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"Heterotopic Ossification of Bilateral Hip Joints post COVID19 infection: A Rare Case Report and Review of Literature''

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Abstract:
Case Report: *A 18 years old male with no significant past medical history, prior trauma, any neurologic/psychiatric disorders developed heterotopic ossification of bilateral hip joints in recovery period after COVID 19 infection.*
Conclusion: *Potential complications after COVID 19 infection are varied and myriad and many more complications are not known to us as it is a naïve virus. Although rare: but heterotopic ossification as a complication after COVID 19 infection is also known. Clinicians should always be alert about development of heterotopic ossification in any patient after COVID 19 infection who complains of pain, local warmth and stiffness of joints.*
Keywords: *Heterotopic ossification, COVID 19, Hip joint, Indomethacin, Myositis ossificans, Radiotherapy*

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I. Introduction:

Heterotopic ossification is the formation of reactive non-neoplastic bone in extraosseous tissues like skeletal muscles, fascia, tendon, ligament, skin, subcutaneous tissue, vessel wall or any site with connective tissue. It is often associated with history of trauma, surgery, massage, neurologic disorders, severe burns and rarely genetic like fibrodysplasia ossificans progressive (Munchmeyer's disease). It is also commonly associated with prolonged immobilisation and sequelae of critical illness. More recently a very few case reports of heterotopic ossification in patients with COVID19 infection who required mechanical ventilation were published. Here we are presenting a rare case report of HO around bilateral hip joint in a patient who had recovered from COVID19.

II. Case History:

A 18 year old male with no significant past medical history presented with complaints of fever and shortness of breath initially followed by an episode of seizure, brief loss of consciousness and altered sensorium. No history of prior trauma, any neurologic/psychiatric disorders was there. Patient was diagnosed with COVID19 by molecular RT-PCR from nasal swab. He was treated with Dexamethasone, Acyclovir, Teicoplanin, Meropenem and Phenytoin. However condition of patient deteriorated with high grade fever, worsening hypoxia and septic shock for which he required mechanical ventilation with high FiO2 and additional antibiotics (vancomycin and Cefuroxime), Nebulization with salbutamol and budesonide and levetiracetam for seizure. Supportive care done in prone positioning. Mechanical ventilation removed after 9 days and tracheostomy done for long term acute care which was subsequently removed after 1 month.

Patient become COVID19 negative after around one month in two successive RT-PCR tests done at 3 days interval. One month later, after becoming COVID19 negative, the patient complained of pain and swelling over his both hips with gradual restriction of range of motion. No pain/stiffness in any other joints. On clinical examination, there was swelling, local rise of temperature with restricted range of motion of both hip joints ***(Fig.1)***.

In laboratory investigations, Serum Alkaline Phosphatase level (ALP) remained normal for initial one month, then there was steep rise in its level with peak value of 363 U/L which coincides with the development of heterotopic ossification. Liver enzymes (ALT/AST) and serum Creatinine Kinase were also elevated during the same duration and followed the same trend. However, serum calcium level remained in lower range

throughout the stay with maximum dip observed at the time of peak level of these enzymes. Renal functions remained within normal limit.

Plain radiograph of pelvis with both hip joints shows well developed irregular opacity with a zonal ossification process and a broad bony stalk with continuity on the cortex of proximal femur and the pelvis suggestive of parosteal Heterotopic ossification (Brooker's Classification type IV). Multiple small opacities were also seen around proximal femur (***Fig. 2***). Later it was confirmed with CT scan to be near bridging HO across the superolateral aspect of proximal femur (***Fig. 3,4,5***). MRI of pelvis with both hip joints shows multiple large sharply delineated lesions in the soft tissue around the hip joint with mainly peripheral calcifications extending from ilium to lesser trochanter suggestive of myositis ossificans ***(Fig.6)***.

Ibandronate and NSAIDS have been started and the patient was followed up at an interval of two

chances of neuromuscular injury during resection. Bone scans may also be used to demonstrate quiescence of the HO prior to surgical excision[5].

Development of HO in patients with COVID19 infection can be correlated in many ways. COVID-19 virus itself or its neuro-invasive potential, or cytokine storm associated with COVID-19 includes upregulation of factors that have been previously associated with the formation of HO[2]. Spike protein of COVID-19 activates IL-6/TNF-@ leading to elevated levels of cytokines and these cytokines are responsible for the pathogenesis of HO[1,6].

Immunosuppressive drugs that target these pathways theoretically may inhibit development of HO in COVID-19 patients but more studies are necessary to prove.

The coronavirus surface proteins itself may incite the inflammatory process resulting in flush release of a certain group of cytokines that triggers the pathogenesis of HO. COVID19 infection related critical illness with prolonged immobilisation and chronic hypoxia may attribute to the development of HO. Fever of long duration or neurological insults due to COVID19 may also trigger HO. Aggressive mobilisation or passive exercises after prolonged hospital stay may also be responsible for the same.In December 2020, **Aziz et al** reported two cases of HO,one around bilateral shoulders about 5.5 months post admission and another in right shoulder about 6 months after admission in patients of COVID19 who underwent mechanical ventilation.

IV. Conclusion:

Potential complications after COVID 19 infection are varied and myriad and many more complications are not known to us as it is a naïve virus. Although rare: but heterotopic ossification as a complication after COVID 19 infection is also known. Clinicians should always be alert about development of heterotopic ossification in any patient after COVID 19 infection who complains of pain, local warmth and stiffness of joints.

The patient was informed that the data concerning the case would be submitted for publication and the patient agreed for the same.

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Figure Legends:

Fig. 1: Clinical photograph of hip joints showing localised swelling.

Fig. 2: X-ray anteroposterior of pelvis with bilateral hip joints showing bilateral periarticular radiopaque opacity suggestive of heterotopic ossification.

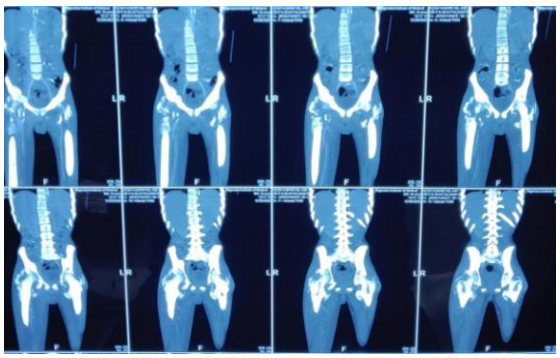

Fig. 3: Coronal section NCCT of pelvis showing bilateral periarticular new bone

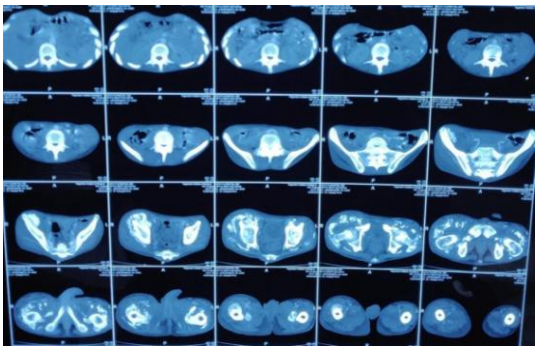

Fig. 4: Axial section NCCT of pelvis showing bilateral periarticular new bone formation.

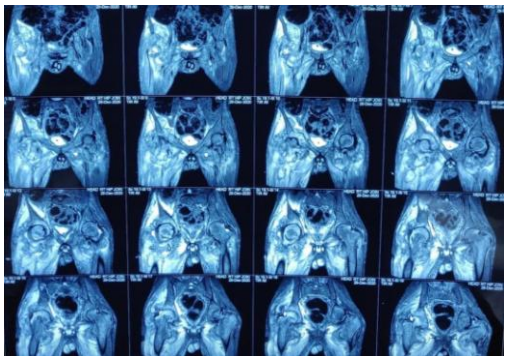

Fig. 5 : Magnetic resonance imaging (MRI) of pelvis with both hip joints shows multiple large sharply delineated lesions in the soft tissue around the hip joints with mainly peripheral calcifications extending from ilium to lesser trochanter suggestive of myositis ossificans.