130.23 | 151,784.32 | 166,409.90 | 174,281.40 | 113,842.98 | 149,646.34 | 157,163.45 |

| Cytokines and chemokines | Patient | | | | | Controls | | |
|--------------------------|----------|----------|----------|----------|----------|----------|----------|----------|
| | Day 5 | Day 6 | Day 9 | Day 23 | Day 44 | N1 | N2 | N3 |
| SCYB16/CXCL16 | 863.50 | 958.28 | 630.81 | 624.50 | 709.56 | 553.42 | 573.47 | 542.07 |
| SDF-1a+b/CXCL12 | 2,704.63 | 2514.82 | 1,580.83 | 1,512.64 | 2,530.59 | 2,178.87 | 1,762.36 | 2,021.26 |
| TECK/CCL25 | 1,045.18 | 1,147.02 | 824.00 | 902.54 | 1,289.05 | 1,052.93 | 1,019.89 | 997.06 |
| TNF-a | 130.18 | 126.50 | 99.40 | 95.10 | 167.69 | 117.97 | 122.05 | 134.08 |
| TNF-b | 279.37 | 265.23 | 274.34 | 306.91 | 339.22 | 287.75 | 320.74 | 304.75 |
| TRAIL | 13.45 | 13.23 | 12.33 | 12.61 | 18.53 | 18.43 | 13.00 | 15.06 |

*Values are expressed in pg/mL. Values below the detection sensitivity are indicated as 0.00.



Appendix Figure 1. Severe acute respiratory syndrome coronavirus 2 anti-spike (full-length) antibody titers from a patient with multisystem inflammatory syndrome in an adult. Antibody induction was observed within 5 days after vaccination. High antibody titers were obtained 23 days after vaccination. Dotted line indicates the positivity criterion, which was based on the negative control mean + 3 SD. NC, negative control; PC, positive control.



Appendix Figure 2. Profile of 67 cytokines and chemokines from a patient with multisystem inflammatory syndrome, compared with those of 3 healthy persons as controls. The controls were infection-free men 34–41 years of age who had received 2 doses of the BNT162b2 vaccine (Pfizer-BioNTech, <https://www.pfizer.com>).

