Dr Jorge do Campo1, Dr Vivienne Taylor2
1Department of Medicine Noosa Hospital, Ramsay Health Care, Noosaville, Queensland, Australia
2Division of General Practice, Department of Medicine, University of Sydney, Sydney, New South Wales, Australia

INTRODUCTION: Since the SARS-CoV-2 (severe acute respiratory syndrome coronavirus2) vaccination started there have been multiple reports of different off target adverse effects related to the vaccination, such as myocarditis, immune mediated thrombosis, thrombocytopenia and allergic reactions. W Murphy and Dan Longo in the NEJM November 2021 reported these adverse effects associated with Anti-idiotype antibodies (Ab2) in SARS-CoV-2 vaccination. The pathologic cascade of Ab2 is described in several ways as the antibodies can bind to the protective normal antibodies (Ab1) resulting in immune complex formation and clearance thus impairing Ab1 efficacy. Another action of the Ab2 could be inhibiting normal ligands affecting interaction with angiotensin converting enzyme 2 (ACE2) receptors or stimulating the ACE2 receptor and down-regulating the ACE2 function. There is also a description of complement-mediated and immune cell attack on ACE2 expressing cells (1). The case reported in this manuscript is related to a severe deterioration in a male with previous diagnosis of ME/CFS with worsening lethargy and cognitive skills after SARS-CoV-2 vaccination.

The outstanding clinical improvement after starting oral Colchicine is the reason for this paper.

CASE REPORT: A 46-year-old male with a previous history of Sarcoidosis and Haemochromatosis had ME/CFS since 2016. He was followed up at Noosa Hospital clinic related to his ME/CFS. His general symptoms related to this condition were under control and he was able to work and study at the University. After the second dose of his SARS-CoV-2 (Pfizer –BioNTech COVID-19) vaccination in August 2021 his general condition deteriorated. During September—October 2021 his cognitive skills declined and he had to stop his university studies. The patient also stopped driving his car because of lethargy and could not do any sport recreational activity. Because of ME/CFS he was on treatment with multivitamins and low dose Naltrexone and Spironolactone before vaccination. After the ME/CFS clinical deterioration the decision was to start Colchicine 0.5 mg a day (November 2021). After four weeks of Colchicine plus his previous medication, his level of energy and cognitive skills recovered to pre vaccination status.

DISCUSSION: The immunologic cascade after SARS-CoV-2 vaccination triggered by Ab2 ended in activation of pyrin domain containing protein3 (NRLP3) inflammasome. This is the pattern of activation of Interleukin1 beta (IL1-beta) cytokine complex which is activated in inflammatory conditions (1).

Colchicine is postulated to work by inhibiting tubulin polymerization and microtubule formation blocking inflammasome activation (2). Spironolactone increased the activity and number of macrophage angiotensin converting enzyme 2 (ACE2) receptors. In the microglia this effect may represent a reduction of neuro-inflammation (3). In this abstract we present ME/CFS patients treated with the synergetic effect of Colchicine and Spironolactone to inhibit Inflammasome and decrease inflammation.

Population and Method: 23 patients (19 females) with positive serology for EBV infection and ME/CFS were included. All the patients were treated with multivitamins. Patients were educated about benefit and adverse effect of spironolactone and colchicine before treatment. The starting dose of Spironolactone was 12.5 mg a day increased to 25 mg a day (during years 2019 to 2021). The introduction of Colchicine 0.5 mg/day on treatment plan was during year 2021. Patient follow-up was in the outpatient clinic and GP clinic.

RESULTS: Total 23 Patients 19 were Females age 37.3±28 and 4 were Males age 61±9. Two patients stop colchicine after 4 weeks. Improvement in cognitive skills was the early manifestation of spironolactone benefit. Patients reported to be less brain foggy, more alert, and they found it easier to focus when doing normal everyday activities. They were also less irritable by noise and light and described themselves to be able to multi-task again. There was an improvement in general condition and everyday activities four weeks after Colchicine started.

Conclusion: Patients with ME/CFS improve their cognitive skills and everyday physical activity tolerance when treated with Colchicine and Spironolactone.

References
1. Murphy J, Longo D. A Possible Role for Anti-Idiotypes Antibodies in SARS-CoV-2 infection and vaccination N Engl J Med November 24,2021
2. Tardif J-C, Kouz S, Waters DD, et al. Efficacy and safety of low-dose colchicine after myocardial infarction. N Engl J Med 2019;381: 2497-2505
3. Mineralocorticoid Receptor Blocker Increases Angiotensin-Converting Enzyme 2 Activity in Congestive Heart Failure. Keidar S, et al. Circ Res.2005;97:946-953.

BEST POSTER PRIZE IN ADULT MEDICINE – FELLOW

CLINICAL IMPROVEMENT IN PATIENTS WITH ME/CFS WITH SYNERGISTIC EFFECT OF COLCHICINE AND SPIRONOLACTONE TARGETING INHIBITION OF INFLAMMASOME ACTIVITY

Dr Jorge do Campo1, Dr Vivienne Taylor2
1Department of Medicine Noosa Hospital, Ramsay Health Care, Noosaville, Queensland, Australia
2Division of General Practice, Department of Medicine, University of Sydney, Sydney, New South Wales, Australia

Background: Myalgic Encephalomyelitis/ Chronic Fatigue Syndrome (ME/CFS) has been associated to Epstein Bar Virus (EBV), Coxsakie virus and Ross River virus infections. Recently a similar condition to ME/CFS has been described as ‘Long Covid’ associated to SARS-CoV-2.

Patients with positive EBV serology and ME/CFS may be carriers of a chronic latent infection that translates in a chronic systemic inflammation with neuroinflammation. The activation of the immunologic cascade after a viral infection or vaccination can trigger the formation of Anti-idiotype antibodies (Ab2) and an activation of pyrin domain containing protein3 (NRLP3) inflammasome. The NRLP3 inflammasome is the pattern of activation for interleukin (IL1-beta) cytokine complex which is activated in inflammatory conditions (1).

Colchicine is postulated to work by inhibiting tubulin polymerization and microtubule formation blocking inflammasome activation (2). Spironolactone increased the activity and number of macrophage angiotensin converting enzyme 2 (ACE2) receptors. In the microglia this effect may represent a reduction of neuro-inflammation (3). In this abstract we present ME/CFS patients treated with the synergetic effect of Colchicine and Spironolactone to inhibit Inflammasome and decrease inflammation.

Population and Method: 23 patients (19 females) with positive serology for EBV infection and ME/CFS were included. All the patients were treated with multivitamins. Patients were educated about benefit and adverse effect of spironolactone and colchicine before treatment. The starting dose of Spironolactone was 12.5 mg a day increased to 25 mg a day (during years 2019 to 2021). The introduction of Colchicine 0.5 mg/day on treatment plan was during year 2021. Patient follow-up was in the outpatient clinic and GP clinic.

RESULTS: Total 23 Patients 19 were Females age 37.3±28 and 4 were Males age 61±9. Two patients stop colchicine after 4 weeks. Improvement in cognitive skills was the early manifestation of spironolactone benefit. Patients reported to be less brain foggy, more alert, and they found it easier to focus when doing normal everyday activities. They were also less irritable by noise and light and described themselves to be able to multi-task again. There was an improvement in general condition and everyday activities four weeks after Colchicine started.

Conclusion: Patients with ME/CFS improve their cognitive skills and everyday physical activity tolerance when treated with Colchicine and Spironolactone.

References
1. Murphy J, Longo D. A Possible Role for Anti-Idiotypes Antibodies in SARS-CoV-2 infection and vaccination N Engl J Med November 24,2021
2. Tardif J-C, Kouz S, Waters DD, et al. Efficacy and safety of low-dose colchicine after myocardial infarction. N Engl J Med 2019;381: 2497-2505
3. Mineralocorticoid Receptor Blocker Increases Angiotensin-Converting Enzyme 2 Activity in Congestive Heart Failure. Keidar S, et al. Circ Res.2005;97:946-953.

WORSENING OF LETHARGY POST SARS-COV-2 VACCINATION IN A PATIENT WITH ME/CFS

Dr Jorge do Campo1
1Department of Medicine Noosa Hospital, Ramsay Health Care, Noosaville, Queensland, Australia

Introduction: Since the SARS-CoV-2 (severe acute respiratory syndrome coronavirus2) vaccination started there have been multiple reports of different off target adverse effects related to the vaccination, such as myocarditis, immune mediated thrombosis, thrombocytopenia and allergic reactions. W Murphy and Dan Longo in the NEJM November 2021 reported these adverse effects associated with Anti-idiotype antibodies (Ab2) in SARS-CoV-2 vaccination. The pathologic cascade of Ab2 is described in several ways as the antibodies can bind to the protective normal antibodies (Ab1) resulting in immune complex formation and clearance thus impairing Ab1 efficacy. Another action of the Ab2 could be inhibiting normal ligands affecting interaction with angiotensin converting enzyme 2 (ACE2) receptors or stimulating the ACE2 receptor and down-regulating the ACE2 function. There is also a description of complement-mediated and immune cell attack on ACE2 expressing cells (1). The case reported in this manuscript is related to a severe deterioration in a male with previous diagnosis of ME/CFS with worsening lethargy and cognitive skills after SARS-CoV-2 vaccination.

The outstanding clinical improvement after starting oral Colchicine is the reason for this paper.

Case Report: A 46-year-old male with a previous history of Sarcoidosis and Haemochromatosis had ME/CFS since 2016. He was followed up at Noosa Hospital clinic related to his ME/CFS. His general symptoms related to this condition were under control and he was able to work and study at the University. After the second dose of his SARS-CoV-2 (Pfizer –BioNTech COVID-19) vaccination in August 2021 his general condition deteriorated. During September—October 2021 his cognitive skills declined and he had to stop his university studies. The patient also stopped driving his car because of lethargy and could not do any sport recreational activity. Because of ME/CFS he was on treatment with multivitamins and low dose Naltrexone and Spironolactone before vaccination. After the ME/CFS clinical deterioration the decision was to start Colchicine 0.5 mg a day (November 2021). After four weeks of Colchicine plus his previous medication, his level of energy and cognitive skills recovered to pre vaccination status.

Discussion: The immunologic cascade after SARS-CoV-2 vaccination triggered by Ab2 ended in activation of pyrin domain containing protein3 (NRLP3) Inflammasome. This is the pattern of activation for interleukin (IL1beta). This may determine a general increase in the...
systemic and microglia inflammation as described in ME/CFS. The clinical manifestation in the present case was worsening in the symptoms of the ME/CFS. The patient was already on Spironolactone targeting the increase on number of macrophages ACE2 receptors as immune modulation.

An anti-inflammatory synergy between Colchicine and Spironolactone is currently the focus of research in atherosclerosis. Colchicine has a direct effect on phagocytes leading to inflammatory inhibition and impaired production of IL-1 beta.

Conclusion: The Colchicine had a beneficial effect in recovering this patient from an exacerbation of his ME/CFS induced by SARS-CoV-2 vaccination.

References
1. Murphy J, Longo D. A Possible Role for Anti-Idiotypes Antibodies in SARS-CoV-2 infection and vaccination N Engl J Med November 24, 2021
2. Tardif J-C, Krouz S, Waters DD, et al. Efficacy and safety of low-dose colchicine after myocardial infarction. N Engl J Med 2019;381: 2497-2505

BEST POSTER PRIZE IN ADULT MEDICINE – TRAINEE

MONASH STATUS EPILEPTICUS STUDY(MOSES): GLASGOW COMA SCORE, AGE AND INPATIENT ONSET, NOT TIME TO TREATMENT, PREDICT IN-HOSPITAL MORTALITY AND MORBIDITY

Dr Yi Chao Foong1, Dr Gabriella Wong1, Dr Goelchin Alan1, Dr Zheng Song1, Dr Pauline Du1, Dr Mitchell Browne1, Dr Stefan Seggase1, Associate Professor Udaya Seneviratne1, Professor Thanh Phan1
1Monash Health, Melbourne, Australia

Background: Status epilepticus (SE) is a medical emergency with high mortality and morbidity. There is ongoing controversy over the predictors of mortality and morbidity.1,2 As a result, many of the mortality prediction tools that have been introduced in status epilepticus have failed to gain widespread acceptance.1,2 Furthermore, there is little literature on the predictors of morbidity in status epilepticus. We aimed to determine the predictors of in-hospital mortality and morbidity in an Australian setting.

Aim: To identify predictors of mortality and morbidity in status epilepticus in an Australian setting.

Methods: We retrospectively reviewed medical records between January 2020 and December 2020 to identify patients diagnosed with status epilepticus. Data regarding in-hospital mortality, modified Rankin Score (mRS), medical history, management and outcomes were collected from the electronic medical records.

Results: We identified 157 patients meeting the inclusion criteria. In-hospital mortality was 20.4% (32/157) and 40.8% (64/157) had an increase in their mRS. Only 67 (42.7%) of patients received first-line therapy with benzodiazepines, and of these only 35 were given within 20 minutes of diagnosis. Hospital mortality was 20.4% (32/157) and 40.8% (64/157) had an increase in their mRS. Only 67 (42.7%) of patients received first-line therapy with benzodiazepines, and of these only 35 were given within 20 minutes of diagnosis.

After adjusting for confounders, age, presenting Glasgow Coma Score (GCS) and inpatient onset of SE were associated with in-hospital mortality. For every 1 year increase in age, the odds of in-hospital mortality were increased by 1.05 (95%CI 1.01-1.09). For every 1 point decrease in GCS, the odds of in-hospital mortality increased by 1.13 (95%CI 1.01-1.25). Inpatient onset had greater odds of in-hospital mortality (Odds ratio (OR) of 4.42, 95%CI 1.71-11.49). Similarly, age, presenting GCS, inpatient onset of SE and independent predictors of increase in the modified Rankin Score. Time to first, second and third-line therapy were not found to be predictors of in-hospital mortality.

Conclusion: This is one of the largest cohorts of status epilepticus in an Australian setting. Status epilepticus was associated with a high rate of mortality and increased morbidity. Less than one-quarter of patients had timely provision of first-line SE treatment. Time to treatment was not associated with short-term mortality in status epilepticus; instead, age, initial GCS and an inpatient onset of SE were the strongest predictors of short-term mortality. These variables also predicted increase in morbidity following SE.

References
1. Sutter R, Semmlack S, Opic P, Spiegel R, De Marchis GM, Hunziker S, Kaplan PW, Rüegg S, Marsch S. Untangling operational failures of the status epilepticus severity score (STESS). Neurology. 2019 Apr 23;92(17):e1948-56.
2. Reindl C, Knappe RU, Spriegel ML, Sembhi JA, Mueller TM, Hamer HM, Huttner HB, Madzar D. Comparison of scoring tools for the prediction of in-hospital mortality in status epilepticus. Seizure. 2018 Mar 1;56:92-7.
3. Rivero Rodríguez D, Scherle Matamoros C, Sam K, DiCapua Sacoto D, Samaniego NM, Permas Y. Evaluation of STESS, mRSTESS, and EMSE to predict high disability and mortality at hospital discharge in Ecuadorian patients with status epilepticus. Neurocritical care. 2018 Dec;29(3):413-8.

BEST POSTER PRIZE IN ADULT MEDICINE – FELLOW

COVID-19 VACCINE RESPONSE IN PATIENTS ON CANCER THERAPY – EVIDENCE FROM AUSTRALIAN DATA

Dr Yada Kanjanapan1,2, Mr George Cavigi1, Mr Andrew Almonte1, Ms Sarah M Hicks2, Dr Teresa Neeman2, Dr Jo-Wai Wang1, Ms Sue Brew1, Professor Ian Cockburn1, Professor Elizabeth Gardiner2, Associate Professor Aude M Fahrer1, Professor Desmond Yip1,2
1Canberra Hospital, Canberra, Australia, 2Australian National University, Canberra, Australia

Background: Cancer patients have increased risk of serious illness or death from COVID-19. Vaccination protects against severe disease, but cancer patients were excluded from COVID-19 vaccine registration trials. Different cancer therapies may have varying impact on immune response. We assessed seroconversion post COVID-19 vaccination among cancer patients in a setting of high vaccine uptake with minimal community transmission.

Methods: Solid tumour patients and healthy controls from Canberra who received COVID-19 vaccination between 3/2021-1/2022 were included. Patients received active cancer therapy within two weeks of COVID-19 vaccination. Blood was collected at baseline, pre 2nd vaccine dose, then one, three and six months post 2nd dose. SARS-CoV-2 anti-spike receptor binding domain and anti-nucleocapsid immunoglobulin G(IgG) levels were measured by enzyme-linked immunosorbent assay and calibrated with the National Institutes of Health serology standard. Primary endpoint was seroconversion three months post 2nd vaccine dose, or within two weeks prior to 3rd vaccine dose in patients.

Results: There were 96 solid tumour patients (76 evaluable for the primary endpoint) and 19 healthy controls. Median age 62 years with 70 (61%) being female. COVID-19 vaccinated included AZD1222 (65%) and BNT162b2 (35%). Majority (69%) of patients had metastatic cancer. Baseline lymphopenia (<1.2x10^9/L) was seen in 41% of patients. Median Charlson comorbidity index score was 7 (2 - 12). Among primary endpoint evaluable patients, 47 (62%) patients received chemotherapy, alone or in combination with other cancer therapy; 8 (11%) received immunotherapy alone; 21 (28%) had targeted therapy.

Seroconversion at three months post vaccination occurred in 86% of cancer patients and 100% of controls (p<0.11). Mean anti-spike antibody titre was 88 binding antibody units (BAU)/ml in cancer patients and 179 BAU/ml in controls, p=0.10. No subjects had positive anti-nucleocapsid IgG confirming absence of past COVID-19 infection. Seroconversion occurred in patients who received chemotherapy alone or in combination (83%), immunotherapy (75%) and targeted therapy (95%; p=0.2). Mean anti-spike IgG levels were 77, 63 and 137 BAU/ml with chemotherapy, immunotherapy and targeted therapy respectively. Age, metastatic disease and lymphocyte count were not associated with anti-spike antibody level. Among cancer patients, 40% and 95% were seropositive after 1 and 2 vaccine doses respectively. A decline in anti-spike antibody titre was seen from three months post the 2nd vaccine dose. Cancer patients had an increase in anti-spike post 3rd vaccine dose, while levels declined in controls (pre booster), at 6 months post the 2nd vaccine dose.

Conclusions: Cancer patients achieved comparable seroconversion rates three months post vaccination compared with healthy controls. Although the anti-spike antibody titre was numerically lower among cancer patients than controls, the difference was not statistically significant. Recent cancer therapy did not appear to significantly affect vaccine response, however, the anti-spike antibody level was numerically lower...