Case Report

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Non-Small Cell Lung Cancer – A Case of the Bazex

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ABSTRACT

Bazex syndrome is a rare form of paraneoplastic syndrome, rarely identified as an underlying cancer at presentation. Predominately found in upper aero-digestive cancers and squamous cell lung carcinomas. Plaques on acral surfaces are common, described as psoriatic, often resolve after underlying anti-cancer therapy. This case presents a 76-year-old male with squamous cell non-small cell lung cancer suffering psoriatic lesions which respond chemotherapy and immunotherapy.

Keywords: Lung Cancer; Bazez Syndrome; Immunotherapy; Chemotherapy

Introduction

Bazex syndrome is a paraneoplastic psoriasiform dermatitis, predominately seen in squamous cell carcinomas (SCC) of aero-digestive tract and non-small cell lung cancers (Räßler, et al. [1]). Lesions are seen mainly in adult males (>60 years old (YO)) >3:1 woman, with an alcohol and smoking history noted in 28% of cases noted to be alcohol and smoking (Räßler, et al. [1]). Clinically, lesions may be erythematous, scaling and appear psoriatic like, which may lead to a delayed diagnosis of cancer while benign skin causes are treated (Räßler, Goetze & Elsner, 2017). Acral lesions may be considered pathognomonic of BAK upon confirmation of carcinoma with common distribution of lesions on: ears (79% & 28%), nails (75% & 57%), nose (63% & 33%), fingers (61% & 29%), hands (57% & 38%), feet (50% & 30%) and less commonly the trunk (13% & n/a), scalp (7% & n/a), elbows (19% & n/a) and cheeks (19% & n/a) (Räßler, et al. [1]). Treatment of the underlying cancer has been found to successfully treat the skin lesions when therapy is established with cases noting response to NSCLC BAK syndrome lesions after chemotherapy, immunotherapy and surgical intervention (Table 1) (Mititelu, et al. [2-4]). The current case reports BAK syndrome in a 76-year-old male following a delayed diagnosis and details his diagnosis and treatment journey to date while he remains on current active first line management. Within the report is a brief review of the lung cancer cases and BAK syndrome, showing literature available via Medline and Pub med from 2011-2021 in the English language using the search term ((Bazex) OR (acrokeratosis)) AND (Title Combined: (lung cancer OR carcinoma)).

Consent

Consent was obtained to use images in relation to this report, identifiers are anonymised and no patient personal information is used within this article.

Time line

December 2020 – January 2023.

Patient Presentation

76-year-old retired white British male presented with 6-month history of psoriatic like plaques on fingers and toes bi-laterally, progressing to the scalp and torso, with >10% weight loss and progressing breathlessness two weeks prior to diagnosis. He has a >40 pack year smoking history and a past medical history of chronic obstructive pulmonary disease (COPD) and hypertension, taking medicines; amlodipine 5mg, acitetin 20mg, atrovastatin 10mg nocte, furosemide 40mg mane, aspirin 75mg, tiotropium 10mcg mane and salbutamol inhaled 100mcg/dose, with no known drug allergies. No family history of Bazex acrokeratosis neoplastica syndrome or lung cancer was present.

Delayed Diagnosis

Initial treatment for scaling dermatosis was initiated by the community doctor with dermol 500 and dermovate cream, which gained no symptomatic benefit over a 6-month period March – September, later given acitetin 20mg with no continued benefit. New shortness of breath triggered a chest x-ray via the community GP which highlighted a supraclavicular mass and a right hilar mass, leading to a two week wait for suspected cancer.

Diagnostics

A computer topography (CT) and a positron emission topography CT scan (PET-CT) confirmed stage 3b lung cancer, with a 7cm mass in the right lower lobe with atelectasis and right upper lobe nodal lesion with a 4cm supraclavicular lesion and a paratracheal node at 3.5cm, confirmed as avid on a positron CT scan. The supraclavicular node was biopsied showing a squamous cell carcinoma with a programmed death ligand -1 as 10% and no actionable mutations, next generation sequencing was not performed.

Stage

T4N3M0 – 3b (Matilla et al. [5]).

Examination

The examination took place prior to cycle one of chemo/immunotherapy, or any anti-cancer treatment on the same day. Comparison over treatment will be detailed in the discussion. Over all the patient was comfortable at rest, with no mobility aids, no oxygen, no indwelling catheters or lines in-situ. The end of bed assessment clearly identified plaques upon finger nails bi-laterally.

Lung Exam

No additional berthing sounds identified, with good air expansion. Saturation was 96% on room air with a respiration rate of 16 breaths per minute at rest.

Heart Exam

No additional sounds or murmurs were identified, with a pulse rate of 58 beats per minute regular and a blood pressure of 103/53.

Abdominal Exam

A single plaque identified in the epigastric area, no scars where noted, with no masses, a soft abdomen on palpation and bowel sounds throughout.

Hands

Plaques (pre-treatment) noted on finger nails bi-laterally, crusting and yellow with thickened perioncychium and mild palm erythema bi-laterally.

Toe nails

Equally to fingers, yellow scaling plaques bi-laterally were noted with erythematous cracks on the heels bi-laterally.

Other

Three lesions were noted on the scalp and one on post oracular on the left side.

Treatment

Triple therapy was initialised based on squamous metastatic NSCLC with a PDL-1 of 10%, given Carboplatin, Paclitaxel and Pembrolizumab was administered in four cycles, following which, Pembrolizumab immunotherapy continued as a single agent treatment (Paz-Ares et al. [6]). Radiotherapy 20 grey in 5 fractions was given to reduced paratracheal mass, with continued Pembrolizumab to 10 cycles before progressive disease n mediastinum and superior vena cava obstruction, before patient died of progressive disease. Scans performed every 3 months measured with iRECIST criteria (Persigehl, et al. [7]), with best outcome partial response (PR) to treatment and an overall time to progression of 10 months from start of treatment.

Discussion

Delayed diagnosis of BAK syndrome may prolong ant-cancer treatment leading to diagnosis at a later stage, limiting treatment options for patients, which parallels the current case who waited 6 months from the onset of plaque lesions to diagnosis of lung cancer (Zarzour, et al. [8]) noted death of a small cell lung cancer patient 6 months following diagnosis despite a 2-year history of hyper pigmented rash over forearms and legs, diagnosed as BAK syndrome (Räßler, et al. [1,8]). Similarly, an epidermal growth factor receptor mutation (EGFR) was diagnosed with metastatic bone lesions after a 5 year history of pruritic, acral lesions, suggesting earlier recognition may of allowed lower diagnostic stage (Zhao et al. [8]). The current case noted a 6 month delay pre-treatment, leading to a diagnosis of 3b NSCLC with supraclavicular lymph node spread, meaning an advanced stage of lung cancer untreatable to radical surgery or radiation, giving a poor prognosis with systemic treatment, although the current treatment regime of chemotherapy combined immunotherapy may lead to prolonged survival (Matilla, et al. [5,6]). Psoriatic lesions occurred in the current case on the hands, feet, nose, nails, auricular helices and scalp in the current case, with a lesion on the trunk suggesting advanced carcinoma correlation (Bazex, et al. [9]). Typically the lesions will respond (Table 1) to anti-cancer therapy as was the case here, the individual who failed to respond died within 6 months of diagnosis, and unusually had SCLC (Zarzour, et al. [8]).

Table 1: Table showing similar cases in lung cancer after a search of Pub med and Medline with the search term '' ((Bazex) OR (acrokeratosis)) AND (Title Combined:(lung cancer OR carcinoma))'' year 2011- 2021, English language. N=No, Y= Yes, M= Male, F-Female, NSCLC= Non-small cell lung cancer, SCLC+ Small cell lung cancer, N/a = Not applicable.

Cases	Cancer	Age &Gender	Smoker Y/N	Lesion/plaques	BAK symptom treatment	Symptom relief Y/N	Plaque resolution with anti-cancer therapy Y/N
Mititelu & Powell, 2019	NSCLC No cell type	72F	Y	Fingers/ toes, Hands, knees	Acitertin Methotrexate	N	Y - surgery
Aoshima et al., 2019	NSCLC adenocarcinoma	69M	Y	Fingers, Ears	No	N/a	Y- Pembrolizumab
Zhao et al., 2016	NSCLC adenocarcinoma	83M	Y	Nose, cheeks, ears, knees, hands, feet, fingers	Topical corticosteroid Oral retinoids	N	Y-Gefitinib
Zarzour, Singh, Andea & Cafardi, 2011	SCLC	58F	Y	Hands, feet, nails, arms and legs, minimal nose.	Topical corticosteroid Oral corticosteroid Hydroxychloroquine	N	N- Chemotherapy
Amano et al., 2016	NSCLC Squamous	82M	Y	Trunk, pams and soles	Topical corticosteroids	N	Y- Surgery
Current	NSLCL Squamous	72M	Y	Fingers, toes, scalp, ear & sternum	Dermol 500 Dermovate cream Acitetin 20mg	N	Y- Carbopltin Pemetrexed and Pembrolizumab

Previous cases have shown symptomatic benefit from adjuvant treatment with acitretin, used to treat severe psoriasis, at 0.25-1mg/kg body weight (Bazex, et al. [4,10]). The current case has shown how Pembrolizumab combined with chemotherapy therapy in advanced/metastatic NSCLC (Paz-Ares, et al. [6]), may reduce plaques in BAK syndrome (Figures 1A-a & 1B-b) which is paralleled by (Aoshima, et al. [2]), who showed a improvement in the distal extremities after 7 cycles of Pembrolizumab. Pathophysiology of BAK syndrome may be related to cross reactivity of tumour antigens irritating the skin, growth factors associated with epidermal growth factor and vitamin deficiency such as Zinc and vitamin A (Amanon, et al. [4,11]) Showed serum immunoglobulin e and eosinophil count elevated in an 82 YO SCC of the lung, with reduced levels after tumour removal, suggesting a role of the Th2-type cytokine response leading to an elevated inflammation, which may cross react causing keratin based skin plaques seen in BAK syndrome, although reactive response to the subcutaneous cancer itself could not be ruled out as well as raised inflammation as a result of patients positive smoking status. The current case survived approximately 12 months post treatment with chemotherapy and pembrolizumab, compared to 15.9 months in the literature for NSCLC SCC patients (Paz-Ares, et al [6,12]). Diagnosis in the current case was on observation capacity, failure to resond to anti-psoriatic medication and response to anti-cancer therapy, although none biopsy may be a limitation here.

Further limitations are a lack of tracked biomarkers throughout treatment, with immunoglobulin E, also not detailed, as suggested to be raised in BAK syndrome by (Amanon, et al. [4,13,14]). Take home messages from the current case highlight that BAK syndrome in SCC NSCLC can be successfully treated with combine chemotherapy and immunotherapy, with lesion/plaque regression corresponding to successful anti-cancer treatment, although the patient did die of advanced NSCLC. Plaques in BAK syndrome are not commonly responsive to psoriatic therapy, and a smoker with a resistant history of psoriatic lesion treatment should be considered for an upper digestive or lung cancer diagnosis to rule out an underlying malignancy (Moore, et al. [15]).

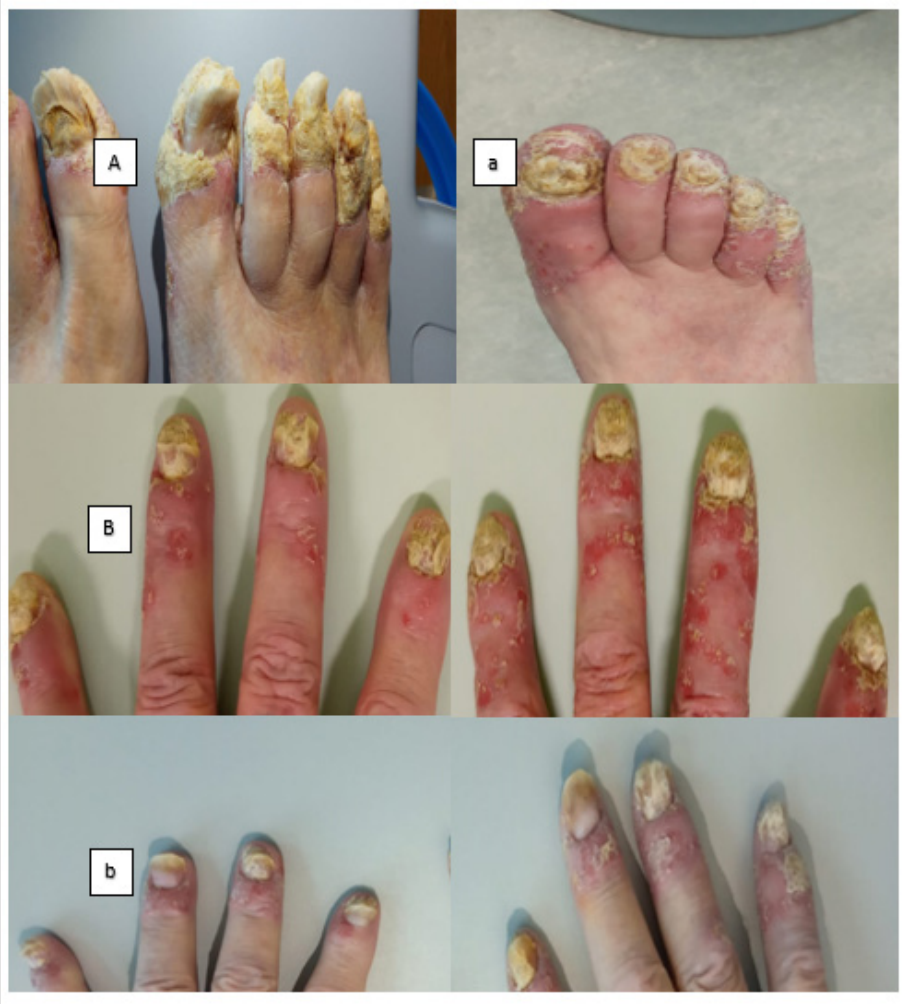

Figure 1: Acral lesions (A & B December 2020, a & b April 2021), predominating on the nails of the hands and feet, noted after 6 cycles of Carboplatin, paclitaxel and pembrolizumab.

Competing Interests

No competing interests.

Ethics Approval

Ethical guidelines were followed, with written consent obtained for images.

De-Identification

All information remains anonymized.

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