Objective

We aim to describe the clinical, laboratory, and radiographic features that characterize patients with progressive multifocal leukoencephalopathy (PML) in the context of sarcoidosis (S-PML).

Background

Sarcoidosis has been associated with CD4+, CD8+, and CD19+ lymphopenia, T-cell anergy, and increased infection risk. S-PML has been reported in approximately 60 cases. PML is often mistaken for neurosarcoidosis, leading to harmful administration of high-dose steroids. Preliminary evidence suggests that experimental therapies such as interleukins 2 and 7, checkpoint inhibitors, polyomavirus-specific T-cell therapy, and infliximab may offer promise for treatment. To ensure optimal outcome, it is crucial to identify S-PML accurately and with minimal delay.

Design/Methods

Data and imaging for patients were collected retrospectively from the electronic medical record from Mass General-Brigham network hospitals, National Institutes of Health, Mayo Clinic, Columbia University Irving Medical Center, University of California San Francisco, University of Michigan, and Beth Israel Deaconess Medical Center.

Results

Twenty-five patients with definite S-PML were identified. Median age at diagnosis of sarcoidosis was 54 years, and median time between sarcoidosis and PML diagnosis was 12 months. Sarcoidosis was isolated to lung in 14/25 patients; 10/25 had multisystem involvement; one patient had isolated dermatologic sarcoidosis. Of all patients, 16/25 patients had never received immunosuppressive medications prior to neurological symptom onset. Median serum lymphocyte count at time of PML diagnosis was 430 cells/uL (range: 50-1490). On MRI, 8/25 patients had infratentorial lesions only, while 8/25 had both infratentorial and supratentorial lesions, and 6/25 showed contrast enhancement. Seven/twenty-five patients progressed to death.

Conclusions

This study characterizes the clinical, laboratory, and imaging features of S-PML patients from seven major US medical centers. These data will be used to identify risk factors for development of PML in the context of sarcoidosis and to investigate any biomarkers that might aid in accurate and timely diagnosis.

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"Trigeminal Tract Sign" in Patients With Herpes Zoster Ophthalmicus: A Case Series of a Novel Imaging Finding

Heather Yong, Carla Wallace, Ronak Kapadia

Objective

Herein, we report three patients presenting with zoster ophthalmicus caused by varicella zoster virus (VZV) with unexpected and novel cervico-medullary findings on magnetic resonance imaging (MRI).

Background

Zoster opthalmicus involves reactivation of latent VZV in the ophthalmic division of the trigeminal nerve producing a dermatomal rash. In a minority of patients this leads to ophthalmic findings and damage to surrounding peripheral nerves through perineural/intraneural inflammation. MRI findings in zoster opthalmicus are often nondescript or normal leading to misdiagnosis and delays in treatment.

Design/Methods

This was a case-series describing patients in Calgary, Alberta who presented with zoster opthalmicus, and who were noted incidentally to have similar appearing lesions in the ipsilateral cervico-medullary region on brain MRI. Standard MRI imaging of the brain and selected high-resolution images of the orbits and globes were reviewed by neuroradiology (CW).

Results

Three patients, with varying phenotypes of zoster opthalmicus, are described: a 70-yo male with ipsilateral decreased visual acuity and oculomotor/abducens palsy; a 75-yo female with ipsilateral oculomotor/facial nerve palsies; and a 35-yo immunocompromised female with ipsilateral blepharoconjunctivitis and optic neuritis. In all 3 cases, MRI revealed profound T2 and fluid-attenuated inversion recovery (FLAIR) hyperintensity along the spinotrigeminal tract of the clinically affected side, extending from the posterolateral pons and medulla into the cervical region.

Conclusions

To our knowledge, hyperintensity within the medulla and spinal trigeminal tract in zoster opthalmicus is a rare imaging finding. We have coined this radiologic finding the "trigeminal tract sign" due to the anatomic structure affected. A thorough radiologic/laboratory workup should be considered in patients with similar presentations; however, a high index of suspicion for zoster opthalmicus should be considered in cases with the aforementioned imaging findings. Whether this radiological finding predicts disease severity or the likelihood of multiple cranial nerve involvement (as was seen in all patients in this series) requires further study.

Disclosure: Dr. Yong has nothing to disclose. Dr. Wallace has nothing to disclose. Dr. Kapadia has nothing to disclose.

Characterization of Clinical and Paraclinical Features Associated With TS-HDS Autoantibody Seropositivity

Mohamed Rezk, Igal Mirman, Sarah Berini, Pitcha Chompoopong, Christopher Klein, John R. Mills, Divyanshu Dubey

Objective

To evaluate neuropathy phenotypes and clinical outcomes associated with trisulfated heparin disaccharide (TS-HDS) autoantibodies.

Background

TS-HDS autoantibody has been reported as a biomarker of immune-mediated neuropathy. However, studies evaluating the clinical associations of this autoantibody are limited.

Design/Methods

Electronic medical records were reviewed to identify TS-HDS autoantibody seropositive patients and characterize their clinical and electrodiagnostic findings.

Results

Seventy-seven TS-HDS-IgM seropositive (titer range 9000-350,000) patients were identified (50 females; median age of onset was 48 years (range 9-83 years). Eleven patients were also positive for FGFR3-IgG (titer range 4000-19,000). 70% (54/77) had clinical/paraclinical evidence of neuropathy (54/77, 70% of TS-HDS-IgM alone; 10/11, 91% of TS-HDS-IgM with coexisting FGFR3-IgG). The managing physician characterized an immune-mediated neuropathy in 30% (23/77) and 54% (6/11) of the TS-HDS-IgM only and TS-HDS-IgM with coexisting FGFR3-IgG seropositive patients, respectively. Small fiber neuropathy presented in 58% (45/77) and 63% (7/11) of TS-HDS-IgM only, and both antibodies seropositive patients, respectively. Length-dependent neuropathy was the most common neuropathy phenotype amongst TS-HDS IgM (43/54, 80%) and dual seropositive cases (7/11, 63%). Forty-one (53%) patients received immunotherapy, predominantly: IVIG (n = 37), IV solumedrol (n = 7), oral prednisone (n = 14), and mycophenolate mofetil (n = 12). Among these, 43% (15/35) with TS-HDS-IgM seropositivity alone had improvement in inflammatory neuropathy cause and treatment (INCAT) disability score or modified Rankin Scale (mRS), while 33% (2/6) of patients with dual seropositivity had INCAT and mRS improvement. TS-HDS-IgM titers had low discriminative ability to identify immunotherapy response with an AUC of 0.621.

Conclusions

Neuropathy associations and clinical phenotypes amongst TS-HDS-IgM seropositive cases are variable. Furthermore, only a minority of cases are immunotherapy responsive, limiting the value of this biomarker in identifying immune-mediated neuropathies.

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BNT162b2 mRNA COVID-19 Vaccine Three-Dose Safety and Risk of COVID-19 in Patients With Myasthenia Gravis

Alon Doron, Yoav Piura, Ifat Vigiser, Hadar Kolb, Keren Regev, Nahum Nesher, Arnon Karni

Objective

To study the COVID-19 vaccine three-dose safety and risk of COVID-19 in patients with myasthenia gravis

Background

Various vaccines, including those against SARS-CoV-2, were reported to trigger or exacerbate myasthenia gravis (MG). As COVID-19 may potentially contribute to the tendency of MG patients to develop respiratory failure, it is important to study the safety of vaccines against SARS-CoV-2 and assess the risk of COVID-19 in MG patients.

Design/Methods

Among 215 MG patients treated in Tel Aviv Medical Center, 160 were interviewed about their response to the three-dose BNT162b2 mRNA vaccine. We assessed exacerbation rate and safety in a period of up to 6 weeks from each vaccine dose, as well as patient morbidity and mortality during COVID-19 compared to the general population.

Results

430 vaccine doses were administered across 150 patients. Thirteen patients (8.7%) complained of exacerbation within 6 weeks (risk period) of each vaccine dose, 8 (5.3%) confirmed by physician report. The exacerbation rates were similar during the risk period (5.6%) compared to corresponding period the previous year (4.8%). MG onset rates during the vaccination period were unaffected compared to previous years. Exacerbation rate among 15 patients who had COVID-19 was significantly higher (40%) compared to rate in the risk period following vaccination, with higher severe or lethal COVID-19 (26.7%) compared to the general population (0.96%), occurring in unvaccinated, steroid-treated, generalized MG patients.

Conclusions

Three-dose BNT162b2 vaccination is neither associated with exacerbation nor the new onset of MG, whereas COVID-19 is associated with severe disease and death in unvaccinated, steroid-treated generalized MG patients. Hence, it is strongly recommended for generalized MG patients to get vaccinated

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