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CASE REPORT

COVID-19 associated Bell's Palsy and lumbosacral neurolymphomatosis in a patient with B-cell lymphoma—Case Report

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This is a case of acute onset unilateral Bell's Palsy during COVID-19 illness, coinciding with development of progressive leg pain, weakness, and sensation change. The patient was ultimately found to have a large B-cell lymphoma mass invading the sciatic nerve, lumbosacral plexus and the spinal canal with compression of cauda equina consistent with neurolymphomatosis. Although COVID-19 infection has been associated with Bell's palsy, Bell's palsy has also been reported with lymphoid malignancy. We review current literature on the association of Bell's palsy with COVID-19 infection and lymphoid malignancy, as well as review the diagnostic challenges of neurolymphomatosis. Providers should be aware of the possible association of Bell's palsy as harbinger of lymphoid malignancy.

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CASE DESCRIPTION

This is a case of a 50-year-old female who developed progressive leg weakness and pain, concurrent with a diagnosis of Bell's palsy and COVID-19. She was otherwise healthy except for a past medical history of implantable cardioverter defibrillator (ICD) placement for Brugada type I syndrome found incidentally on electrocardiogram.

In the spring of 2020, she developed an acute left Bell's Palsy as well as cough, shortness of breath, fever, myalgias, and fatigue, for which she sought care in the emergency department (ED). She was diagnosed with COVID-19 and was treated symptomatically. She did not require hospitalization. She was treated symptomatically for upper respiratory symptoms, which resolved in a couple weeks. Acyclovir was prescribed by the ED, and the Bell's Palsy improved over time. She reported that during the time of her acute illness, she developed vague pain in the left gluteal area and left foot, although these were not significant at the time of initial ED evaluation and treatment. Over the next few weeks however, she developed progressive left foot drop, gluteal weakness and subsequent gait changes resulting in tripping. She was seen multiple times for these symptoms in the ED and was referred to multiple providers, including Rheumatology, Neurology and Podiatry with no diagnosis. She was referred for lumbar spine Magnetic Resonance Imaging (MRI) for presumed lumbar radiculopathy, but imaging was unremarkable. She experienced acute worsening of pain and distal weakness after a greater trochanteric corticosteroid injection for presumed left greater trochanteric pain syndrome. Two weeks later, she was referred by Neurology to Physical Medicine and Rehabilitation for electrodiagnostic (EDX) evaluation. At the time of EDX examination, over one year after onset of symptoms, she was found to have a dense left foot drop. She had significant loss of sensation over the left groin, perineal and posterior gluteal area, with extension to the lower leg, though the femoral nerve distribution was spared. The right lower extremity motor and sensory status were affected to a lesser degree. EDX demonstrated a sensorimotor axonal process affecting the lower lumbosacral plexus versus sciatic nerves. Neurology service was contacted by the physician performing the EDX, with suspicion of plexus abnormality, and the patient was admitted for evaluation. Pelvic MRI revealed a left pelvic mass measuring approximately 11 cm in transverse direction, 9 cm anteroposterior and 8 cm in craniocaudad extent, infiltrating the lower lumbosacral plexus, sciatic nerve and surrounding pelvic and gluteal musculature (Fig. 1). Biopsy showed diffuse large B-cell lymphoma, with lymphoid cells positive for CD20, PAX-5, Bcl-6, Mum-1, Bcl-2 and c-myc, negative for CD10 and cyclin D1. Fluorodeoxyglucose-positron emission tomography (FGD-PET) showed no distant disease. She was treated with Rituximab, Cyclophosphamide, Doxorubicin Hydrochloride, Vincristine Sulfate, Prednisone chemotherapy in spring 2021. Repeat PET scan after completion of chemotherapy showed interval resolution of the left pelvic mass, no metastatic disease, and severe denervation atrophy of the left calf and left deep and superficial gluteal musculature. She had interim improvement in sensation in the left lower extremity but continued to suffer from left calf and posterior gluteal pain. She ambulated with a rolling walker due to persistent gluteal weakness, and dense foot drop was treated with ankle foot orthosis (AFO).

In early October 2021, she developed new right foot drop, numbness, and pain. Lumbosacral spine MRI imaging revealed a homogeneous mass in the left S2-S3 epidural spinal canal extending through the left S2-S3 neural foramina and invading

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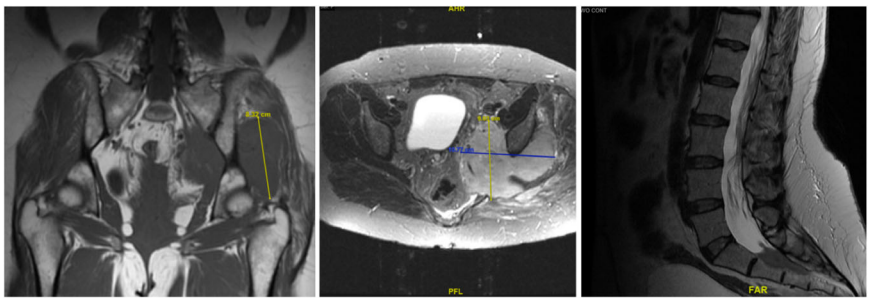

Fig. 1 Pelvic MRI without contrast T1 coronal (left) and axial (middle) showing mass measuring 11 × 9 × 8 cm infiltrating the lower lumbosacral plexus, sciatic nerve and surrounding pelvic and gluteal musculature. Lumbosacral spine MRI without contrast T2 sagittal image (right) showing recurrence of lymphoma with new invasion of the sacral canal.

the sacrum (Fig. 1). Computed tomography (CT) abdomen/pelvis redemonstrated soft tissue densities within the presacral space and within the sacral canal, extending into the left sacral neural foramen, right sciatic foramen and left gluteal musculature, concerning for recurrent malignancy. Biopsy of left gluteal mass confirmed focal post-treatment lymphoma. She was hospitalized and underwent palliative chemoradiation, but had progression of disease with further compromise of the cauda equina due to mass growth into the sacral canal and lumbosacral neuroforamina with bony erosion of the posterior sacrum, as well as interim development of multiple liver lesions. She was ultimately discharged to home hospice in January 2022.

DISCUSSION

This case showcases an unfortunate outcome of a rare disorder with initially vague symptoms delaying diagnosis, and rapid deterioration following COVID-19 infection. Apart from temporal coincidence, the association between Bell's palsy (BP), B-cell lymphoma, and COVID-19 infection in this patient is not clear. Although occurrence of BP in the presentation of this patient may be incidental, there are described cases of BP with B-cell lymphoma, as well as BP and COVID-19 infection.

BP is a sudden onset unilateral facial weakness due to dysfunction of the facial nerve of unknown cause. Facial paralysis or paresis can occur due to various mechanisms of injury, including central nervous system lesions such as those resulting from stroke or brain tumors, direct injury or compression of the nerve, direct and indirect infectious causes, and immune-mediated mechanisms. Although often used interchangeably, not all patients with facial paralysis have BP, which generally refers to cases that are self-limiting and for which no other specific cause can be identified [1]. Multiple cases of BP in association with SARS-CoV-2 infection have been described, as well as with COVID-19 vaccination [2, 3]. This association was explored early in the pandemic with a 2020 systematic review evaluating the cases of COVID-19 positive patients with BP as the only neurological manifestation. This review found 20 such cases. In nine cases, BP was the first neurological manifestation, while in eleven cases, BP was noticed multiple days after other clinical manifestations [4]. Other studies also found supporting evidence of the association of BP and COVID-19 illness. A retrospective study of 348,088 patients with COVID-19 infection found 284 cases (0.08% of total) of BP within the first 2 months of COVID-19 diagnosis, which is higher than the baseline incidence of BP [2]. There are published cases of pre-symptomatic patients with SARS-CoV-2 infection who presented with BP as first symptom [5]. These patients presented for evaluation with unilateral facial weakness and no respiratory symptoms, and tested positive for SARS-CoV-2, with symptomatic improvement with oral corticosteroids and valaciclovir. Other studies looking at a sample of individuals with isolated BP, found a SARS-CoV-2 IgM + IgG antibody test positivity rate of 24.3% [6]. In a study of 34 patients who presented to the emergency department with facial paralysis, peripheral facial paralysis was detected as an initial finding in 5 patients who tested positive for COVID-19 on RT-PCR, and 3 patients developed facial paralysis 7–12 days after diagnosis of COVID-19 [7].

Conversely, a review of cases of peripheral facial paralysis in one hospital system prior to and during the pandemic did not find an increased incidence of BP and suggested that a co-diagnosis of BP and SARS-CoV-2 infection may be an incidental finding [8]. Similarly, a study evaluating data from 235 cases of BP during 14 months of the COVID-19 pandemic also concluded there was no increase in the incidence of BP proportionate to the increase in incidence of SARS-CoV-2 virus in the population [9].

Although the association between SARS-CoV-2 infection and BP remains to be determined, the association of BP with lympho-proliferative malignances has been reported in literature since at least 1985, when Cartwright et al. reported 8 cases of BP occurring out of 780 total cases of lymphoid malignancy [10]. Of the 8 cases reported, 3 of them were in patients with non-Hodgkin's lymphoma, while 4 were found in acute lymphoblastic leukemia cases. Interestingly, in all cases, the BP preceded the diagnosis of malignancy. It was initially thought that the association between BP and lymphoid malignancy was due to tumor spread via the facial nerve. Although direct invasion or compression causing BP may potentially occur, such as with Burkitt's lymphoma in pediatric patients, direct invasion is not typically the case [11]. Indirect immunological mechanism causing BP are especially more likely when BP is found in association with various distant malignancies, such as in cases of facial paralysis found preceding leukemia in children [12]. In a recent study looking at oncologic diagnosis within 60 days of pediatric BP diagnosis, 17.1% were diagnosed with leukemia, and 4.9% with lymphoma [13]. Specific to our case, other cases of BP in association with B-cell lymphoma in adults have been described. In one recently published case with BP preceding diagnosis of high-grade B-cell lymphoma, the neoplastic cells had a slightly different profile than the B-cell lymphoma in our patient, and were positive for CD20, CD10, BCL2, Cyclin D1, MYC with high Ki67 proliferation rate (4+) [14].

In our patient's case, although it is possible that the Bell's palsy was either entirely incidental, connected to COVID through some yet-unclear mechanism, or associated with an underlying lymphoma, its onset coinciding with the vague leg symptoms at time of initial presentation to ED illustrates the complexity of diagnosis of atypical neuropathic pain. This patient had persistent leg symptoms for over a year before eventual diagnosis. Although mass compression of the lumbosacral plexus and cauda equina nerves in the sacral canal likely contributed to nerve injury in our patient, there was indication of direct invasion of the sciatic nerve and growth of the recurrent tumor along the sacral nerves suggestive of neurolymphomatosis. Neurolymphomatosis (NL) is a rare and diagnostically challenging condition characterized by direct lymphomatous infiltration of the peripheral nervous system

[15]. The estimated prevalence of NL is 0.2% in non-Hodgkin lymphoma. A review of 82 published NL cases found that diffuse large B cell lymphoma was the most common malignancy type in both primary and secondary NL cases (76%) [16]. Although most patients have some variation of painful weakness, the clinical presentation is varied and dependent on the distribution of nerves involved [17–19]. MRI may demonstrate enhancing T2-weighted hyperintense fusiform enlargement or nodularity of the nerves and/or plexus with associated FDG activity on fluorodeoxyglucose positron-emission tomography (FDG-PET) [20]. FDG-PET and biopsy are essential for diagnosis [17, 21]. Treatment involves chemotherapy with a Rituximab-containing regimen. However, the prognostic outcome of NL is not favorable. Despite aggressive rituximab-containing chemotherapy treatment, retrospective case analysis of 12 patients noted median survival after diagnosis of NL was 9.4 months [22].

In the case of our patient, she unfortunately exhibited the general poor prognosis of NL, and had local recurrence and metastatic disease within months after completion of treatment.

CONCLUSIONS

This case highlights a challenging diagnosis and is the first to present the association of onset of COVID-19, Bell's palsy and neuropathic pain associated with B-cell lymphoma. It is unclear whether there is a common COVID-19 associated immune event triggering Bell's Palsy or involved in development or rapid progression of lymphoma after COVID-19 infection. Providers should be aware of these atypical signs and symptoms of BP as possible clues of lymphoid malignancy, and a high degree of suspicion for a malignant cause of vague progressive neuropathic pain, whether or not COVID-19 illness is present.

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AUTHOR CONTRIBUTIONS

ZP contributed to idea, patient work-up and evaluation, initial write-up, editing and final submission, SO contributed to chart review, literature review, write-up, creation of figure and table, editing and final submission.

COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

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