A Review of Nail Changes in Acrokeratosis Paraneoplastica (Bazex Syndrome)

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Keywords
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Abstract
Acrokeratosis paraneoplastica (Bazex syndrome) is a rare paraneoplastic dermatosis associated with internal malignancies. Clinical presentation is characterized by erythematous or violaceous scaly plaques involving the digits, nose, ears, palms, and soles. Nail changes commonly present concurrently with cutaneous manifestations. In this review, we characterize nail changes associated with acrokeratosis paraneoplastica. A total of 48 cases were analyzed. Nail findings were nonspecific, with the most common being nail plate thickening, onycholysis, subungual hyperkeratosis, longitudinal ridging, discoloration, and nail plate loss. In most patients, nail changes involved the majority of fingernails and toenails and most often appeared prior to the diagnosis of malignancy. The most common associated underlying malignancies were squamous cell carcinomas of the head and neck. A diagnosis of acrokeratosis paraneoplastica should be considered in patients with onychodystrophy involving multiple nails with accompanying atypical psoriasiform dermatoses. Screening for internal malignancies may significantly decrease morbidity and mortality for these patients.

Introduction
Bazex’ acrokeratosis paraneoplastica is a rare dermatological condition characterized by erythematous and hyperkeratotic plaques, involving the nose, ears, palm, and soles. Bazex syndrome is associated with internal malignancies, commonly of the upper aerodigestive tract [1–3]. Cutaneous manifestations commonly appear prior to cancer diagnosis and typically follow 3 distinct clinical stages. Nail dystrophy often presents during the first stage concurrently with papulosquamous plaques on the distal digits, nose, and ears [1, 4]. Nail findings are common amongst acrokeratosis paraneoplastica patients [1]. Our objectives were to characterize nail changes associated with acrokeratosis paraneoplastica, which may be important clues to the presence of internal malignancies.
| Author                        | Age, years | Sex | Skin type | Race | Cancer type | Stage | Metastasis | Treatment | Nails involved | Nail changes | Timing of nail changes in relation to cancer | Cutaneous manifestations                                                                 |
|------------------------------|------------|-----|-----------|------|-------------|-------|------------|-----------|----------------|-------------|---------------------------------------------|------------------------------------------------------------------------------------------|
| Jacobsen et al. [11]         | 63 M       | Not specified | Not specified | Not specified | Epidermoid carcinoma of lung | Not specified | Liver metastases | None, patient died of broncho-pneumonia | All finger and toenails | Tender nail folds. Fingernails: hypertrophic, onycholytic, crumbling, and partially destroyed. Toenails: yellow, hypertrophic, onycholytic | 6 months prior | Pityriasiform scaling of tip of nose, ear, helices, toes and distal fingers. Violaceous keratodermatofingermucous, palms, toes, and soles Palmar and plantar regions with hyperkeratosis |
| Richard et al. [12]          | 55 M       | Not specified | White | SCC of esophagus | Not specified | Cervical metastases | Radiotherapy | Majority of fingernails and toenails | Thickened and friable | 4 months prior | Erythema with violaceous hue of nose, lips, cheeks, chin, ears, elbows, and knuckles. Palmoplantar regions with hyperkeratosis |
| Bologna et al. [1]           | 52 M VI    | Black | Metastatic SCC of esophagus | Not specified | R upper lobe nodules and R hilar adenopathy; dermal metastasis SCC | Radiation therapy and cisplatin | All finger and toenails | Thickened, yellow/brown discoloration subungual hyperkeratosis and horizontal and longitudinal ridging | 9-10 months prior | Scaling of toes, fingers, and soles. Hyperpigmentation of nose and ears |
| Douglas et al. [13]          | 82 M       | Not specified | Not specified | Adenocarcinoma of esophagus | Not specified | Mediastinal lymphadenopathy | Palliative radiotherapy | Majority of fingernails and toenails | Longitudinal ridging and distal thickening of nail plates | 24 months prior | Blush erythema and scaling of skin over fingers, toes, fingers, and soles. Keratotic lesions on nose and ears |
| Handfield-Jones et al. [14]  | 73 F II    | Caucasian | Poorly differentiated SCC | Not specified | Intrapulmonary metastasis | Radiotherapy | All fingernails and toenails | Ridgeting splitting clubbing | 2 months prior | Papillary discolouration of fingers and toes with tissue swelling and poikiloderma scaling |
| Handfield-Jones et al. [14]  | 65 M II    | Caucasian | Anaplastic carcinoma of indeterminate origin | Not specified | Cervical lymphadenopathy | Radiotherapy | Toenails only | Loose with sterile paronychia. Subungual and perungual hyperkeratosis | 2 months prior | Surrounding skin swollen and purple |
| Handfield-Jones et al. [14]  | 73 M II    | Caucasian | SCC of R main bronchus | Not specified | Not specified | Not specified | All finger and toenails | Severe flaking and cracking of nails and warty thickening and fissuring of the nail folds | 2 months prior | Dry scaly skin around nails. Thickened and scaling on soles of feet. Purple discoloration of arms and knees. Thickening of skin of axilla |
| Mounsey et al. [15]          | 66 M II    | White | SCC of the glottis | T-3, N-0, M-0 | No | Total laryngectomy, L anterior neck dissection, L hemithyroidectomy | Palliative radiotherapy | Majority of fingernails and toenails | Longitudinal ridging and nail plate destruction | Not specified | Palm and plantar hyperkeratosis and superficial pitting |
| Poskitt et al. [16]          | 70 M II    | Not specified | SCC of esophagus | Not specified | Metastasis to tonsil | Excised, digoxin, Navidox ® and Oravox SR | All fingernails and toenails | Longitudinal ridging | 5 years post | Erythema of scaling of nose and ears, swollen and cyanotic fingers with swelling; erosion and crusting of cuticles |
| Arregui et al. [17]          | 41 M II    | White | SCC of esophagus | Not specified | Lymph node metaplasia in the mediastinum and bilateral pulmonary metastases | Palliative treatment with radiotherapy | All fingernails and toenails | Severe onychodystrophy, unspecified | 11 months prior | Erythema and mosaic clavus eruption in perungual area of fingers and toes. Fine scales at tips of nose and external ears |
| Arregui et al. [17]          | 73 M II    | White | Recurrence of transitional cell carcinoma of the bladder | Not specified | Treatment of local bladder recurrence with mitomycin C | All fingernails and toenails | Distal shedding and yellowish discoloration | Few weeks prior | Erythema and mosaic clavus eruption in perungual skin. Moderate plantar hyperkeratosis and desquamative cheilitis |
| O'Brien et al. [9]           | 67 F V     | Not specified | Oropharyngeal carcinoma | Not specified | 5-fluorouracil and carboplatinum | Not specified | Loss of the nail plate | Simultaneously with recurrence | Pachyonychiform eruption on fingers and toes extending onto dorsum of hands and feet | 5-fluorouracil and carboplatinum | Erythema and mosaic clavus eruption in perungual skin. Moderate plantar hyperkeratosis and desquamative cheilitis |

**Table 1.** Demographics, malignancy, treatment, nail changes, and cutaneous manifestations of patients with Bazex syndrome [1, 9–28, 30–38, 40–52]
### Table 1 (continued)

| Author                        | Age, years | Sex | Skin type | Race       | Cancer type                  | Stage | Metastasis | Treatment                      | Nails involved                  | Nail changes                      | Timing of nail change in relation to cancer | Cutaneous manifestations                                                                 |
|-------------------------------|------------|-----|-----------|------------|-----------------------------|-------|------------|--------------------------------|----------------------------------|------------------------------------|------------------------------------------|------------------------------------------------------------------------------------------|
| Hara et al. [18]              | 54         | M   | III       | Japanese   | Cutaneous SCC of the lower leg | Not specified | Not specified | Cutaneous SCC excision | All fingernails and toenails | Distal onycholysis. Subungual hyperkeratosis and paronychial erythema | 3 months prior | Scaling, erythematous plaques on nose, ears, trunk and proximal limbs. Erythematous, thick hyperkeratosis with deep fissures of thenar areas, soles, and palms. Verrucous and alopecic areas of the scalp |
| Laccourreye et al. [19]       | 62         | M   | Not specified | Not specified | Well-differentiated SCC of the pyriform sinus | Not specified | Distant metastasis | Unresectable. Palliative radiotherapy | Not specified | Paronychia and thickening of partly destroyed onycholytic nail | 6 months prior | Violaceous psoriasis and scaling of fingers. Swelling of finger with perungual acrokeratosis |
| Wareing et al. [20]           | 71         | M   | II        | Caucasian  | SCC of unknown primary origin | Not specified | Enlarged mediastinal nodes | Radiotherapy                                  | All finger and toenails                    | Fingernails and toenails                   | 18 months prior                  | Violaceous psoriasis scaling of fingers, lower shins and buttock. Hyperpigmentation over bridge of the nose |
| Sarkar et al. [21]            | 61         | M   | III       | White      | SCC of the L pyriform sinus | T-3, N-0, M-0 | No                | Total laryngectomy, partial pharyngectomy, left radical neck dissection | All fingernails and toenails | Yellowish discoloration and periungual swelling | 5 years prior                              | Acral hyperkeratotic skin lesions and squamous skin lesions at elbows, hands and feet. Painful fissures and scales on heels |
| Mutasim et al. [22]           | 67         | M   | VI        | Black      | Moderately differentiated SCC of the larynx and vocal cords | Not specified | Not specified | Total laryngectomy, R-1 radical neck dissection, and L modified radical neck dissection | Majority of fingernails and toenails | Loss of the cuticles, swelling of the nail folds, subungual hyperkeratosis, transverse and longitudinal ridging with nail loss | Few weeks prior                                | Hemorrhagic weals of dorsal fingers, hands, feet, ankles, and knees. Erythematous/scaly fissured papules and plaques on palmar hands and fingers. Dry, erythematous swelling of the nose and ears |
| Hsu et al. [23]               | 63         | M   | IV        | Not specified | Adenocarcinoma of colon | Stage B1 | No | Low anterior resection | All toenails only | Dystrophic toenails and subungual hyperkeratosis | 1 month prior                               | Pruritic lesions and vesicles on both feet. Dense scale of palms and soles, with fissures on feet. Similar skin lesions on both ears |
| Buxtorf et al. [24]           | 58         | M   | Not specified | Not specified | Low-differentiated SCC of the larynx | T-2, N-1, M-0 | No | Chemotherapy and radiotherapy | All fingernails and toenails | Subungual hyperkeratosis and onycholysis | 4 months prior                                | Scleroderma, violaceous plaques on ears and tip of nose with hyperkeratosis of toes and fingers |
| Gill et al. [25]              | 59         | M   | Not specified | Not specified | SCC of the L pyriform fossa | Not specified | Not specified | Not specified | Majority of fingernails and toenails | Nail dystrophy, thickened, and friable | 4 months prior                                | Tense bullae on lateral feet with erythematous hyperkeratotic skin. Violaceous plaques of dorsum nose, outer elbows and R lateral lower leg |
| Chave et al. [26]             | 65         | M   | V         | Indian     | Well-differentiated thymic carcinoma | Stage B1 | Lung parenchyma and pleural metastases | Surgically debulked and radiation therapy | All toenails | Thickened and dystrophic | 2 months prior                                | Violaceous hyperkeratotic plaques on trunk and limbs |
| Rao et al. [27]               | 62         | M   | V         | Indian     | Adenocarcinoma of rectosigmoid junction | Not specified | Not specified | Not specified | A few nails of the hands and feet | Thickening and brownish discoloration of nail plates with subungual hyperkeratosis | 24 months prior                                | Hyperpigmented scaly papules and plaques over dorsum and palmoplantar surfaces of hands and feet. Thickening of phalanges and hyperkeratotic plaques on palms and soles. Hyperpigmented plaques and scaly on nasal dorsum and both ears |
| Valdivielso et al. [28]       | 64         | M   | III       | Not specified | SCC of the lung | Stage B1A (T-3, N-2, M-0) | No | Chemotherapy with carboplatin and paclitaxel | All fingernails and toenails | Longitudinal streaks, subungual hyperkeratosis, and onychomadesis | 2 months prior                                | Symmetrical and violaceous plaques on dorsum of fingers, hands and feet. Thickening of phalanges and hyperkeratotic plaques on palms and soles. Hyperpigmented plaques and scaly on nasal dorsum and both ears |

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| Author                  | Age, years | Sex   | Skin type | Race             | Cancer type                        | Stage      | Metastasis                     | Treatment                                                                 | Nails involved                                      | Nail changes                                                                                     | Timing of nail changes in relation to cancer | Cutaneous manifestations                                                                 |
|------------------------|------------|-------|-----------|------------------|------------------------------------|------------|---------------------------------|---------------------------------------------------------------------------|---------------------------------------------------|-----------------------------------------------------------------------------------------------|---------------------------------------------------|---------------------------------------------------------------------------------------------|
| Viteri et al. [29]     | 51         | M     | II        | Not specified    | Metastatic SCC of esophagus        | Not specified | Metastatic                     | Early death of pt                                                         | Not specified                                      | Nail detachment with subungual hyperkeratosis                                               | Simultaneously                        | Hyperkeratotic symmetrical lesions on palms, soles, groin, and scalp                           |
| Karabulut et al. [30]  | 57         | F     | Not specified | Not specified | Adenocarcinoma of the choledoche  | Not specified | Not specified                  | Refused further medical/surgical therapy                                 | Not specified                                      | Subungual hyperkeratosis and longitudinal ridging                                              | 2 months prior                          | Dusky red poikiloderma plaques, with fine scales on scaly, eyebrows, nasal radix, cheeks, auricular helices and genital areas; moderate hyperkeratosis on palms and soles |
| Sator et al. [31]      | 71         | M     | II        | Not specified    | Liposarcoma in the retroperitoneum| Not specified | Not specified                  | Two tumor extirpations and radiation therapy                              | All fingernails                                      | Yellowish discoloration and were slightly thickened                                           | 4 months post                          | Erythematous poikilodermatosus plaques on knuckles, fingernails, fingertips, palms, ears, elbows, and neck; diffuse reddening with telangiectatic changes in face and upper chest |
| Strobel et al. [32]    | 58         | M     | Not specified | Not specified | SCC of L upper lobe of lung       | Not specified | Cervical lymph node metastasis| Radical neck dissection and radiation therapy. Partial lung resection and radical hilar and mediastinal lymphadenectomy | Not specified                                      | Subungual hyperkeratosis with onycholyisis                                                     | Not specified                          | Poikiloderma dermatitis of the nose, helix of the ears, fingers and toes                       |
| Poligone et al. [33]   | 62         | M     | VI        | Black            | SCC of the esophagus              | Stage II   | No lymphadenopathy             | Localized radiation therapy with 5-fluorouracil and cisplatin              | Not specified                                      | Thickening with ridging                                                                        | 2 months prior                          | Hyperpigmented, erythematous plaques with scales on ears and dorsal surfaces of metacarpophalangeal, proximal interphalangeal, and distal interphalangeal joints of hands and feet |
| Taher et al. [10]      | 68         | F     | II        | Caucasian        | Invasive lobular carcinoma of the L breast | Not specified | Metastatic infiltration of the lungs, bones (cervical spine, femur, pelvis), and mediastinal lymph nodes | Mastectomy and radiation, Dactylarthropathy and epirubicin alpha            | Majority of fingernails and toenails                                                         | Simultaneously with recurrence                | Hyperkeratotic plaques and ulceration on dorsum of hands. Fissured, scaly plaques and papules on periorbital skin, nose, forehead, chin, and ears |
| Backet et al. [34]     | 63         | F     | III       | Korean            | Adenocarcinoma of colon           | T-3, N-1, M-0 | No                             | L hemicolectomy                                                          | Majority of fingernails and toenails                                                         | Onycholyisis                                                                                  | 1 month prior                          | Yellowish punctuate hyperkeratotic lesions on palms and soles                                |
| Medinica et al. [35]   | 50         | M     | IV        | White            | SCC of the esophagus              | Not specified | No                             | Esophageal resection, subtotal esophagectomy                              | All fingernails                                      | Yellowish, dystrophic, with subungual hyperkeratosis                                           | 3 months prior                          | Violaceous erythema, edema, and yellow crusts on nose, chin and antecubital fossae and boundary hyperkeratotic plaques on elbows and knees. Palmar and plantar regions with diffuse yellow hyperkeratotic changes and fissure |
| Crucitti et al. [36]   | 55         | M     | I         | White            | Adenocarcinoma of lung            | T-2, N-0, M-0 | No                             | Upper lobectomy                                                          | All fingernails and toenails                                                                      | Yellowish discoloration with onycholyisis                                                    | 3.5 years prior                         | Erythematous hyperkeratotic plaques on the periangual region                                   |
| Ljubenovic et al. [37] | 56         | M     | Not specified | Not specified   | Metastatic metastatic carcinoma   | Not specified | Yes                            | Patient died                                                              | Some finger and toenails                                                                             | Moderate dystrophic changes, unspecified                                            | 1 month prior                          | Hyperkeratotic skin changes on his palms, fingers, soles, tip of nose and earlobes              |
| Author | Age, years | Sex | Skin type | Race | Cancer type | Stage | Metastasis | Treatment | Nails involved | Nail changes | Timing of nail change in relation to cancer | Cutaneous manifestations |
|--------|------------|-----|-----------|------|-------------|-------|------------|-----------|---------------|-------------|------------------------------------------|------------------------|
| Santos-Silva et al. [38] | 61 | M | Caucasian | SCC on lateral border of the tongue | T-2, N-0, M-0 | No | | | | | | Ulcerations involving lips, buccal mucosa and tongue; Scales on dorsal surfaces of metacarpophalangeal and interphalangeal joints of hand; Mucosa of the glans penis exhibit diffuse red patches |
| Goto et al. [39] | 75 | M | Japanese | Hepatocellular carcinoma (HCC) | Not specified | Not specified | | | | | | | Thickenig of skin, erythroderma, erosions on lips, buccal mucosa and tongue. Scales on dorsal surfaces of metacarpophalangeal and interphalangeal joints of hand. |
| Zarrouk et al. [40] | 58 | F | African American | Small cell lung carcinoma | Not specified | Not specified | | | | | | | Thin hyperkeratotic plaques on hands and joints. Hyperpigmented plaques over dorsal arms and lower legs. |
| Rodriguez Jimenez et al. [41] | 73 | F | | SCC of the esophagus | Not specified | Not specified | | | | | | Violett, desquamative lesions on nose, auricular parotid, dorsum Hands, feet and toes. Symmetric palmar/plantar keratoderma, with latticework desquamation |
| Fleming et al. [42] | 70 | F | | Metastatic undifferentiated SCC (SCC), primary lesions not identified | Not specified | Not specified | | | | | | Painful, swollen, and erythematous plaques with scale on dorsal surface. Fine scale in the corneal bowls, antihelix and left ear lobule |
| Grivas et al. [43] | 60 | M | | Basaloid SCC of the supraglottic region | Not specified | Not specified | | | | | | Hyperkeratotic, erythematous and hyperpigmented papules/plaques on chest, back, bilateral palms and arms. |
| Robert et al. [44] | 73 | F | | Gastric adenocarcinoma | Not specified | Ovarian metastases | | | | | | Hyperkeratotic erythematous plaques on bilateral palms and soles |
| Amano et al. [45] | 82 | M | Japanese | R lung (SCC), hx of tongue, and gastric cancer | Not specified | | | | | | | Scales hyperpigmented plaques on bilateral hands and perinasal skin of fingers, with fissuring. Bilateral planar feet de monstrates hyperkeratosis. Xerotic scaling and excoriations on bilateral upper arms, lower legs, and lower back |
| Squires et al. [46] | 56 | F | | Cervical SCC | Not specified | FGFR3 stage IIB | | | | | | | |
| Vatandoust et al. [47] | 69 | M | | Metastatic cutaneous SCC of the forearm | Not specified | | Excision, exsanguination and 5-fluorouracil | | | | Hyperkeratotic and desquamation |
| Zhao et al. [48] | 83 | M | | Pulmonary adenocarcinoma of R lower lobe with local metastatic nodes | Not specified | | Gefitinib tablet 250 mg | | | | Infiltrative erythematous plaques with scales on nose, cheeks, ears and dorsa of interphalangeal joints. Erythema covered with yellow thick crust on knees |

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Methods

The PubMed database was reviewed for the keywords "Bazex Syndrome and nail," "Acrokeratosis paraneoplastica and nail," "Acrokeratosis paraneoplastica," and "Bazex Syndrome." The search was limited to articles in the English language published between January 1, 1972, and July 15, 2020. In the initial search, 103 articles were identified and 36 were excluded because they did not pertain to acrokeratosis paraneoplastica, leaving 67. Of the 67 remaining articles, 19 did not report any nail changes, leaving a total of 48 articles for final analysis. Cases were analyzed for age, gender, Fitzpatrick skin type, race, primary cancer type, cancer staging, presence of metastasis, and cutaneous findings. Fitzpatrick skin type was determined by examining photos in the articles and using the article's description of the patient's skin. Tumor type was determined by examining the article's description of the primary tumor. The timing of nail changes was determined by examining the article's description of when nail changes occurred relative to cancer.

Table 1 (continued)

| Author          | Age, years | Sex | Skin type | Race | Cancer type                      | Stage | Metastasis | Treatment          | Nails involved | Nail changes                                           | Timing of nail changes in relation to cancer | Cutaneous manifestations                                      |
|-----------------|------------|-----|-----------|------|----------------------------------|-------|------------|---------------------|----------------|-------------------------------------------------------|-------------------------------------------------------------|------------------------------------------------------------------------------------------------|
| Shikino et al.  | 84         | M   | III       | Not specified | Not specified | Poorly differentiated laryngeal SCC | T-4a, N-2c, M-0 | No | Radiation therapy | All fingernails | Yellow discoloration and proximal detachment | 2 months prior | Symmetric hyperkeratotic plaques of distal hands and feet. Vulvar desquamation on ears and nose |
| Adelman et al.  | 56         | F   | II        | Not specified | Not specified | Poorly differentiated laryngeal SCC | T-2, N-2c, M-0 | No | Chemoradiation with cisplatin | All finger and toenails | Ridging of nail beds and lifting of nails | 2 months post | Sclerodermatosus plaques of finger and toe. Dry gangrene of distal third digit |
| Dabas et al.    | 50         | M   | V         | Not specified | Not specified | Poorly differentiated SCC of base of the tongue | T-2, N-2c, M-1 | None, patient died | Chemotherapy        | All finger and toenails | Subungual hyperkeratosis, yellowish discoloration and thickening | 5 weeks prior | Symmetrical lichenoid scaly plaques on ears, and dorsum of hands |
| Mitriloc et al. | 72         | F   | III       | Not specified | Not specified | NSCLC | Not specified | Resection of the R upper lung lobe. Declined adjuvant chemotherapy | All finger and toenails | Thickened with longitudinal ridging and yellow discoloration | 4 months prior | Hyperkeratotic and fissured erythematous plaques on bilateral plantar surfaces and lateral digits. Mild scaling on livers |

NSCLC, non-small-cell lung carcinoma; SCC, squamous cell carcinoma.
the Fitzpatrick classification guidelines [5]. If photos or descriptions of the patient’s skin type were unavailable or photos were black and white, they were recorded as not specified.

**Results**

There were 48 cases of acrokeratosis paraneoplastica with nail changes included in the final analysis. Demographics and case findings are shown in Table 1. Of these patients, 25% were female, with a mean age of 62.5 years (range 41–84 years). Fifteen patients (31%) were classified as Fitzpatrick skin type I–II, 13 patients (27%) as type III–IV, eleven (23%) patients as type V–VI, and 9 patients (19%) not specified. Eleven patients (23%) were described as either Caucasian or White, 4 patients (8%) African American or Black, 7 patients (14%) Japanese, Korean, or Indian, and the races of 26 patients (55%) were not specified.

Primary malignancies were most often localized to the head and neck region (42%) and were most commonly squamous cell carcinomas (SCCs) of the esophagus. SCCs of the larynx, tongue, and oropharynx were also common forms of malignancies within the head and neck region. The lung was the second most common site of malignancy (21%), with mostly SCCs (6 patients). Gastrointestinal carcinomas represented 12% of the cases, most commonly adenocarcinomas. Genitourinary, cutaneous, breast, and thymic carcinomas were also reported as primary malignancies. Approximately 8% of the cases involved carcinomas were of indeterminate origin (Table 2). Metastases were present in 22 cases (46%), not present in 12 cases (25%), and not specified in 14 (29%) cases.

Nail changes in acrokeratosis paraneoplastica patients were nonspecific and varied (Table 3). The most common nail findings were nail plate thickening (35%), subungual hyperkeratosis (31%), yellow/brown nail plate discoloration (27%), onycholysis (27%), longitudinal ridging
(25%), and loss or destruction of the nail plate (13%) (Fig. 1, 2). Paronychia was seen in 6% of the cases, often causing pain. Many patients had 2 or more nail findings concurrently; nail plate thickening and subungual hyperkeratosis were most common. Approximately, 79% of the patients had nail findings prior to cancer diagnosis, with onychodystrophies on average presenting in the preceding 10 months. In about 10% of the patients, nail changes occurred following malignancy diagnosis with an average of 14 months post-diagnosis. Nail findings presented concurrently with the diagnosis of cancer in about 6% of the cases, and the timing of nail findings were not specified in 5% of the cases. The majority of fingernails and toenails were involved in all cases except for one in which the onychodystrophy was limited to one fingernail.

Discussion

In our review of 48 cases of acrokeratosis paraneoplastica with nail findings, 36 patients (75%) were males, with a mean age of 62.5 years, and the majority of patients were either Caucasian or White (23%). The majority of patients were of Fitzpatrick skin type I–II (31%), followed by skin type III–IV (27%), and skin type V–VI (23%). Our findings are consistent with those of Bolognia et al. [1], who reviewed 93 cases of acrokeratosis paraneoplastica (with and without nails findings) and reported that 89/93 patients were males (96%) with a mean age of 60 ± 8.5 years. In a more recent review on Bazex syndrome (not nail specific) by Räßler et al. [6], 54/70 (77%) patients were males, with mean ages of 65 and 62 years for patients with nail findings and no nail findings, respectively.

In our study of Bazex patients with nail findings, malignancies were most commonly localized to the head and neck (44%), followed by the lung (21%), and gastrointestinal tract (12%). In addition, metastatic anaplastic tumors and SCCs of unknown primary origins accounted for 8% of the cases. Other types of carcinomas in our review included cervical SCC, transitional-cell carcinoma of the bladder, lobular carcinoma of the breast, liposarcoma, cutaneous SCCs, and thymic carcinoma. SCCs of the head and neck were also the most commonly reported underlying malignancies in Bazex syndrome, in patients with and without nail findings, in prior reviews. Bologna et al. [1] reported that 57/93 patients (61%) had SCC of the esophagus, larynx, or pharynx. Other common sites included the lung and the gastrointestinal tract. Räßler et al. [6] reported that 11/77 patients (14%) had a primary malignancy of the lung, 8/77 patients (11%) had adenocarcinoma of the gastrointestinal tract, and 6/77 cases (8%) had metastatic anaplastic tumors of unknown origins with lymph node metastases of occult carcinomas. There was a case of T-cell lymphoma [7] and a neuroendocrine tumor [8] in patients with acrokeratosis paraneoplastic; however, those patients did not present with any nail changes.

We found that nail changes presented at an average of 10 months prior to malignancy diagnosis for 79% of the Bazex patients. In 2 cases, nail changes presented simultaneously with carcinoma recurrence [9, 10]. Our nail data are consistent with those of Bologna et al. [1], who reported that in 63% of the Bazex patients, cutaneous manifestations preceded the diagnosis of malignancy, at an average time of 11 months. Nail findings typically appeared concurrently with the initial cutaneous manifestations; Bazex and Griffiths [4] described the cutaneous presentation of acrokeratosis paraneoplastica occurring in 3 stages. In the first stage, papulosquamous plaques present on the distal digits, nose, and ears, along with nail dystrophy [1, 4]. In the second stage, the papulosquamous plaques extend to the cheeks, palms, and soles. In the third stage, typically when metastases occur, the plaques spread to the elbows, knees, and dorsae of the hands and feet [1].

In our review, the most common nail changes were nail plate thickening, subungual hyperkeratosis, yellow or brown nail plate discoloration, onycholysis, longitudinal ridging, and loss or destruction of nail plate. Presentation with 2 or more nail changes simultaneously was frequent. Paronychia, while less common than some of the other nail findings, is an important source of morbidity in these patients. Bologna et al. [1] reported on similar nail findings associated with acrokeratosis paraneoplastica as in our study; less common nail changes were macerated nails, atrophy, slow growth, and nail plate loss.

Our review is subject to several limitations. Due to the rarity of Bazex Syndrome, there were only 48 cases with associated nail findings published. In some case reports, photograph quality was insufficient to characterize specific nail changes, and/or detailed descriptions of nail findings and digits affected were lacking. Patient demographics were not reported in some cases, and Fitzpatrick skin types were not discernible for others.

A broad variety of nail findings are associated with acrokeratosis paraneoplastica, with many patients presenting with more than one type of onychodystrophy. The changes often affected most or all nails and presented concurrently with cutaneous findings. No nail changes were diagnostic or specific. The presence of subungual...
hyperkeratosis, onycholysis, nail plate thickening, longitudinal ridging, onychomadesis, yellow or brown nail plate discoloration, paronychia, nail plate loss and less common changes such as horizontal ridging, onychomycosis, atrophy, clubbing, pitting, and fissuring involving most or all nails should raise suspicion for acrokeratosis paraneoplastica, especially accompanied by the characteristic cutaneous lesions. When a patient presents with papulosquamous plaques on the skin accompanied by nail dystrophy, psoriasis is an important diagnostic consideration. Nail clippings and/or cultures may be performed to rule out other nail conditions in the differential diagnosis, such as onychomycosis or nail psoriasis. In the absence of hyphae, infiltration of neutrophils, and subungual hyperkeratosis in nail plate clippings, dermatologists should be prompted to perform a thorough review of systems, physical examination with palpation of lymph nodes, and referral to primary care for age appropriate malignancy screening and further testing if dictated by physical findings. Since nail changes typically present almost a year prior to diagnosis of malignancy, careful examination of the nails, hands, and digits and appropriate malignancy workup may be lifesaving. In addition, nail alterations in patients with acrokeratosis paraneoplastica should be monitored closely, since onychodystrophies may present during disease recurrence.

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