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TITLE: Clinical improvement in psoriatic nail disease and psoriatic arthritis with tildrakizumab treatment

RUNNING TITLE: Tildrakizumab in Psoriatic Disease

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KEY WORDS: Psoriatic Nail Disease, Psoriatic Arthritis, Tildrakizumab

CONFLICT OF INTEREST: Professor Rodney Sinclair was a Principal Investigator in Sun Pharma Global FZE Phase 3 Clinical Trial evaluating the efficacy and safety of tildrakizumab in moderate-to-severe Chronic Plaque Psoriasis.

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We report on a 40-year-old man with psoriatic nail dystrophy and psoriatic arthritis who had an excellent clinical response to the anti-interleukin-23 (IL-23) monoclonal antibody tildrakizumab. His past medical history included bipolar disorder, asthma and long-standing lumbar back pain following an injury. His regular medications included carbamazepine, lithium, sertraline, ziprasidone, budesonide/formoterol and metformin.

In 2016, he was diagnosed with left first toe osteomyelitis requiring surgical debridement, including removal of the nail bed, followed by a 3-month course of antibiotics. When the nail regrew it had an unusual appearance that was initially diagnosed as onychomycosis, however, nail scrapings revealed no evidence of fungal infection and a trial of systemic antifungal

therapy and nail lacquer was ineffective. One year later he developed abnormalities in the left second fingernail and left fourth toenail.

Shortly after this he developed an asymmetrical polyarthritis and was referred to a rheumatologist. Examination revealed synovitis of the left second distal interphalangeal (DIP) joint, right second metacarpophalangeal (MCP) joint, right ankle, right second and third and left second metatarsophalangeal (MTP) joints. Radiographs of his hands and feet revealed a solitary erosion of the left second DIP joint. Serum rheumatoid factor was negative, supporting a diagnosis of psoriatic arthritis. Treatment was commenced with methotrexate 20mg weekly and folic acid 10mg weekly. After four months of treatment, methotrexate was replaced by sulfasalazine 1g twice daily, due to ongoing synovitis.

He then presented to a dermatologist for management of his nail dystrophy. Examination revealed significant onycholysis, proximal onychomadesis and oil drop changes to the left second fingernail, onychauxis of the left fourth toenail and pitting of multiple other nails, consistent with psoriatic nail disease. Monthly triamcinolone acetonide injections were administered to the affected nails in addition to clobetasol dipropionate 0.05% ointment. After 7 months on this treatment regimen, there was minimal clinical improvement. His psoriatic arthritis remained active and methotrexate 20mg weekly was restarted.

This patient did not meet eligibility criteria for biologic therapy for psoriatic arthritis on the Australian Pharmaceutical Benefits Scheme (PBS) due to his low C-reactive protein (CRP)

level of 5 and low joint count while taking treatment with methotrexate and sulfasalazine. Tildrakizumab was obtained through special-access scheme approval from the Australian Therapeutic Goods Administration (TGA). Screening investigations, including viral hepatitis serology and Quantiferon-TB Gold, were negative.

Tildrakizumab 100mg was administered subcutaneously at weeks 0 and 4. Twelve weeks later, when he presented for his third dose of tildrakizumab, there had been significant improvement in his nail dystrophy (Figures 1 and 2) and arthritis. The patient recorded the time taken for his pain to ease in the morning after waking during the first 9 weeks of tildrakizumab treatment. There was an overall reduction in the time taken for pain to ease in the affected joints (Table 1). He reported no adverse effects.

Tildrakizumab is a humanised monoclonal antibody that inhibits the p19 subunit of IL-23 and is currently approved by the TGA, Food and Drug Administration (FDA) and European Medicines Agency (EMA) for the treatment of patients with moderate-to-severe plaque psoriasis[1]. Tildrakizumab has also been reported to be efficacious in patients with psoriatic arthritis[2,3].

The IL-23/IL-17 axis plays a central role in the pathogenesis of psoriatic disease[4]. IL-23 antagonists, IL-17 antagonists, IL-12/23 antagonists and tumour necrosis factor (TNF) antagnosits, are approved for use in moderate-to-severe plaque psoriasis[4]. Ustekinumab,

secukinumab and TNF antagonists are also approved for the treatment of psoriatic arthritis. Ustekinumab has been shown to improve psoriatic nail disease[5].

The clinical response observed in this patient suggests that tildrakizumab may be an effective treatment option for both refractory psoriatic nail disease and psoriatic arthritis.

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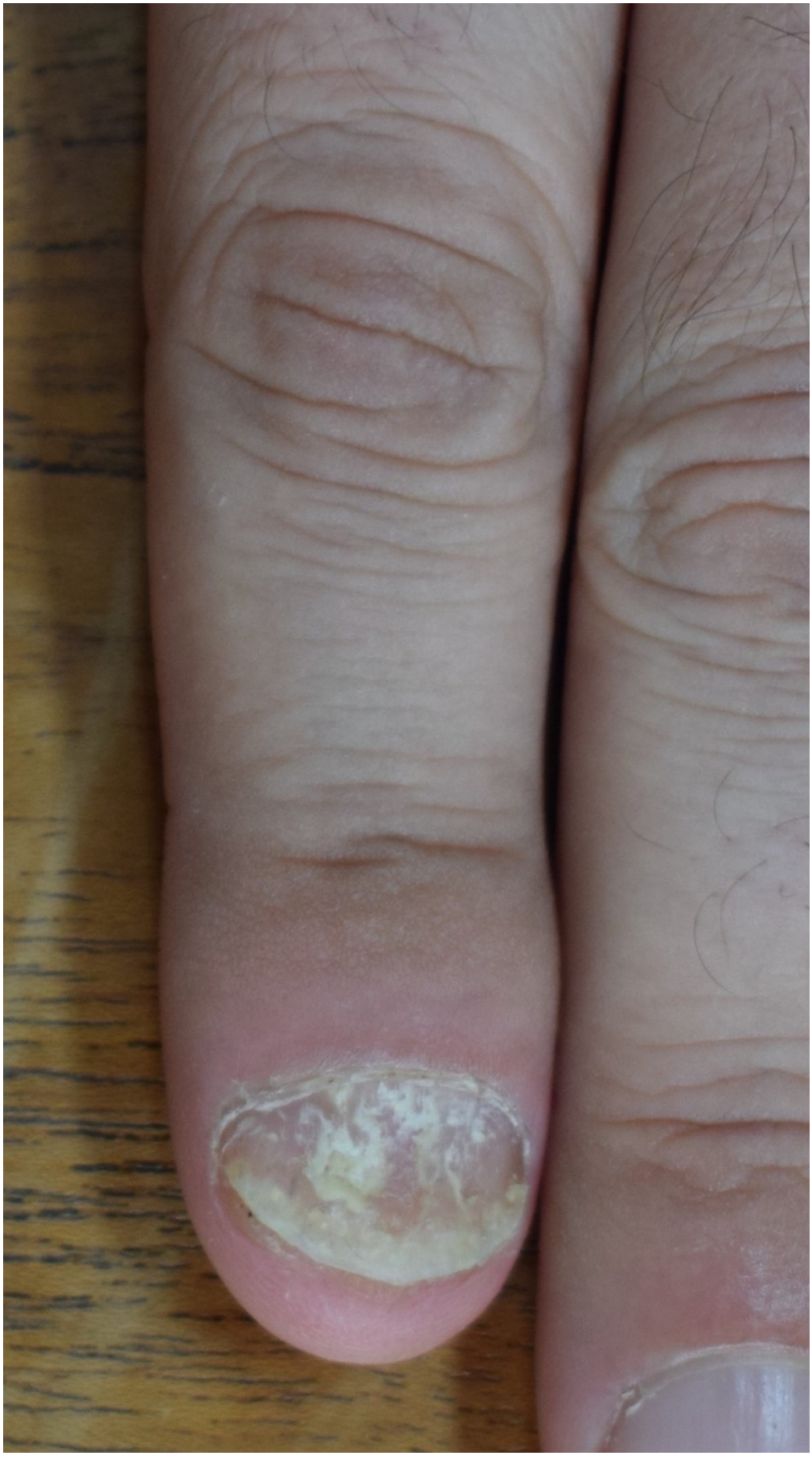
FIGURE LEGENDS

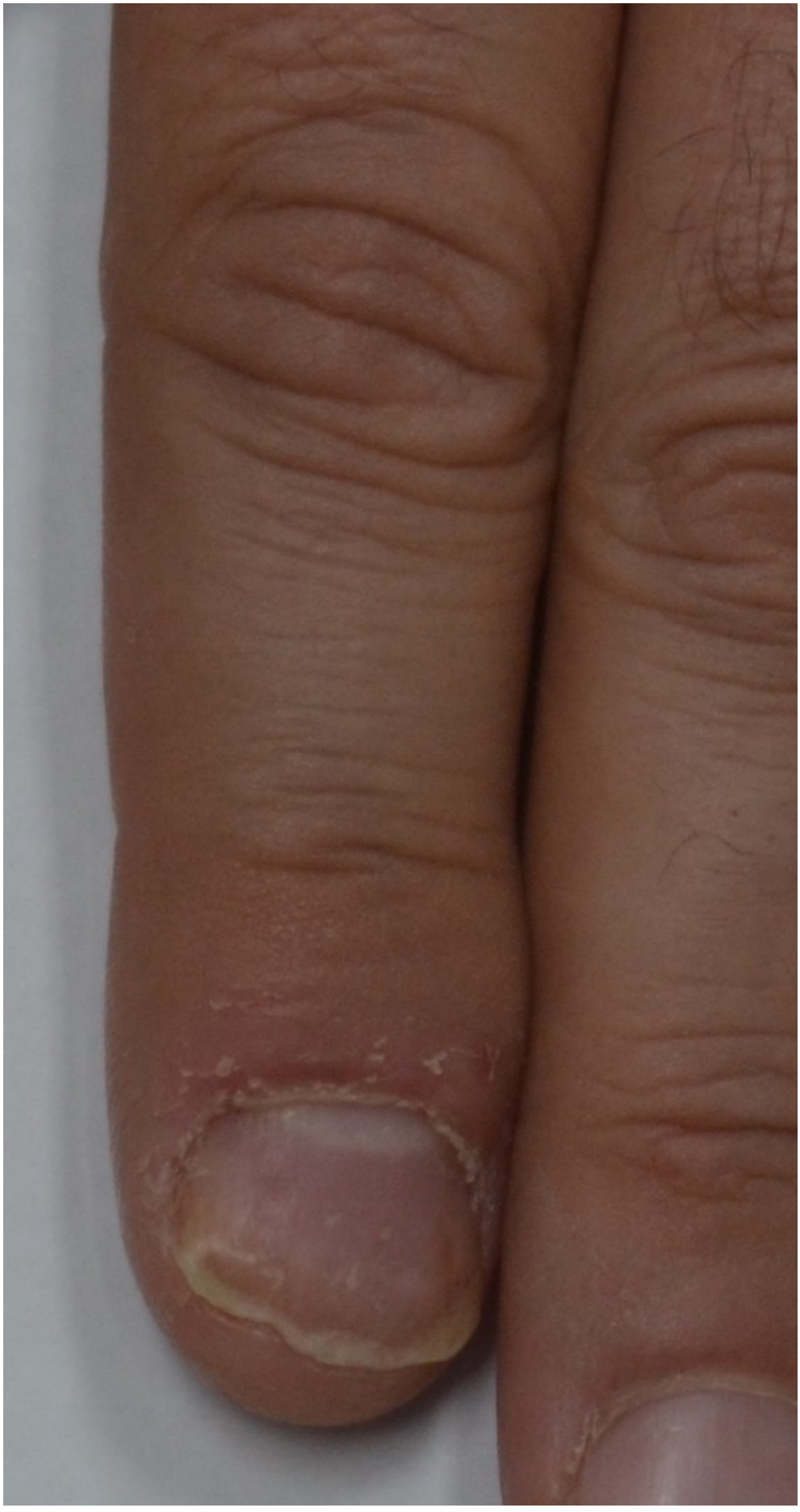
Figure 1: Appearance of the left second fingernail prior to treatment with tildrakizumab

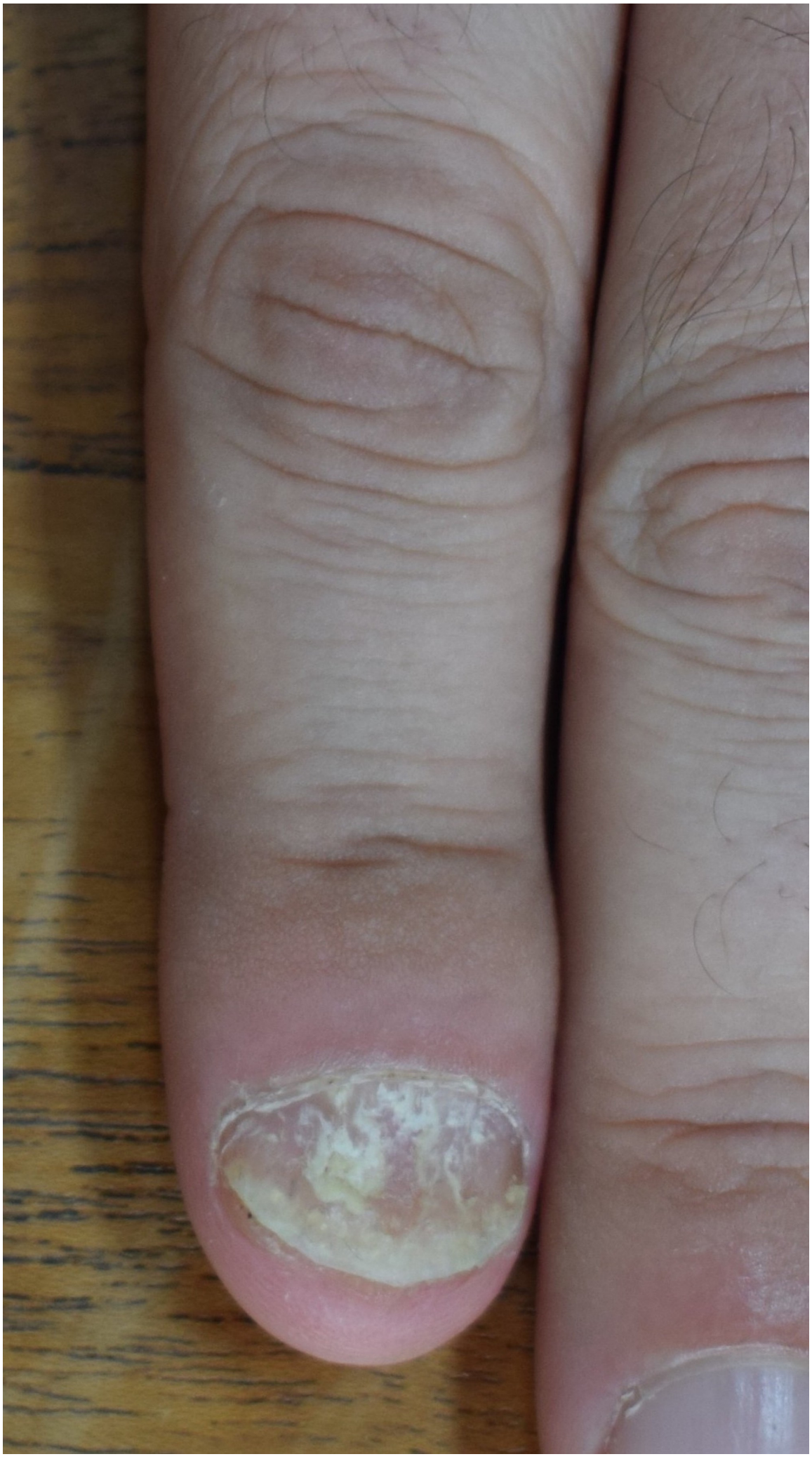
Figure 2: Appearance of the left second fingernail after 2 doses of tildrakizumab

Table 1: Average time (minutes) taken for arthritis to ease upon waking

	Fingers/hands	Wrists	Toes/feet	Ankles
Week 1	111	28	65	26
Week 2	91	42	55	52
Week 3	85	28	88	73
Week 4	54	21	77	55
Week 5	78	16	95	20
Week 6	62	10	72	20
Week 7	58	0	40	21
Week 8	68	3	23	11
Week 9	10	0	13	0







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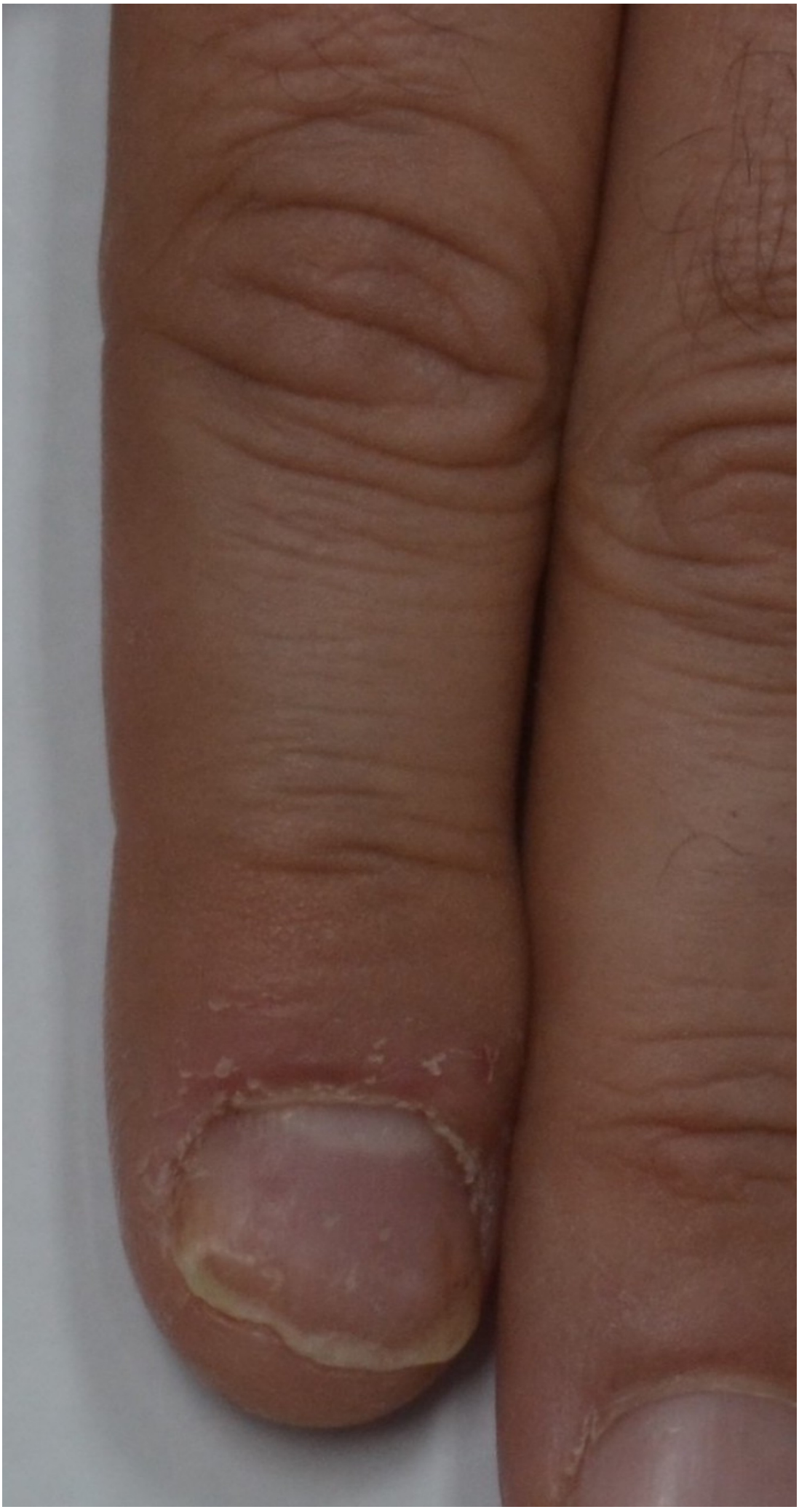

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