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Infectious Diseases

Supplementary appendix

This appendix formed part of the original submission. We post it as supplied by the authors.

Supplement to: Mehta P, Bunker CB, Ciurtin C, et al. Chilblain-like acral lesions in long COVID-19: management and implications for understanding microangiopathy. *Lancet Infect Dis* 2021; published online March 8. http://dx.doi.org/10.1016/S1473-3099(21)00133-X.

Online supplement

Figure 1 Management of Chilblain-like lesions in Adults (A) and Children and Young People (B) following confirmed/suspected COVID-19

DNA for genetic screening of interferonopathies, deficiency of adenosine deaminase type 2 (DADA2) and monogenic lupus. Patients with large vessel vasculopathy or vasculitis may have 4 limb BP discrepancy. Skin biopsy may indicate vasculitis or occlusive vasculopathy. ANA=anti nuclear antibodies; ENA=extranuclear antibodies; ACE=angiotensin converting enzyme; IFN=interferon; CFI=complement factor I; ADA2=adenosine deaminase 2

Chilblain-like lesions in ADULTS following confirmed/suspected COVID

History and examination:
- Long standing history of chilblain lesions? or
- Suggestion of systemic inflammatory disease?

Yes →
- Specialist Rheumatology consultation
- Lifestyle measures
- Treat as per persistent/severe

No →
Lifestyle measures
e.g. keeping extremities warm (gloves, socks, avoiding cold), smoking / vaping cessation advice if relevant and patient information leaflet for Raynaud's

Persistent (> 30 days) or severe (e.g. pain, severe erythema or swelling) chilblain-like lesions

Aspirin 75mg once daily
(if no contraindications)

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Corticosteroids
- Topical (first-line) e.g. Dermovate two-three times daily
- If severe add oral (second line) e.g. prednisolone tapering from 15mg to 5mg over two weeks (reducing by 5mg every week), then stop. Proton pump inhibitor if dyspepsia

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Investigations:
- (COVID-19 PCR / serology – may be negative)
- FBC, U&E, LFT, CRP, ESR, clotting profile
- ANA, anti-dsDNA, ENA, ANCA, anti-cardiolipin Abs, anti-B2GP1 Abs, lupus anticoagulant, C3/C4, Immunoglobulins and protein electrophoresis
- HIV test, hepatitis B sAg, core Ab, Hepatitis C
- Hb electrophoresis (sickle screen), serum ACE
- Cryoglobulins and cold agglutinins (if available)
- Chest radiograph (?sarcoid)
- Nail fold Capillaroscopy if available

Refer for specialist input, as appropriate

if no response after 3 months

Hydroxychloroquine 200-400mg daily (max 5mg/kg/day)
- *Baseline Optical Coherence Tomography (OCT) if high dose HCQ (>5mg/kg/day), concurrent tamoxifen, impaired renal function (eGFR<60ml/min/1.73m^2) - refer to Ophthalmology
- All patients should have OCT screening at 5 years (alert primary care physician)

**Royal College Ophthalmology, December 2020*

if no response after 3 months

Calcium channel blocker e.g. nifedipine 10mg sustained release twice daily
OR
Angiotensin-II-receptor blocker e.g. losartan 25mg nocte
(Advise patients re: postural hypotension, caution if suspected autonomic dysfunction)

if no response after 3 months

Specialist Rheumatology consultation
- may consider fluoxetine, sildenafil, iloprost

Chilblain-like lesions in CHILDREN AND YOUNG PEOPLE following confirmed/suspected COVID

History and examination:
- Long standing history of chilblain lesions? or
- Suggestion of systemic inflammatory disease?
- Or absent pulses/4 limb BP discrepancy

Yes

- Specialist Rheumatology consultation
- Lifestyle measures
- Treat as per persistent/severe

No

Investigations:
- COVID PCR/serology (may be negative)
- FBC, U&E, LFT, CRP, ESR, clotting profile, d-dimer, ferritin, LDH, urine dipstick

Lifestyle measures

e.g. keeping extremities warm (gloves, socks, avoid cold), analgesia, patient information leaflet for Raynaud's

Persistent (> 30 days) or severe (e.g. pain, severe erythema or swelling) chilblain-like lesions

Consider the following investigations and refer to rheumatology:

- COVID PCR/serology (may be negative)

- ANA, anti-dsDNA, ENA, ANCA, anti-cardiolipin Abs, anti-B2GP1 Abs, lupus anticoagulant, serum ACE, urine dipstick
- Cryoglobulins and cold agglutinins
- Hb electrophoresis
- C3/C4, complement function, C1q, CFI
- Immunoglobulins
- IFN gene expression signature and ADA2 enzyme activity
- DNA (genetic screening)
- Chest radiograph
- Echocardiography
- Nail fold Capillaroscopy
- Doppler studies, angiography, CT brain (calcification)
- Skin biopsy

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Lifestyle measures

e.g. keeping extremities warm (gloves, socks, avoiding cold) and patient information leaflet for Raynauds

+

Other treatments:
- Aspirin (3-5 mg/kg)
- Calcium channel blockers (e.g nifedipine)
- GTN patch
- Angiotensin II receptor blockers

If no response may need to consider the following:
- Corticosteroids:
  - Topical (first-line) e.g. dermovate two-three times daily
  - If severe, add oral (second line) e.g. prednisolone
- Hydroxychloroquine (5-6 mg/kg/day)
- Epoprostenol or epoprostenol analogue (iloprost), sildenafil
- Other anti inflammatory treatments are to be targeted to underlying diagnosis