Acne keloidalis nuchae and hypertension in black subjects: a case–control study

Bayaki Saka1*, Julienne Noude Teclessou2, Sefako Abla Akakpo1, Soulemane Pessinaba3, Piham Gnossike4, Garba Mahamadou1, Panawé Kassang1, Abas Mouhari-Toure5, Koussake Kombate2 and Palokinam Pitché1

Abstract

Objective: The aim of this case–control study was to look for an association between hypertension and acne keloidalis nuchae (AKN) in black subjects.

Results: We recruited 303 consenting subjects comprising 101 patients with AKN and 202 controls, case-matched by age (±5 years). The mean patients age was 34.9±10.7 years versus 35.6±11.2 years for controls. The average duration of AKN progression in cases prior to consultation was 1831 days (5 years). The most frequently observed AKN lesions were papules (73/101; 72.3%), fibrous scars (42/101; 41.6%) and folliculitis/pustules (41/101; 40.6%). In terms of quality of life, the mean score of dermatology life quality index was 8.3±5.2 (extremes: 0 to 22). In multivariate analysis, having a BMI of 25 kg/m² or more (OR = 4.91; p < 0.001) and having systolic hypertension (OR = 1.22; p = 0.010) were associated with AKN.

Keywords: AKN, Hypertension, Black subject

Introduction

Acne keloidalis nuchae (AKN) is a chronic scarring folliculitis observed mainly in men of African descent [1, 2]. Contributing factors appear to be varied and involve androgens, inflammation, infections, trauma, genetics and ingrown hairs [3]. Piecemeal data suggest a possible relationship between hypertension and AKN [1, 4]. Verma and Wollina already reported one case of AKN associated with hypertension in 2010 [4]. In addition, hypertensive patients are 6.75 times more likely to have extraoccipital/extra-nuchal lesions than non-hypertensive patients [1]. Given that AKN mainly affects men of African descent [1, 2], and that hypertension is more frequent and more severe in black subjects than in Caucasian subjects [5], is there a link between hypertension and AKN? We therefore conducted a case–control study to look for a possible association between hypertension and AKN in the black subject.

Main text

Method

We conducted a case–control study from January to December 2018 in three dermatology departments (CHU Sylvanus Olympio, CHU campus and Gbossier centre) in Lomé, Togo. Cases were male patients, over 18 years of age, seen in dermatology for AKN located at the neck and/or extending to other parts of the scalp. For the controls, any lesion suggestive of AKN (papular, pustular, hypertrophic or keloid lesion) of the neck was a non-inclusion criteria. Each case was matched with two controls per age (±5 years). Cases were recruited at outpatients dermatological clinics and controls recruited at outpatients dermatological clinics and then in other hospital departments. The recruitment was consecutive and comprehensive. The questionnaire used for general and dermatological examination was developed for this study (Additional file 1), and was the same for both cases.
and controls, except for the part concerning AKN. Each case and control was subjected to a general examination (including blood pressure measurement) and dermatological examination. Blood pressure was taken using a cuff and needle manometer by auscultatory method on a seated subject. We defined systolic hypertension as systolic blood pressure $\geq 140$ mmHg and diastolic hypertension as diastolic blood pressure $\geq 90$ mmHg at two separate consecutive visits, two weeks apart. For defining hypertension, participants were brought back for a second visit to the clinic (either for dermat follow-up or specifically for blood pressure measurement). In both cases and controls, we excluded known hypertensive subjects under treatment, even if, blood pressure is normal (because if they’re on antihypertensive drugs, it’s because they have hypertension, and that would be a selection bias). We also did not include patients undergoing treatment (history of intra-leaved corticosteroid injections) which could influence blood pressure. Also, between the first and second visit, topical steroids or IL-1 steroids to treat AKN were not used in order to not affect blood pressure. For cases, in addition to the general and dermatological examination, quality of life (QOL) was assessed according to the Dermatology Life Quality Index (DLQI) [6], with a total score between 0 and 30. A DLQI score less than or equal to 1 reflected no effect of AKN on the patient’s QOL, a score between 2 and 5 reflected a small effect, a score between 6 and 10 reflected moderate effect, a score between 11 and 20 reflected a large effect, and finally a score between 21 and 30 reflected an extremely large effect on the patient’s QOL.

**Statistical analysis**

The questionnaires were entered using EPIDATA software version 3.1. Descriptive statistics were conducted and the results presented in the form of frequency and percentage tables for the qualitative variables. Quantitative variables were presented as means (± standard deviation). Comparisons of means were made using the Student’s test for matched samples and qualitative variables with the McNemar test. These tests made it possible to study the existence of statistical links between the factors considered and the AKN. Conditional logistic regression was used to identify the factors associated with AKN. Factors with a value of $p < 0.20$ in univariate analysis were taken into account for the multivariate model with a significance level of 5%. All analyses were performed using R® software.

**Results**

We recruited 303 consenting subjects comprising 101 patients with AKN and 202 controls. The mean patients age was $34.9 \pm 10.7$ years versus $35.6 \pm 11.2$ years for controls. The average duration of AKN progression in cases prior to consultation was 1831 days (5 years). The most frequently observed AKN lesions were papules (73/101; 72.3%), fibrous scars (42/101; 41.6%) and folliculitis/pustules (41/101; 40.6%) (Table 1). We found other lesions associated with AKN such as acne (29 cases; 28.7%), pubic folliculitis (13 cases; 12.9%) and folliculitis of the axillary hollows (4 cases; 4%). In terms of quality of life, the mean score of DLQI was $8.3 \pm 5.2$ (extremes: 0 to 22). Almost all patients (99/101; 98%) had an altered QOL. More than half of the patients (60/101; 59.5%) had mild to moderate changes in their QOL and more than a third (39/101; 38.6%) had significant or very significant changes in their QOL.

In univariate analysis, having a BMI of $25 \text{ kg/m}^2$ and above was associated with the risk of AKN ($p < 0.001$). Systolic hypertension ($\geq 140$ mmHg) was present in 33.7% of cases versus 7.9% of controls ($p = 0.009$). Diastolic hypertension ($\geq 90$ mmHg) was present in 33.7% of cases versus 29.2% of controls ($p = 0.461$) (Table 2).

In multivariate analysis, adjusted for other variables, having a BMI of $25 \text{ kg/m}^2$ or more (OR = 4.91; $p < 0.001$) and having systolic hypertension (OR = 1.22; $p = 0.010$) were associated with AKN (Table 3).

**Discussion**

The frequency of AKN and the difficulty of their management are arguments for researching the factors associated with these conditions, in order to prevent them if possible. It is a condition that so impairs the QOL of patients who suffer from it [3, 7], as in our study where almost all patients had an impairment in their QOL. We evaluated the association between hypertension and AKN in 101 patients compared to 202 matched controls. Our study is the first of its kind, to our knowledge, involving two groups matched with untreated patients in an African country where the prevalence of hypertension and AKN are relatively high. By matching

| Lesions observed in 101 patients | Number | % |
|--------------------------------|--------|---|
| Papules                        | 73     | 72.2 |
| Fibrous scars                  | 42     | 41.5 |
| Folliculitis/pustules          | 41     | 40.6 |
| Keloids scars                  | 30     | 29.7 |
| Ulceration                     | 29     | 28.7 |
| Nodules                        | 21     | 20.8 |
| Alopecia                       | 12     | 11.9 |
| Pus                            | 9      | 8.9 |
| Atrophic scars                 | 7      | 6.9 |
In our study, not only were mean systolic (p < 0.001) and diastolic (p = 0.001) arterial pressures higher in cases than controls, the calculation of the odds ratio shows an association between systolic hypertension and the presence of AKN. Furthermore, the risk of AKN increases with BMI, as shown by the OR, which was 4.91 in overweight or obese subjects (BMI ≥ 25 kg/m²). Although high BMI is thought to be a mechanical risk factor for AKN (more folds in the occipital region, more risk of incarceration), it is a risk factor for high blood pressure. Our study therefore confirms that there is an association between AKN and systolic hypertension, as previously suggested by other authors [1, 4]. Although AKN and keloids do not have the same physiopathology, stage 3 of AKN leads to keloid formation according to the classification of Mahé et al. [8]. With regard to keloids, while some studies have found no association with hypertension [9], others have shown that hypertension is associated with their development, with both occurring more frequently in people of African descent than in Caucasians [10, 11]. Patients with keloid disorders are more likely to have concomitant hypertension than patients without keloid disorders [12]. There is an interaction between these factors that may be mediated by an alteration in the ratio of metalloproteinase-1 matrix to tissue inhibitor of metalloproteinase-1 (MMP-1/TIMP-1) that promotes the deposition of extracellular matrix. Endothelial dysfunction, which also occurs in high blood pressure, may also be involved in the pathogenesis of keloid disorders [13]. In addition, activation of the renin-angiotensin system is known to cause angiotensin II-induced arterial vasoconstriction resulting in elevated blood pressure. Similarly, the association between the renin-angiotensin system and tissue fibrosis is well documented [14, 15]. The mechanism highlighting the association between renin-angiotensin system activity and fibrosis is thought to be an increased expression of growth factor (TGF-1) caused by angiotensin II, which plays a central role in fibrogenesis [16]. This role of angiotensin II in both hypertension and fibrogenesis may also partly explain the significant association between hypertension and AKN. For example, improvement of keloid lesions in hypertensive patients has been observed

| Table 2 Comparisons of measured variables and calculation of odds ratio: in univariate analysis |
|-----------------------------------------------|-----------------------------------------------|-----------------------------------------------|
| Variables                                     | Cases (n = 101)                               | Controls (n = 202)                            | p-value                                      |
| Mean age (years) ± standard deviation         | 34.91 ± 10.7                                  | 35.62 ± 11.2                                 | NC                                           |
| Mean BMI (kg/m²) ± standard deviation         | 27.0 ± 4.5                                    | 23.7 ± 2.9                                   | < 0.001 T                                    |
| Mean systolic blood pressure (mmHg) ± standard deviation | 126.7 ± 22.50 | 115.7 ± 14.24 | < 0.001 T                                    |
| Mean diastolic blood pressure (mmHg) ± standard deviation | 83.07 ± 15.86 | 75.74 ± 13.06 | 0.001 T                                      |
| BMI (kg/m²), n (%)                            |                                              |                                              |                                              |
| < 25                                          | 36 (35.6)                                     | 147 (72.8)                                   |                                              |
| ≥ 25                                          | 65 (64.4)                                     | 55 (27.2)                                    | < 0.001 a                                    |
| Blood pressure, n (%)                         |                                              |                                              |                                              |
| Systolic hypertension                         |                                              |                                              |                                              |
| No                                            | 77 (76.2)                                     | 186 (92.1)                                   | 0.009 a                                      |
| Yes                                           | 24 (23.8)                                     | 16 (7.9)                                     |                                              |
| Diastolic hypertension                        |                                              |                                              |                                              |
| No                                            | 67 (66.3)                                     | 143 (70.8)                                   | 0.461 a                                      |
| Yes                                           | 34 (33.7)                                     | 59 (29.2)                                    |                                              |

| Table 3 Association between AKN and hypertension in black subjects; conditional logistic model (N = 303) |
|---------------------------------------------------------------|---------------------------------------------------------------|---------------------------------------------------------------|
| Multivariate analysis                                         | Multivariate analysis                                         | Multivariate analysis                                         |
| aOR                                                          | 95% for a OR                                                  | p-value                                                      |
|---------------------------------------------------------------|---------------------------------------------------------------|---------------------------------------------------------------|
| BMI (kg/m²)                                                   |                                                              |                                                              |
| < 25                                                          | 1                                                             | –                                                            |
| ≥ 25                                                          | 4.91 [2.96–8.28]                                              | < 0.001                                                      |
| Systolic hypertension                                         |                                                              |                                                              |
| No                                                            | 1                                                             | –                                                            |
| Yes                                                           | 1.22 [1.10–3.11]                                              | 0.010                                                        |
| Diastolic hypertension                                        |                                                              |                                                              |
| No                                                            | 1                                                             | –                                                            |
| Yes                                                           | 0.84 [0.75–1.36]                                              | 0.574                                                        |
after treatment with antihypertensive drugs, such as calcium channel blockers and angiotensin converting enzyme inhibitors [17, 18]. However, we didn’t find a pathogenic explanation between AKN without keloids (stages 1, 2) and hypertension.

Limitations of study
The main limitation of this study is that, we have not evaluate the association between, AKN severity and hypertension, because of the number of patients. Ideally, the link between the severity of AKN and hypertension should be assessed. A multicentre study to have a larger number of cases will be necessary to look for this link between AKN severity and hypertension. Secondly, we did not assess the quality of life in the controls to make a comparative study on this point.

Supplementary information
Supplementary information accompanies this paper at https://doi.org/10.1186/s13104-020-05274-0.

Abbreviations
AKN: acne keloidalis nuchae; BMI: body mass index; DLQI: dermatology life quality index; MMP: matrix metalloproteinase; QOL: quality of life; aOR: adjusted odds-ratio; TIMP: tissue inhibitors of metalloproteinases; TGF: transforming growth factor.

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Authors’ contributions
BS, JNT, SAA, GM, PP were responsible for the conception of the study, participated in the study design, undertook the field study, conducted the data collection, analysis and interpretation, and wrote the manuscript. They have revised and finalized the manuscript. BS, JNT, SAA, SP and PK were involved in the data collection, analysis and interpretation. They wrote and finalized the manuscript. AMT and KK were involved in data analysis and interpretation. All the authors were responsible for the overall scientific management of the study, for analysis and interpretation, and the preparation of the final manuscript. All authors read and approved the final manuscript.

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Availability of data and materials
All data generated or analysed during this study are included in this published article.

Ethics approval and consent to participate
This study was approved by the head of the dermatology department of the Sylvanus Olympio University Hospital (Ref No. 07/2017/DER/CHUSO). We obtained consent from patients that participated in the study. For each respondent, the objectives and benefits of participating in the survey and its conduct were clearly stated, as well as their right to interrupt the interview without justification. An informed consent form signed after the verbal explanation was made by the investigating officer in the language understood by the participant.

Consent to publish
Not applicable.

Competing interests
The authors declare that they have no competing interests.

Author details
1 Service de Dermatologie et IST, CHU Sylvanus Olympio, Université de Lomé, BP 30785, Lome, Togo. 2 Service de Dermatologie et IST, CHU Campus Université de Lomé, Lome, Togo. 3 Service de Cardiologie, CHU Campus Université de Lomé, Lome, Togo. 4 Centre National de Dermatologie de Gossiimé, Lome, Togo. 5 Service de dermatologie et IST, CHU Kara, Université de Kara, Kara, Togo.

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References.
1. East-Innis ADC, Stylianou K, Paolino A, Ho JD. Acne keloidalis nuchae: risk factors and associated disorders—a retrospective study. Int J Dermatol. 2017;56:828–32.
2. Alexis A, Heath CR, Halder RM. Folliculitis keloidalis nuchae and pseudo-folliculitis barbae: are prevention and effective treatment within reach? Dermatol Clin. 2014;32:183–91.
3. Ogunkbiyi A. Acne keloidalis nuchae: prevalence, impact, and management challenges. Clin Cosmet Investig Dermatol. 2016;9:483–9.
4. Verma SB, Wollina U. Acne keloidalis nuchae: another cutaneous symptom of metabolic syndrome, truncal obesity, and impending/overt diabetes mellitus? Am J Clin Dermatol. 2010;11:433–6.
5. Burt VL, Whelton P, Roccella EJ, Brown C, Cutler JA, Higgins M, et al. Prevalence of Hypertension in the US Adult Population: results From the Third National Health and Nutrition Examination Survey, 1988–1991. Hypertension. 1995;25:305–13.
6. Finlay AY, Khan GK. Dermatology Life Quality Index (DLQI): a simple practical measure for routine clinical use. Clin Exp Dermatol. 1994;19:210–6.
7. Adegbidi H, Atadokpede F, Ango-Padonou F, Yedomon H. Keloidacne of the neck: epidemiological studies over 10 years. Int J Dermatol. 2005;44(Suppl 1):49–50.
8. Mouhari-Toure A, Saka B, Akakpo SA, Kombaté K, Tchangaï-Walla K, Pitché P. Keloids and hypertension in black subjects: a case-control study. Ann Dermatol Venereol. 2013;140:134–7.
9. Mahé A. Traitement de l’acné chéloïdienne de la nuque : recommandations. Ann Dermatol Venereol. 1999;126:541–2.
10. Arima J, Huang C, Rosner B, Akaishi S, Ogawa R. Hypertension: a systemic key to understanding local keloid severity. Wound Repair Regen. 2015;23:213–21.
11. Louw L. Keloids in rural black South Africans. Part 1: general overview and essential fatty acid hypotheses for keloid formation and prevention. Prostaglandins LeukotEssent Fatty Acids. 2000;63:237–45.
12. Snyder AL, Zmuda J, Thompson P. Keloid associated with hypertension. Lancet. 1996;347:465–6.
13. Noishiki C, Takagi G, Kubota Y, Ogawa R. Endothelial dysfunction may promote keloid growth. Wound Repair Regen. 2017;25:976–83.
14. Shi Y, Liu T, Yao L, Xing Y, Zhao X, Fu J, et al. Chronic vitamin D deficiency induces lung fibrosis through activation of the renin-angiotensin system. Sci Rep. 2017;7:3312.
15. Kilimster EJ, Paterson C, Brasch HD, Davis PF, Tan ST. The role of the renin-angiotensin system and vitamin d in keloid disorder—a review. Front Surg. 2019;6:1–12.
16. Murphy AM, Wong AL, Beuzly M. Modulation of angiotensin II signaling in the prevention of fibrosis. Fibrogenesis Tissue Repair. 2015;8:7.
17. Ardekani GS, Aghaie S, Nemati MH, Handjani F, Kasraee B. Treatment of a postburn keloid scar with topical captopril: report of the first case. Plast Reconstr Surg. 2009;123:112e–e11313.
18. D’Andrea F, Brongo S, Ferraro G, Baroni A. Prevention and treatment of keloids with intraleosomal verapamil. Dermatology. 2002;204:60–2.

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