Poster Round
海報目錄

時　間：113 年 12 月 15 日(星期日)15：15-15：45

地　點：新竹喜來登大飯店 3F 海報區

主持人：楊登和醫師

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海報摘要 TCR39

Increased pyruvate carboxylase expression during the macrophage differentiation and regulated its biologic activity

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巨噬細胞分化過程中丙酮酸羧化酶表現增加並調節其生物活性

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Background: The activation of macrophages dramatically changes it metabolic program. Current study suggested the gluconeogenesis could affect the function of tumor infiltrating macrophages through pyruvate carboxylase (PC), an important enzyme for gluconeogenesis. Therefore, we hypothesized that the inhibiting the expression of pyruvate carboxylase could affect the function of macrophages.

Methods: PC knockout (KO) U937 cells were generated using transfection by plasmid encoding short-hairpin RNA. The protein levels of PC and the phosphorylation of MAPKs in U937 cells, differentiated macrophages, and macrophages stimulated with lipopolysaccharides (LPS) were analyzed by Western blotting. The expression of proinflammatory cytokines was analyzed by real-time PCR and ELISA. The mitochondrial membrane potential, and apoptosis of PC KO macrophages were studied via flow cytometry.

Results: The protein and mRNA expression of PC increased after the macrophage differentiation and the addition of LPS to macrophages further increased its expression levels. PC KO would decreased the mRNAs expression and cytokines secretion of interleukin (IL)-1, tumor necrosis factor (TNF)-α, and IL-6 in differentiated macrophages, and macrophages stimulated with LPS. PC KO further impaired mitochondrial membrane potential, increase apoptosis and the phosphorylation of MAPKs in macrophages.

Conclusion. We found the expression of PC is upregulated in the differentiation and activation of macrophages. PC KO could suppressed IL-1, TNF-α, and IL-6 section via MAPK pathway and impaired mitochondrial membrane potential, and increase apoptosis in macrophages.

海報摘要 TCR40

Novel effective & practical vaccine against hepatitis C virus infection:α2-3,6,8,9 Neuraminidase A-modified HCVpp

一種新型有效且實用的丙型肝炎病毒感染疫苗:α2-3,6,8,9神經氨酸酶A修飾的HCVpp

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Abstract

Background

Worldwide over 170 million people are chronically infected with the hepatitis C virus (HCV). Currently there is no vaccine available.

Viral attachment and entry are major targets of adaptive humoral responses. The viral proteins responsible for cell attachment and entry of HCV are the glycoproteins E1 and E2, which are highly glycosylated, leading to the evasion of HCV from the humoral immune response.

Methods

HCV pseudoparticles (HCVpp) are produced by transfecting 293T cells with three vectors required to assemble infectious pseudo-particles.

The vaccine ($HCV_{Neura-A}$) is generated by hydrolysis of sialic acid residues from glycoproteins on HCVpp by using α2-3,6,8,9 Neuraminidase A.

Results

With the sera from $HCV_{Neura-A}$-immunized mice, levels of suppression on infection of Huh7.5 cells by HCVpp are correlated with priming and boosting times, suggesting neutralizing activities increased in the same way.

Conclusion

In short, hydrolysis of sialic acid residues from glycoproteins on HCVpp by α2-3,6,8,9 Neuraminidase A elicits the production of neutralizing antibody and effectively inhibits infection of Huh7.5 cell line by HCVpp. This strategy opens a new direction for vaccine design. Actually, this research has already created encouraging results with patent (Taiwan: Patent number I844199, June 1, 2024; USA, EU, and China: in process) and potentially clinical use in the near future.

海報摘要 TCR41

Alternation of N6-methyladenosine modification on mRNAs of T cells in response to chronic exposure to TNF-a

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T 細胞長期暴露於 TNF-α 其 mRNA 上 N6-甲基腺苷修飾的變化

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Background: Ankylosing spondylitis (AS) is a chronic inflammatory disease. A growing body of studies has revealed that N6-methyladenosine (m6A) modification of RNA engages in a variety of inflammatory processes of autoimmune disorders. However, the role of m6A modification on mRNAs of T cells in contribution to AS pathogenesis remained characterized. In this study,

Methods: Jurkat cells were activated by treatment with chronic exposure to TNF-a and the resulting mRNAs were isolated and fragmented to 60-200 nucleotides. The m6A modified RNA fragments were immunoprecipitated and were subjected to analysis by high-throughput RNA sequencing. Quantitative real-time PCR was used to measure the expressions of m6A writers, erasers and readers.

Results: Compared with the controls (without TNF-a treatment), 183 and 118 m6A modified mRNAs in Jurkat cells were up-regulated and down-regulated more than log2 fold change with p value < 0.05, respectively. mRNAs of involved in signaling pathways of immune response and inflammation, including MAPK signaling pathway, PI3K-Akt signaling pathway, cytokine/cytokine receptor interaction, TNF-a signaling pathway and IL-17 signaling pathway. The mRNA expression levels of most m6A writers, erasers and readers were altered.

Conclusions: Chronic exposure to TNF-a altered the m6A modification of many mRNAs of Jurkat cells and affected signaling pathways of immune response and inflammation. The expression levels of m6A writers (ZC3H13, METTL14, RBM15B, CBLL1, RBM15, and KIAA1429), eraser (FTO) and readers (YTHDC2, ELAVL1, FMR1, hnRNPA2B1, and IGF2BP1) were altered in response to chronic exposure to TNF-a.

海報摘要 TCR42

The anti-inflammatory effect of Ferulic Acid in the mouse model of collagen-induced arthritis

在膠原蛋白誘導關節炎小鼠模型之阿魏酸抑制發炎效果

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Abstract

Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease with presentations of multiple arthritis and synovitis. Active arthritis also can be observed in in the collagen-induced arthritis (CIA) mouse model. Ferulic acid (FA) exhibits anti-inflammatory and immunoregulatory effects, according to prior research. This research seeks to investigate the pharmacological effects of FA in a mouse model of CIA.

Methods: The CIA model was built using male DBA/1J mice. FA was given to the mice for three weeks. Throughout the trial, clinical arthritis scores and hind paw volume were measured.

Results: Immunization of DBA/1 mice with a bovine CII emulsion led to the progression of arthritis, characterized by paw swelling, erythema, edema, and joint rigidity; however, this was steadily reduced when the mice were orally administered FA (100 mg/kg) daily for 3 weeks without significantly affect body weight changes . To further analyze arthritis, slices of ankle joints stained with hematoxylin and eosin on day 42 postimmunization were examined histologically. According with clinical scoring data, FA-treated animals exhibited substantial decreases in synovial hyperplasia, cartilage degradation, and bone erosion in the ankle joints.

Conclusion: The significant anti-inflammatory effect of FA was observed from our study. FA may serve as a potential therapeutic candidate for RA.

海報摘要 TCR43

Hydroxychloroquine Reduces the Risk of Hepatocellular Carcinoma in Patients with Hepatitis B Virus Infection

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煙氯奎寧降低 B 型肝炎病毒感染患者罹患肝細胞癌之風險性

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Abstract

Background: Hydroxychloroquine (HCQ) may protect against cancer, but its effects in patients with hepatitis B virus (HBV) remain unexplored. We investigated the association of HCQ use with hepatocellular carcinoma (HCC) risk in patients with HBV.

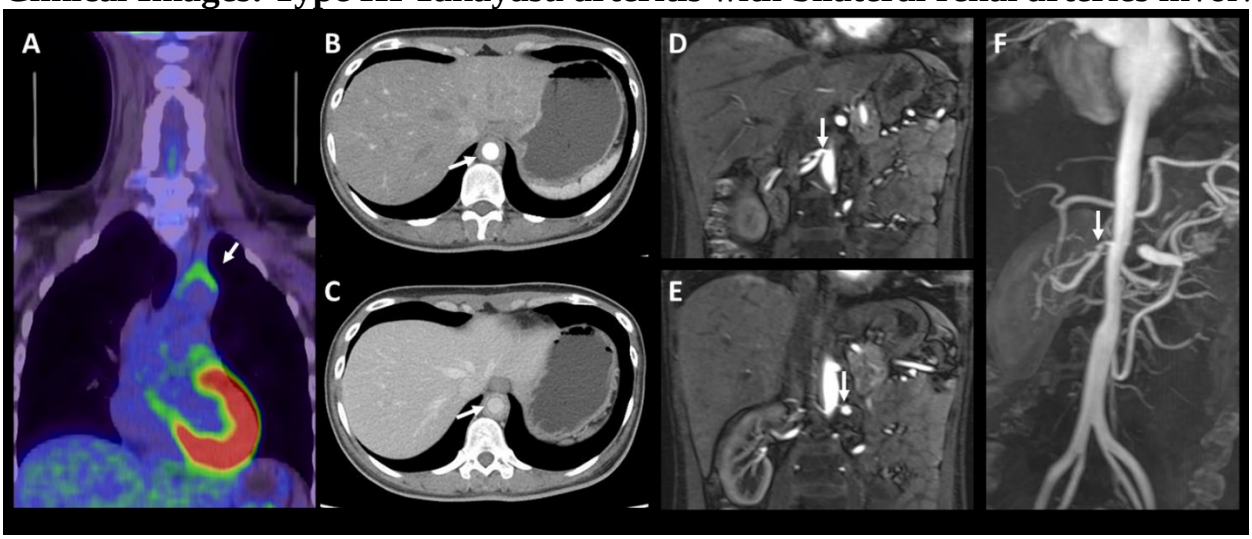
Methods: This population-based cohort study selected the data of patients with HBV infection during 2006–2016 from Taiwan's National Health Insurance Research Database. We performed multivariate and stratified analyses using the Kaplan–Meier method and Cox proportional hazards regression to evaluate the association of HCQ use with HCC risk in the HBV cohort.

Results: We included 688,295 patients with newly diagnosed HBV infection. During follow-up, patients with HBV who used HCQ had a significantly lower HCC risk than did those who did not use HCQ (adjusted hazard ratio [aHR], 0.47; 95% confidence interval [CI], 0.32–0.69). Furthermore, we stratified the patients into subgroups according to cumulative defined daily dose (cDDD) and average cDDD per year. We observed that compared with those obtained for HCQ nonusers (cDDD < 28), the aHRs obtained for HCQ users in the 28 ≤ cDDD < 89.92, 89.92 ≤ cDDD < 293.41, and cDDD ≥ 293.41 subgroups were 0.42 (95% CI, 0.23–0.78), 0.55 (95% CI, 0.32–0.95), and 0.44 (95% CI 0.23–0.83), respectively. Similarly, compared with those obtained for HCQ nonusers, the aHRs obtained for the average cDDD < 18.49, 18.49 ≤ average cDDD < 61.40, and average cDDD ≥ 61.40 subgroups were 0.32 (95% CI, 0.16–0.62), 0.55 (95% CI, 0.32–0.94), and 0.61 (95% CI 0.34–1.10), respectively.

Conclusion: Among patients with HBV infection, HCQ use was associated with a reduced HCC risk. Further research should elucidate the underlying mechanisms.

海報摘要 TCR44

Clinical Images: Type III Takayasu arteritis with bilateral renal arteries involvement



A 34-year-old woman with no prior systemic disease presented with a fever of unknown origin. Initial physical examination showed no significant findings, but an autoimmune workup revealed elevated CRP and ESR levels. A positron emission tomography scan showed patchy FDG uptake at the aortic arch (SUVmax.eq = 2.8), suggesting large vessel vasculitis (Panel A, arrow). She was started on immunosuppressive therapy. Subsequently, she developed unintentional severe hypertension with systolic blood pressure exceeding 200 mmHg, without significant symptoms. A computed tomography angiography revealed mural thickening of the descending aorta (Panel B, arrow), and a "double ring sign" was observed on the venous phase of the scan (Panel C, arrow). Further evaluation with magnetic resonance imaging (MRI) confirmed wall thickening of the abdominal aorta and focal stenosis at the orifice of the bilateral renal arteries (Panel D&E, arrow). A reformatted MRI of the aorta highlighted significant narrowing of the renal arteries (Panel F, arrow). The final diagnosis was Type III Takayasu arteritis involving bilateral renal arteries. Intensified treatment led to a gradual normalization of the patient’s blood pressure.

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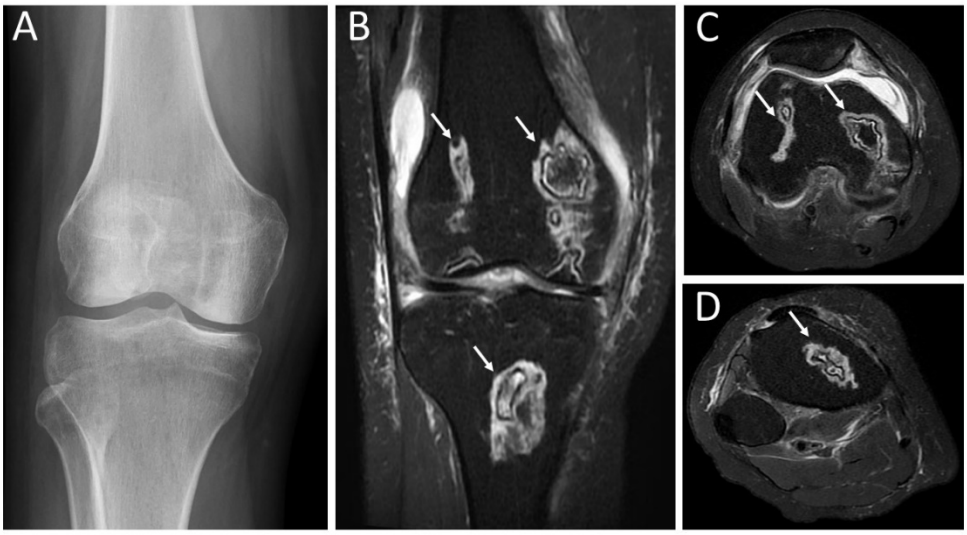
海報摘要 TCR45

Clinical Images: Spontaneous Osteonecrosis of the Knee (SONK) in a Patient with Immune-Related Adverse Event(irAE)



Spontaneous osteonecrosis of the knee (SONK) is a debilitating condition characterized by the sudden onset of knee pain and functional impairment, primarily affecting the medial subchondral bone of the femoral condyles.

We present a case of a 40-year-old female diagnosed with right triple-negative breast cancer (TNBC), with a tumor size of approximately 2.0 cm, staged cT2N0M0. She was subsequently treated with a combination of pembrolizumab, lipodox, and cyclophosphamide. During the 3rd course of treatment, the patient developed polyarthritis, initially affecting both knees and progressively involving the shoulders and elbows. There was no steroid exposure during anti-cancer treatment. This was diagnosed as an immune-related adverse event (irAE) associated with her immunotherapy after evaluation. An autoimmune survey showed no remarkable findings, and the patient responded well to steroid treatment for arthritis.

During arthritis evaluation, an X-ray of the right knee (Panel A) showed mild osteoarthritic changes. Additionally, right knee MRI revealed avascular necrosis of both the femoral condyle and tibial plateau. The MRI coronal view (Panel B, arrow) indicated a double line sign on T2-weighted imaging (T2WI) in the distal femur and proximal tibia. Transverse views at the femur level (Panel C, arrow) and tibia level (Panel D, arrow) also indicated the same findings. Combining the patient's clinical presentation and imaging results, the diagnosis was consistent with SONK. Although SONK typically affects the medial femoral condyle, it can occasionally involve the tibial plateau, as observed in this patient. Currently, there is no literature establishing a relationship between SONK and irAEs, indicating a need for further case collection and study to explore this potential association.

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海報摘要 TCR46

Heart transplantation rescues a case of myocarditis in multisystem inflammatory syndrome in adults: a case report

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Background: Multisystem inflammatory syndrome in adults (MIS-A) is a rare and severe condition occurring within 12 weeks post-COVID-19 infection, affecting organs such as the heart, lungs, and gastrointestinal tract. First-line treatments typically include glucocorticoids and intravenous immunoglobulin (IVIG), though there is no consensus on the treatment for refractory cases. Here, we report the successful recovery of a refractory MIS-A patient following heart transplantation.

Methods: The patient is diagnosed based on criteria: age ≥ 21, illness requiring hospitalization, fever for over 24 hours within the first three days of hospitalization, severe cardiac disease, shock, abdominal pain, elevated CRP, elevated IL-6, and positive SARS-CoV-2 test.

Results: A 54-year-old unvaccinated female developed COVID-19 on November 20, 2023. She presented with epigastric pain and cough on December 29. On December 31, she was referred to our emergency department for suspected acute myocardial infarction. Coronary angiography revealed patent coronary arteries and she was admitted to the ICU with suspected myocarditis with cardiogenic shock. During hospitalization, PCR assays for the respiratory panel were negative for all pathogens. Initial treatment with antibiotics and antiviral drugs was ineffective. Subsequently, IVIG was administered, resulting in rapid clinical improvement and transfer to a general ward. However, she experienced another episode of cardiogenic shock in the general ward, necessitating heart transplantation. Post-transplant, her condition stabilized, improving her ejection fraction from 20% to 57%, and she was discharged successfully.

Conclusion: This is the first reported case worldwide of heart transplantation successfully treating MIS-A, suggesting that transplantation may be considered in refractory cases.

海報摘要 TCR47

Clinical image:A 21-year-old male with postauricular mass, elevated serum IgE levels and eosinophilia

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21歲男子耳後結節合併高免疫球蛋白 E 及嗜伊紅血症

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A 21-year-old Vietnam male patient presented to the surgical outpatient department with the complaint of right postauricular mass for the past 5 years which was insidious in onset and gradually progressive. He had no history of any constitutional symptoms. On examination, a 6x5 cm non-tender, movable mass was seen in the right postauricular area. Hematological examination revealed Hb 12.5 gm/dl, WBC 12,100 cells/cumm (Eosinophils 58%), IgE 1114 IU/ml(<100), Eosinophil count 5950/ml(150-300) and without proteinuria. Excision biopsy was performed. Histopathological section revealed lymphoid infiltrate in fibrous tissue with formation of lymphoid follicles with germinal centers, accompanied by many eosinophils. Eosinophilic micro-abscesses (*) and vascular hyperplasia(⇓) are also present (200x,
H&E statin) (Fig.1). Recurrent mass over the right postauricular area around 1.7x1.8cm was noted around 8 months after excision (Fig.2). He was transferred to the rheumatologic clinic and prednisolone 20mg/d was prescribed and the mass shrank around 2 weeks later. Kimura disease is characterized by predominant lymphoid proliferation, sparse vascular components with minimal epithelioid endothelial changes, and consistently numerous eosinophils, unlike epithelioid hemangiomas like angiolymphoid hyperplasia with eosinophilia (ALHE) where eosinophils may be sparse or absent. Kimura disease should be considered as a differential diagnosis in patients presenting with head & neck mass with eosinophilia and elevated serum IgE levels. [1,2]

References

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2. Wenig BM, Childers EL, Richardson MS, Seethala RR, Thompson LD. Non-Neoplastic Diseases of the Head and Neck; American Registry of Pathology in collaboration with the Armed Forces: Washington, DC, USA, 2017: 435.

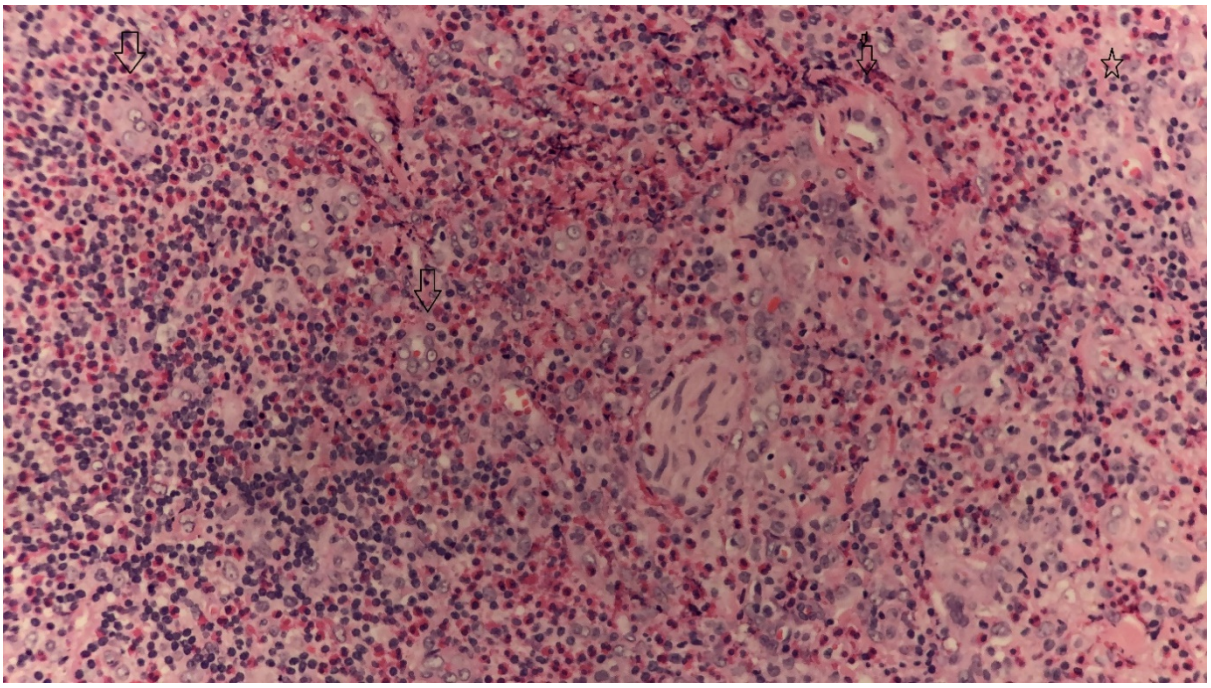
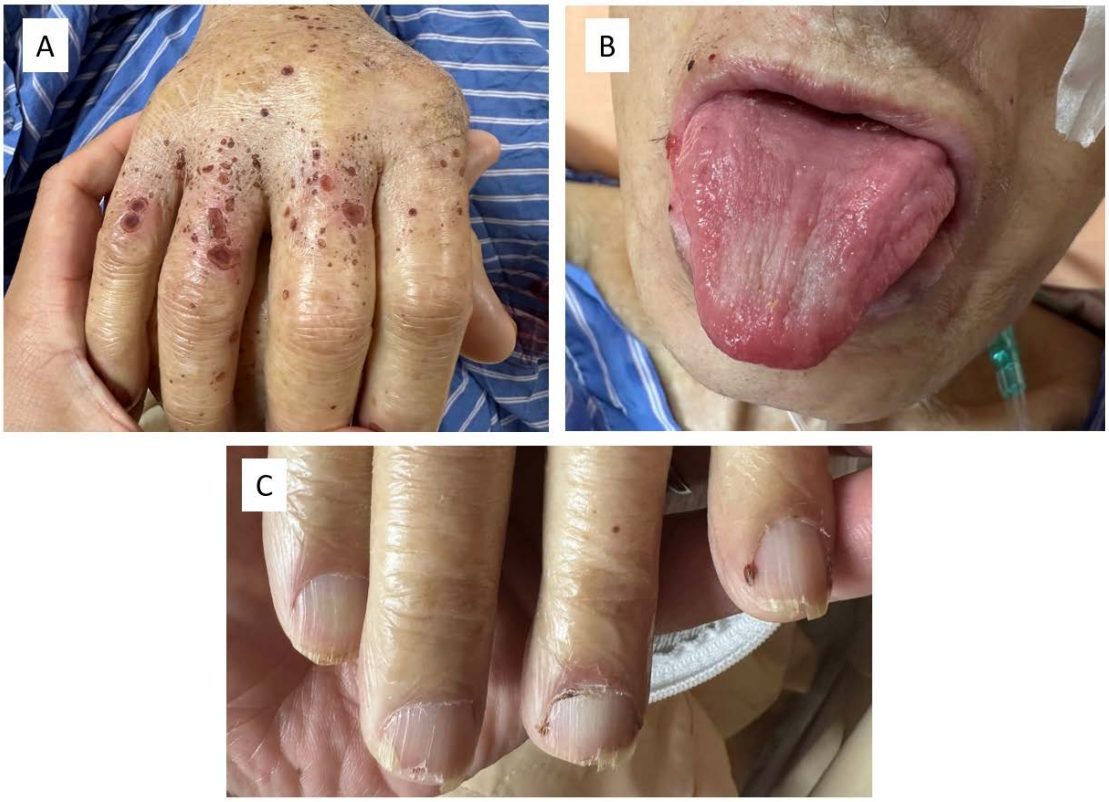


Figure 1

Figure 2

海報摘要 TCR48

Clinical Images: Vitamin B12 Deficiency With Skin Erosions



The patient, an 88-year-old male with dementia, was admitted due to a falling accident and functional decline. Physical examination revealed multiple skin erosions, papules, and macules with hemorrhagic crusts on the bilateral hands and thighs (Figure A), onychorrhexis (Figure B), glossitis, and angular cheilitis (Figure C). Blood tests indicated megaloblastic anemia and thrombocytopenia. Survey for vasculitis was negative. A skin biopsy of the erosion showed intracorneal pustules. Lab tests reported vitamin B12 levels at <100 pg/ml (reference range: 197-771 pg/ml). A bone marrow biopsy indicated erythroid hyperplasia. After vitamin B12 supplementation, the skin erosions improved.

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臺北榮民總醫院

海報摘要 TCR49

A rare case of Eosinophilic fasciitis, post-COVID infection related

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This 34-year-old female with no significant past medical history, had COVID-19 infection in January, 2024. Several weeks later, she began to notice progressive skin and fascia tightness over her both fingers & toes and extending up to elbows and knees. There was no Raynaud's phenomenon, no dysphagia, no telangiectasia, no facial skin tightness, no calcinosis. On arrival to our out-patient department in April, the physical examination revealed skin and fascia tightness from both fingers & toes to elbows & knees, positive groove sign, and finger contracture. Her lung function test showed a reduced DLCO SB/Pred (70% on 2024/04), which could point to pulmonary involvement. Lab data indicated eosinophilia 17.8%, E.S.R 32 mm/hr, IgG 2457 mg/dl on 2024/04. Nailfold capillaroscopy showed no SD/D pattern but only abnormal nailfold capillaroscopy pattern, characterized by abnormalities of the microcirculation to be evaluated in the clinical contest.

Given the clinical presentation and preliminary findings, the working diagnosis is eosinophilic fasciitis. After glucocorticoid medications, lab data revealed eosinophil 2.6% , and E.S.R 15 mm/hr on 2024/06; and tightness skin got improved.

Fig. 1 Groove sign positive when forearm elevated

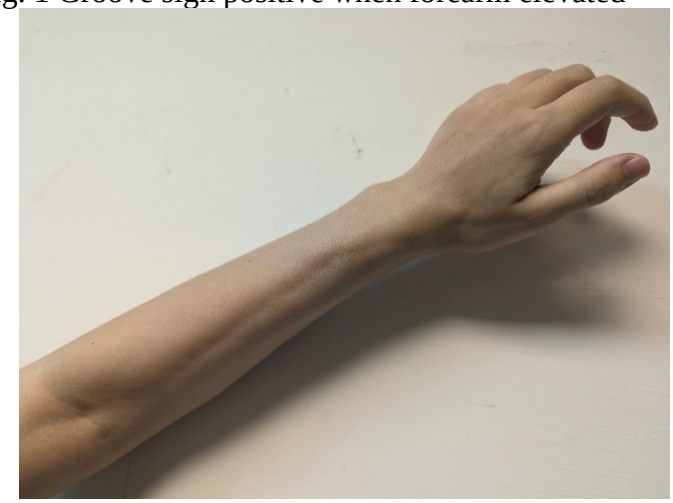
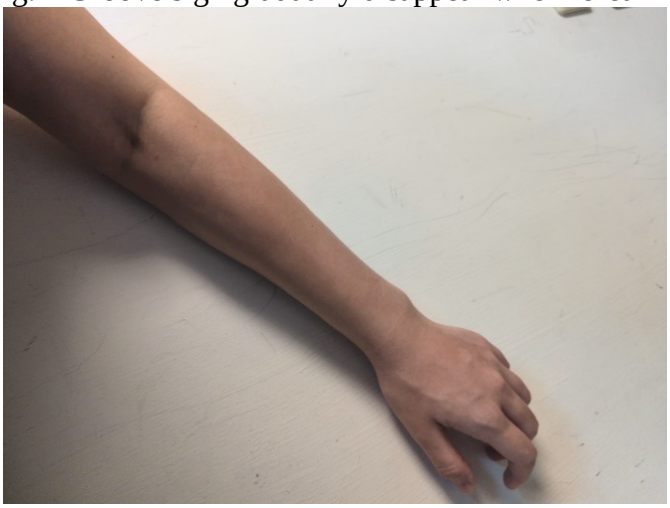


Fig. 2 Groove sign gradually disappear when forearm drop down



海報摘要 TCR50

Diffuse-weighted MRI and Histopathological Findings in an Asian patient of Neuro-Behçet's disease manifested as acute cerebellar ataxia

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A 45-year-old man with a history of BD came to our emergency department because of acute onset of ataxia for 3 days. BD was diagnosed one year ago with the presentations of recurrent oral ulcers above three times in one year, recurrent genital ulcerations, skin papulopustular lesions, positive pathergy test, and uveitis observed by an opthalmologist which resulted in left eye total blindness about half a year ago.

3 days ago prior to admission, he suffered from acute onset of ataxia with right side deviation while walking. Initially there was no focal weakness, but progressive right side clumsiness was noted within 2-3 days. On neurologic examination, direct fundoscopy showed only mild pale on optic disc of left eye, and dysmetria on right extremities. On the magnetic resonance imaging study, T1-wighted image and T2-weighted fluid attenuated inversion recovery images showed multiple hyperintensity ovoid spots without obvious enhancement in bil periventricular white matters, subcortical white mater of left frontal lobe, left cerebral peduncle and left cerebellum, and apparent diffusion coefficient showed round lesion with increased intensity in right cerebellum.

Brain biopsy from the lesion on left frontal lobe was performed and the histologic examination found mild gliosis with abundant foamy histiocytes and no accumulation of inflammatory cells within vessels on H-E stain. CSF was clear and colorless with 21 RBC and 4 WBC per microliter. Elevated CSF protein was also noted. Pulse therapy with methylprednisolone 1000mg QD for 5 days was given and the neurological deficits got gradually improved after treatment.

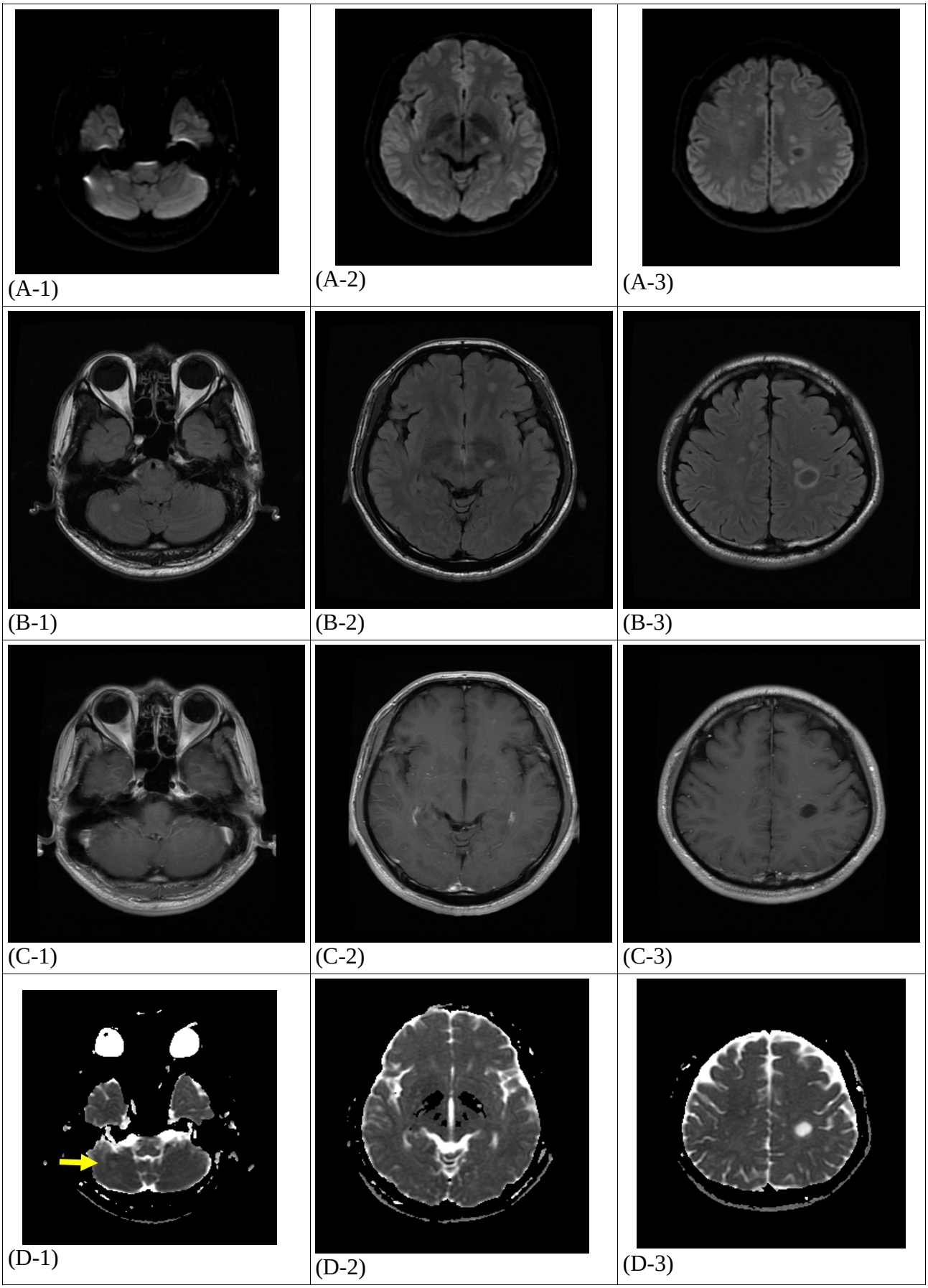

Figure 1: Brain MRI (A)DWI (B)T2 FLAIR (C)T1 with contrast (D)ADC showed multiple white matter lesions over bilateral hemispheres and cerebellum. Only (D-1) showed low ADC measures (arrow).

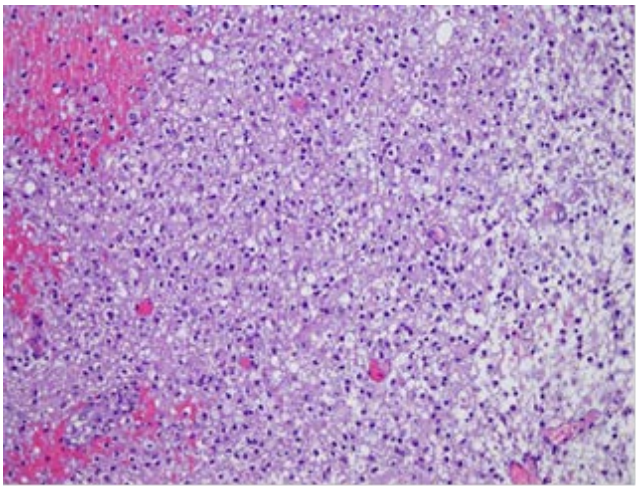
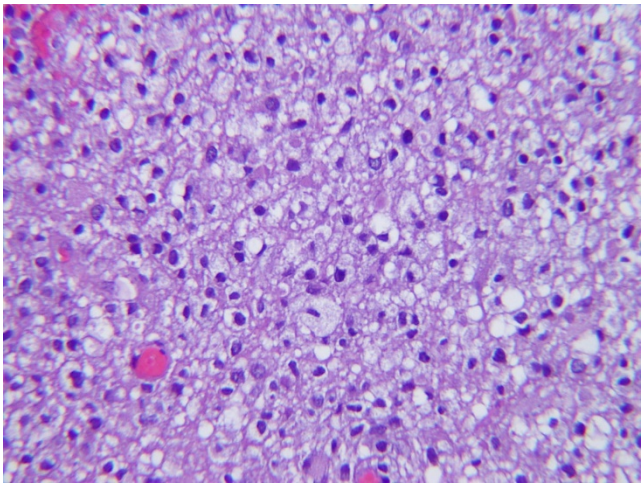

Figure 2: Brain biopsy, left frontal lobe, showed mild gliosis with abundant foamy histiocytes and no accumulation of inflammatory cells within vessels on H-E stain, favored demyelination. The sampled vessels did not show obvious evidence of vasculitis.

海報摘要 TCR51

Disseminated Cryptococcus Infection in an IgG4-related Disease Patient: A Case Report

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Abstract: This case report discusses a 71-year-old man with IgG4-related disease who developed IgG4-associated cholangitis and subsequently a disseminated Cryptococcus infection after steroid and azathioprine treatment. Despite initial clinical improvement, he presented with symptoms leading to the diagnosis of Cryptococcus neoformans. The case highlights the challenges in managing IgG4-RD and preventing serious infections.

Background: Immunoglobulin G subclass 4 (IgG4)-related disease (IgG4-RD) stands as a nascent immune-mediated condition and is gaining more attention by clinicians for its various manifestations. IgG4-associated cholangitis (IAC), as part of a spectrum of IgG4-RD, is one of the most common extra-pancreatic manifestations of IgG4-RD. Subsequent treatments with steroids and immunosuppressants may predispose patients to infections.

Methods: We present the case of a 71-year-old man who presented with symptoms suggestive of cholangiocarcinoma with images revealed a mass lesion in common bile duct. IgG4-associated cholangitis was later confirmed by biopsy results and responses to steroids. Following treatment with steroids and azathioprine effectively managed the disease; however, he subsequently developed disseminated Cryptococcus infection.

Results: The patient was prescribed prednisolone 40 mg daily, leading to clinical improvement and normalized liver function. He followed a steroid tapering plan, reducing by 5 mg every two weeks, and was given azathioprine 50 mg daily for better disease control. Three weeks later, he presented with left upper quadrant pain. Vital signs were stable, but lab tests showed bandemia of 11.2%. Blood cultures identified Cryptococcus neoformans, with serum Cryptococcal antigen >1:2560 and negative HIV. He was treated with liposomal amphotericin B 300 mg IV daily and oral flucytosine 1,250 mg every six hours. Lumbar puncture confirmed a Cryptococcal antigen titer of 1:80 and positive culture. Chest CT showed ground-glass opacities, while brain CT showed no lesions. After three weeks of antifungal therapy, he was discharged with a two-week fluconazole regimen without neurological dysfunction.

Conclusion: We highlight the diagnostic challenges and treatment complexities encountered in managing IgG4-associated cholangitis. The successful management of the patient's condition with steroids and azathioprine was overshadowed by the development of disseminated Cryptococcus infection, emphasizing the delicate balance required in treating IgG4-RD to prevent serious infectious complications.

海報摘要 TCR52

Anti-Interferon Gamma Autoantibodies with Disseminated NTM Infection

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Case Presentation

A 53-yea r-old man was admitted to Taipei Veterans General Hospital with sudden-onset right-sided facial palsy and hemiplegia. He had progressive palpable nodules in the cervical and supraclavicular areas since February 2024. A previous lymph node biopsy at another hospital showed no malignancy or tuberculosis, and he was empirically treated for sarcoidosis with low-dose prednisolone and colchicine. As his condition worsened, he sought further treatment.

On examination, multiple enlarging lymph nodes and soft tissue masses were found in the neck and submandibular regions, with erythematous papules and nodules on the face, neck, trunk, and limbs (Fig. 1). Chest CT revealed enlarged lymph nodes in the lower neck, axilla, and mediastinum, while brain MRI showed multiple small lesions in the pons (Fig. 2). A lymph node biopsy indicated suppurative granulomatous inflammation, but TB PCR was negative, suggesting disseminated nontuberculous mycobacterial (NTM) infection. We then detected the presence of anti-interferon-γ (IFN-γ) autoantibodies. The QuantiFERON-TB test was indeterminate, and the neutralization test confirmed anti-IFN-γ autoantibodies. The final diagnosis was anti-interferon-γ autoantibody syndrome with disseminated NTM infection.

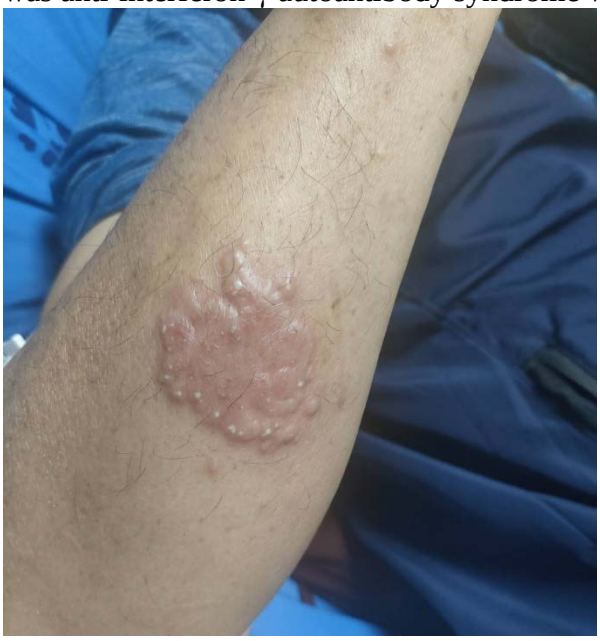

Figure 1. Patient on admission, presented with erythematous papules in his arm.

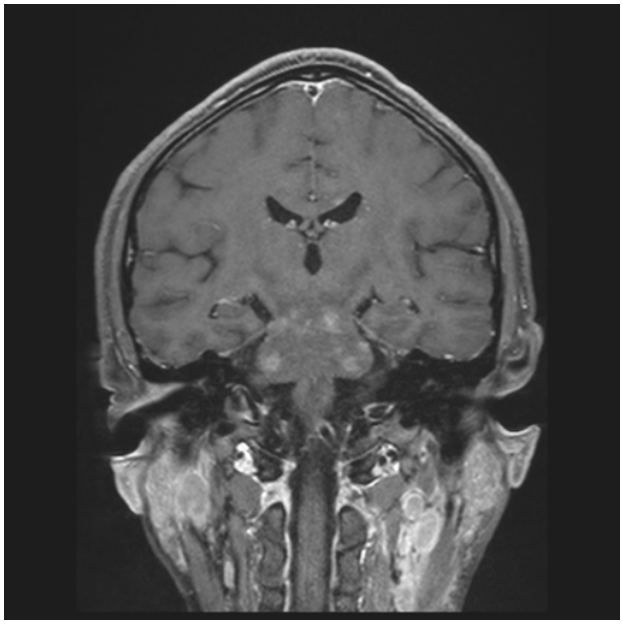

Figure 2. Brain MRI showed Multiple small lesions in almost the whole pons

Discussion

Anti-IFN-γ autoantibodies neutralize IFN-γ, impairing the immune response against intracellular pathogens and leading to severe infections. Patients typically present with disseminated infections, including those caused by NTM, non-typhoidal Salmonella, Cryptococcus neoformans, and Talaromyces marneffei, and may also develop reactive skin conditions like Sweet syndrome and erythema nodosum. Diagnosis requires detection of anti-IFN-γ autoantibodies, and treatment involves prolonged antimicrobial therapy and possibly immunomodulatory treatments like cyclophosphamide and rituximab to reduce autoantibody levels and improve outcomes.