

Table 1 Data summary including demographic data and treatments used

Variable	Frequency, n (%)	Treatment	Patients improved, n/N
Sex		Phototherapy	7/21
Male	12 (30)	Citalopram	4/11
Female	28 (70)	Cognitive behavioural therapy	3/9
Age (years)		Haelan Tape	3/8
< 30	2 (5)	Amitriptyline	2/8
30–49	12 (30)	Antihistamines	4/7
50–69	18 (45)	Oral antibiotic/antiviral	3/8
≥ 70	8 (20)	Topical steroids	1/5
Ethnicity		Trimovate	3/4
White	31 (78)	Habit reversal	2/4
Afro-Caribbean	4 (10)	Risperidone	2/4
Asian	2 (5)	Fluoxetine	1/3
Mixed	2 (5)	Diprobase, Dermol 500/600	1/4
Egyptian	1 (3)	Psychotherapy (other)	1/3
Time since diagnosis		Sertraline	0/2
< 1 year	4 (10)	Oral steroids	1/2
1–5 years	22 (55)	Fucibet/Fucidin	2/2
> 5 years	14 (35)	Doxepin	0/1
		Alcohol cessation	0/1
		Topiramate	1/1
		Self-prescribed herbals	0/1
		Pregabalin	0/1


psychodermatology multidisciplinary team due to stable disease in our patient cohort. However, they may have a role in the treatment of some of our patients in the future should their condition become refractory to current therapy.

The remission rate of NP was low. Out of the 40 patients, only 16 (40%) had improved at the time the data were collected and had been discharged. Of those, 14 were on a range of combination therapies and the remaining two were on monotherapy.

Limitations of our study include lack of adjustment for confounding and inability to form conclusive inferences on treatment outcomes due to the study design and small patient cohort, although a cohort of 40 patients is relatively large in NP research.

In conclusion, we acknowledge that the IFSI guidelines are a step forward towards a standardized treatment for NP; however, we are yet to see the most effective combination of treatments trialled in large-scale studies. We do believe that NP management is complex and requires a multidisciplinary approach within a specialist psychodermatology clinic. There remains hope with preliminary data available on monoclonal antibodies and Janus kinase inhibitors in NP.<sup>5</sup> However, at present based on our findings, patients with NP who showed

improvements were on a combination of treatments that manage the skin and the mind concurrently, which is the main point we hope this study emphasizes.

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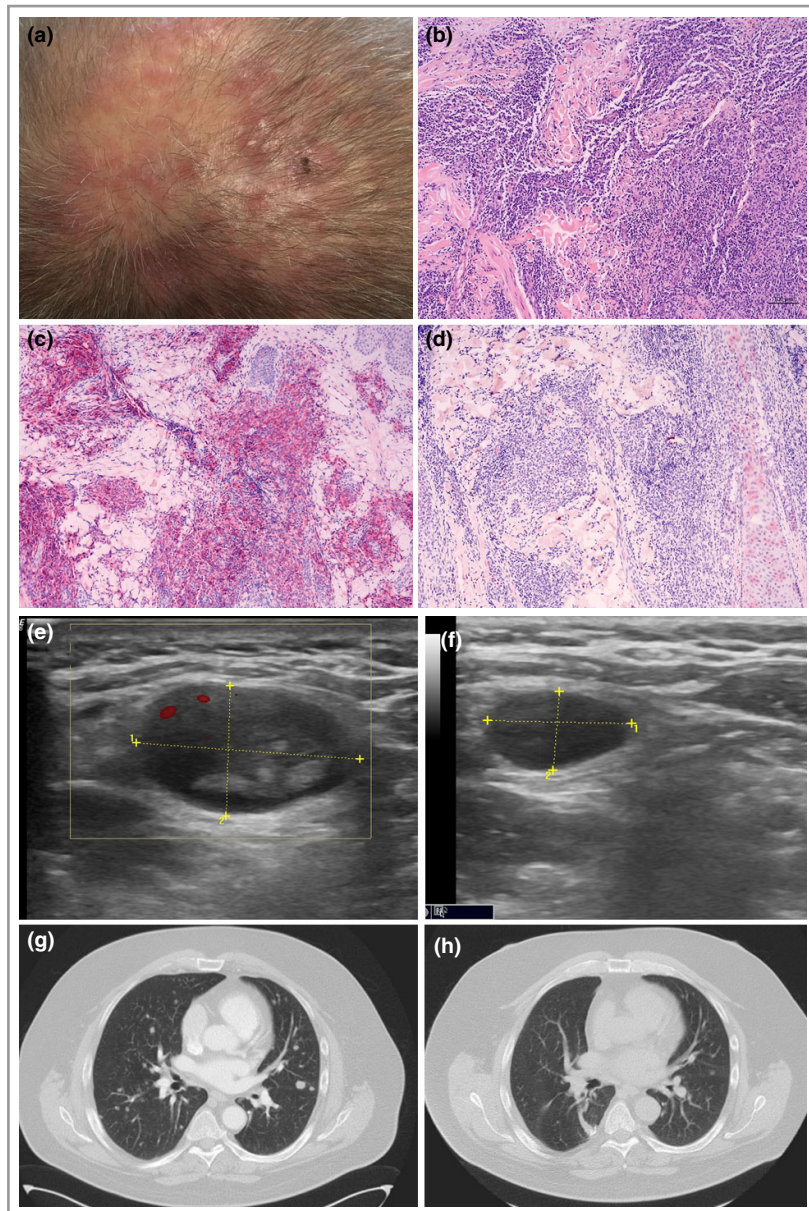
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## Primary cutaneous anaplastic large-cell lymphoma with marked spontaneous regression of organ manifestation after SARS-CoV-2 vaccination

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DEAR EDITOR, Primary cutaneous anaplastic large-cell lymphoma (pcALCL) belongs to the primary cutaneous CD30+ T-cell



**Figure 1** (a) A male patient is shown with recurrent primary cutaneous anaplastic large-cell lymphoma (pcALCL) on the scalp. (b) Haematoxylin & eosin histology revealed dense dermal infiltrates with large lymphocytes (scale bar = 100 µm) showing (c) strong CD30 positivity and (d) CD15 negativity on immunohistochemistry. (e) Ultrasound revealed a pathologically enlarged cervical lymph node (1 = 2.2 cm, 2 = 1.29 cm). (g) Thoracic computed tomography showed diffuse bilateral pulmonary disease with numerous tumour nodules. Shortly before treatment initiation the patient had received his first SARS-CoV-2 vaccination. (f) A few days later, the size of the lymph node was significantly decreased (1 = 1.23 cm, 2 = 0.71 cm) and pulmonary manifestation had almost completely spontaneously regressed (h).

lymphoproliferative disorders.<sup>1</sup> Systemic involvement is relatively rare and pcALCL is generally confined to the regional lymph nodes.<sup>1</sup> In this research letter, we describe a patient with recurrent pcALCL and diffuse lung manifestation that spontaneously regressed after one SARS-CoV-2 vaccination.

We report a 57-year-old male patient with a 10-year history of biopsy-proven [CD30+, CD3+, CD4+, anaplastic lymphoma kinase (ALK)-, clonal T-cell receptor gamma-chain rearrangement] pcALCL with frequent local relapses predominantly affecting his scalp and neck. Moreover, the patient had a

history of suspicious waning and waxing cervical lymph nodes (partly biopsy-proven) over the last 5 years. Pretreatments included methotrexate, brentuximab, gemcitabine and radiotherapy. The last treatment (radiotherapy) of cutaneous lesions (Figure 1a–d) was performed in February 2021, resulting in complete remission. At the end of March 2021, ultrasound again revealed a pathologically enlarged cervical lymph node (Figure 1e). Thoracic computed tomography (CT) showed innumerable bilateral pulmonary nodules that were suspicious for new pcALCL manifestation or second malignancy

(Figure 1g). Bone marrow was not involved. A lung wedge resection was scheduled, which included a histological confirmation by a haematopathology reference centre. Histopathology of several lesions of the lung revealed infiltrates of Hodgkin/Reed–Sternberg-like cells that were positive for CD30, CD3, CD4, TGP and CD15 and negative for Bcl-6, epithelial membrane antigen and ALK-1. On multiplex polymerase chain reaction, there was a monoclonal T-cell receptor gamma- (tube A, 244 bp) and beta-chain (tube A, 254 bp; tube B, 255 bp) rearrangement in the lung tissue, which was exactly the same pattern as observed in biopsies of skin lesions 5 years and 9 years previously. Rechallenge with brentuximab was discussed by the interdisciplinary tumour board. A few days before initiation of brentuximab therapy, the patient noticed shrinking of the suspicious cervical lymph node, which was confirmed by means of ultrasound (Figure 1f). Moreover, thoracic CT revealed an almost complete resolution of the diffuse lung lesions (Figure 1h). Importantly, 1 week before pcALCL restaging, the patient had received his first COVID-19 vaccination (Comirnaty®, BioNTech/Pfizer, Mainz, Germany).

pcALCL is a rare lymphoma with an excellent prognosis as indicated by a 10-year survival rate of about 90%. However, the recurrence rate of pcALCL is high. Notably, 10–42% of patients diagnosed with pcALCL may experience spontaneous remission.<sup>1</sup> We detected identical clonal T-cell receptor gamma-chain rearrangements in lung lesions and previous skin lesions, together proving that the pulmonary lesions very likely originated from pcALCL. Eberle et al.<sup>2</sup> demonstrated that systemic manifestations of pcALCL frequently show Hodgkin/Reed–Sternberg-like infiltrates and that the coexpression of CD30 and CD15 in these cases may result in a mistaken diagnosis of classical Hodgkin disease.<sup>2</sup> Diffuse pulmonary disease stemming from pcALCL, as described in the present letter, is certainly unusual, as is spontaneous regression of such a tumour load, even though pcALCL is often associated with spontaneous regression as mentioned before.<sup>1,2</sup>


The most frequently reported triggers of spontaneous remission of malignancies include surgical trauma, infections and vaccines. Several vaccines, including the vaccines for smallpox, tetanus-diphtheria-pertussis, rabies and the Bacillus Calmette–Guérin vaccine, have previously been reported to be associated with spontaneous cancer remission. Accordingly, medical research has focused on cancer microbial vaccine immunotherapy.<sup>3,4</sup> Our patient received the COVID-19 vaccination 1 week before the detection of the almost complete resolution of his untreated lymphoma manifestations. After his COVID-19 vaccination, he noticed that the suspicious cervical lymph node regressed, indicating that the remission process likely began after the vaccination. Hence, the temporal sequence strongly suggests, but does not prove, that the SARS-CoV2 vaccine was the causal factor of the marked spontaneous regression of organ manifestation observed in the present case.

Dotan et al.<sup>5</sup> proposed that the most likely mechanism to have the potential for contributing to the development of

autoimmunity in COVID-19 is the capability of SARS-CoV-2 to overstimulate the immune system in addition to the molecular mimicry between self-components of the host and the viral components. There is growing evidence that autoimmunity owing to COVID-19 infection can also be triggered by SARS-CoV-2 vaccines.<sup>5–7</sup> The combination of a genetically predisposed individual with an overstimulated immune system owing to SARS-CoV-2 vaccination may trigger autoimmune phenomena or diseases such as myasthenia gravis, Henoch–Schönlein purpura or Rowell's syndrome.<sup>5–7</sup> Thus, we speculate that SARS-CoV-2 vaccines have the potential not only to trigger autoimmunity, but also to enhance antitumour responses owing to overstimulation of the immune system. In contrast, Brumfield et al.<sup>8</sup> recently reported on the recurrence of a primary cutaneous CD30-positive lymphoproliferative disorder following COVID-19 vaccination.

In conclusion, we observed marked spontaneous regression of organ manifestation in a patient with recurrent pcALCL following their first SARS-CoV-2 vaccination. However, as up to 42% of pcALCL cases may show spontaneous regression, we cannot fully exclude the possibility that this occurred in the present case.

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## Can artificial intelligence be used for accurate remote scoring of the Psoriasis Area and Severity Index in adult patients with plaque psoriasis?

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DEAR EDITOR, A 47-year-old man with chronic plaque psoriasis and type II diabetes mellitus on ustekinumab 45 mg 12-weekly injections, his first biologic therapy, was switched to adalimumab 40 mg alternate weeks (10 February 2020) when his Psoriasis Area and Severity Index (PASI) was 11.4 due to loss of effectiveness. Owing to the COVID-19 outbreak, the UK Prime Minister advised clinically vulnerable people, including people on immunosuppressive medication with comorbidities including diabetes, to stay home avoiding face-to-face contact (23 March 2020). To understand whether it was possible, with artificial intelligence (AI) assistance, to remotely assess the patient's response to adalimumab, we performed a critically appraised review.

The PASI is the most widely utilized and validated method of evaluating plaque psoriasis severity. PASI scoring using AI algorithms could allow remote psoriasis severity assessment, reduce inter- and intraobserver variability,<sup>1</sup> enable more reliable comparisons and save time and costs. Computing power and image classification algorithm advances have enabled recent AI breakthroughs in image-based medicine including dermatology.<sup>2</sup> Our aim was to identify and critically appraise the studies reporting AI algorithms designed to assess PASI in adult patients with plaque psoriasis vs. clinician in-person PASI assessment.

A literature search in Ovid MEDLINE (database inception 31 October 2020), using a search strategy by index test set using AI terms (including 'artificial intelligence', 'machine learning'), diagnosis terms (including 'diagnosis') and target condition sets (including 'psoriasis'), identified 61 publications. Inclusion criteria were studies assessing AI algorithm accuracy in scoring severity of any PASI component (erythema, desquamation, induration or lesion area) in adults with psoriasis. After duplication, titles and abstracts were screened (B.R.S.) and reviewed (Z.Z.N.Y.); 52 publications were removed. Nine full-text articles were assessed for eligibility; two met the inclusion criteria. The included article bibliographies were reviewed, identifying 15 additional relevant studies (B.R.S./

M.DB.): one was included. Three studies in total were included.<sup>4–6</sup> The main reasons for exclusion were no PASI output or a method not classed as AI. Risk of bias and applicability were assessed with the Quality Assessment of Diagnostic Accuracy Studies 2 tool.<sup>3</sup> (Full details are available on request from the authors.)

Table 1 outlines the included studies' characteristics. Ihtatho *et al.*<sup>4</sup> developed an algorithm to assess PASI area; Raina *et al.*<sup>5</sup> PASI erythema of elbows and knees; and Lu *et al.*<sup>6</sup> PASI erythema and scaling. Ihtatho *et al.* externally validated their algorithm by calculating exact matches between algorithm-assessed PASI and manual PASI from digital images. The algorithm correctly scored PASI lesion area in 30 of 32 regions (93.8%). Raina *et al.* and Lu *et al.* did not use separate reference tests and only performed internal validation from using leave-one-out cross-validation and 10-fold cross-validation, respectively. The algorithm in Raina *et al.* matched dermatologist-assessed PASI erythema in 39 of 80 images (48.8%), while Lu *et al.* found exact-match PASI erythema for 78.9% and PASI scale for 88.7% of images.

Risk of bias was high for all three studies. All used convenience or undisclosed sampling methods to recruit small numbers of participants. Raina *et al.* was limited to elbows and knees while Lu *et al.* only included lesions scored identically by two dermatologists, reducing applicability. Lu *et al.* and Ihtatho *et al.* used optimal image-taking conditions not reflective of real-world variability, introducing bias in the algorithm's favour. Lu *et al.* and Raina *et al.* only performed internal validation, leaving them at high risk of bias. Test blinding was not explicitly described for any study, biasing in favour of the algorithm. Ihtatho *et al.* did not specify the qualification and experience of the person responsible for scoring PASI for reference. The generalizability of these results is unclear; algorithms trained on nondiverse data may be inaccurate when applied to diverse populations. Most studies did not report on ethnicity (except Ihtatho *et al.*) or sex, and failed to recruit sufficient ethnically diverse participants.

In summary, we identified three studies reporting on algorithms for PASI scoring of area, erythema alone, and erythema and scale. Studies were small, incompletely reported and, in two cases, not externally validated. No algorithm was validated for scoring all four PASI components, and none assessed induration, an ongoing challenge for AI-based assessment. Psoriasis severity measures not utilizing induration may be more amenable to AI assessment.

Research investigating AI in dermatology for inflammatory disease severity categorization, compared with malignant lesion categorization, is scarce.<sup>7</sup> The included studies are > 4 years old. As AI is rapidly evolving and deep learning methods are leading to increasingly sophisticated algorithms, we recommend repeating this literature search in 3 years.<sup>8</sup>

Without a reliable AI algorithm, remote assessment of the patient via telephone or video consultation was necessary. Due to patient global assessment of severe, widespread disease, on 4 May 2020, the patient was escalated to weekly adalimumab dosing.