Background During the COVID-19 pandemic, a high incidence of patients with perniosis was observed worldwide. Classically, perniosis is secondary to cold exposure, hemoproliferative and autoimmune diseases. Although the pathomechanism of perniosis is incompletely characterized, lupus pernio is associated with a Type I interferon (IFN-I) signature. Therefore we explored the role of IFN in patients with perniosis.

Methods Antibodies to SARS-COV-2 were tested by protein microarray. Expression of IFN-I, IFN stimulated genes (ISGs) and other inflammatory cytokines in peripheral blood were determined by qPCR. Inflammatory cytokine proteins in serum were quantified by Biologic LegendPlex. Immunohistochemistry was used to detect expression of the IFN-induced protein, Myxovirus resistance protein A (MxA) in lesional skin. STING protein phosphorylation in CD14 monocytes was determined by flow cytometry. The effect of patient sera on microvessels-on-a-chip was determined by Von Willebrand Factor (vWF) protein release to the vessel lumen. Statistical significance was determined by Student’s t-test.

Results Between April-September 2020, 7 patients (3M;4F age 31-56) with pernio of the toes and/or fingers were studied (figure 1A and B). Two patients had previous Raynaud’s phenomenon but none had prior or co-existing autoimmune disease. 1/5 patients tested was ANA+. 4/7 patients reported suspected COVID-19 symptoms prior to onset of perniosis. Antibodies to COVID antigens were negative in all patients. Blood studies showed an increase in TNF gene expression in perniosis patients compared to healthy matched controls (p=0.02). While there was a trend toward increased mRNA expression of IFNb (p=0.07) and the ISG CXCL10 (p=0.07), the results did not reach statistical significance. Phosphorylation of STING in CD14+ monocytes was higher in perniosis than healthy controls (n=3 per group), with borderline statistical significance (p=0.05). Lesional skin biopsies in perniosis (n=2) showed striking expression of MxA in tissue (Fig1. C&D). 4 patient sera induced high vWF release into the lumen on the microvessel 3D chip.

Conclusions The frequency of perniosis during the COVID pandemic, suggests a relationship between these two conditions although direct evidence of COVID-19 infection has been limited. We observed a trend toward higher IFN-b gene expression in PBMC as well as higher phospho-STING protein expression in CD14 monocytes and, most significantly, strong expression of MxA in skin. While the small number of patients preclude a definitive explanation, our data suggest that COVID associated perniosis is an interferonopathy. We propose that acute, transient COVID infection led to monocyte activation, IFN-I production and damage to the small vessels, likely aggravated by cold exposure.

Abstract 1203 Figure 1 Clinical appearance of perniosis in study patients showing red and purple papules over several toes some with near blisters (A and B). MxA staining of skin from perniosis lesion (D) showing lymphocytic inflammation in the dermis with perivascular and periadnexal inflammation. There is prominent MxA staining in the epidermis, dermal inflammatory infiltrate and in the superficial endothelial cells indicating interferon activation in skin. This is compared to no MxA staining in normal skin (C).