

**TABLE 1** Demographics of good and poor responders

	Good responders, N = 114	Poor responders, N = 112
Age, mean (s.d.), years	55 (10)	52 (12)
% male	111 (98)	111 (98)
BMI, mean (s.d.), kg/m <sup>2</sup>	31.1 (5.0)	33.1 (5.9)
European, n (%)	89 (78.1)	86 (76.8)
Days on febuxostat prior to day 0, mean (s.d.)	46 (119)	32 (52)
Serum urate at day 0, mean (s.d.), mg/dl	4.1 (0.64)	6.3 (1.12)
ABCG2 rs2231142 allele count (freq.) GG/GT/TT	65 (0.57)/37 (0.32)/12 (0.11)	57 (0.51)/46(0.41)/9 (0.08)

ABCG2: ATP-binding cassette transporter G2.

grants from Ardeabiosciences unrelated to the submitted work. L.K.S. reports speaker fees from Amgen unrelated to the submitted work. R.T. report no conflicts of interest.

**Lisa K. Stamp<sup>1</sup>, Ruth Topless<sup>2</sup>, Jeffrey N. Miner<sup>3</sup>, Nicola Dalbeth<sup>4</sup> and Tony Merriman<sup>2</sup>**

<sup>1</sup>Department of Medicine, University of Otago, Christchurch, <sup>2</sup>Department of Biochemistry, University of Otago, Dunedin, New Zealand, <sup>3</sup>General Atomics Court, Viscentio Bio, San Diego, CA, USA and <sup>4</sup>Department of Medicine, University of Auckland, Auckland, New Zealand

Accepted 17 November 2018

Correspondence to: Lisa K. Stamp, Department of Medicine, University of Otago, Christchurch, PO Box 4345, Christchurch, New Zealand. E-mail: [lisa.stamp@cdhb.health.nz](mailto:lisa.stamp@cdhb.health.nz)

## References

- 1 Khanna D, Fitzgerald J, Khanna P *et al.* 2012 American College of Rheumatology Guidelines for the Management of Gout. Part 1: systematic nonpharmacologic and pharmacologic therapeutic approaches to hyperuricemia. *Arthritis Care Res (Hoboken)* 2012;64:1431–46.
- 2 Wen C, Yee S, Liang X *et al.* Genome-wide association study identifies ABCG2 (BCRP) as an allopurinol transporter and a determinant of drug response. *Clin Pharm Ther* 2015;97:518–25.
- 3 Roberts RL, Wallace MC, Phipps-Green AJ *et al.* ABCG2 loss-of-function polymorphism predicts poor response to allopurinol in patients with gout. *Pharmacogenomics J* 2017;17:201–3.
- 4 Wallace M, Roberts R, Nanavati P *et al.* Association between ABCG2 rs2231142 and poor response to allopurinol: replication and meta-analysis. *Rheumatology (Oxford)* 2018;57:656–60.
- 5 Ichida K, Matsuo H, Takada T *et al.* Decreased extra-renal urate excretion is a common cause of hyperuricemia. *Nat Commun* 2012;3:764.
- 6 Miyata H, Takeda T, Toyoda Y *et al.* Identification of febuxostat as a new strong ABCG2 inhibitor: potential applications and risks in clinical situations. *Front Pharmacol* 2016;7:518.
- 7 Dalbeth N, Jones G, Terkeltaub R *et al.* Lesinurad, a selective uric acid reabsorption inhibitor, in combination with febuxostat in patients with tophaceous gout. *Arthritis Rheum* 2017;69:1903–13.

- 8 Price A, Patterson N, Plenge R *et al.* Principal components analysis corrects for stratification in genome-wide association studies. *Nat Genet* 2006;38:904–9.

Rheumatology 2019;58:548–550

doi:10.1093/rheumatology/key317

Advance Access publication 8 November 2018

## Nasal carriage of *Staphylococcus pseudintermedius* in patients with granulomatosis with polyangiitis

### Rheumatology key message

- Patients with granulomatosis with polyangiitis can be colonized by *Staphylococcus pseudintermedius*, with unclear contribution to disease pathogenesis.

SIR, granulomatosis with polyangiitis (GPA, formerly Wegener's granulomatosis) is characterized by necrotizing granulomatous inflammation usually involving the upper and lower respiratory tract, and necrotizing vasculitis affecting predominantly small to medium vessels, frequently leading to glomerulonephritis [1]. Disease etiopathogenesis is complex but includes a genetic background, epigenetic modifications and environmental factors. There are several lines of evidence indicating an association of nasal colonization with *Staphylococcus aureus* and GPA. *S. aureus* is an independent risk factor for relapse of GPA in carriers, and therapeutic administration of trimethoprim-sulfamethoxazole has been shown to reduce relapse rates during a treatment period of 2 years [2]. Little is known about other bacterial species that colonize the noses of GPA patients.

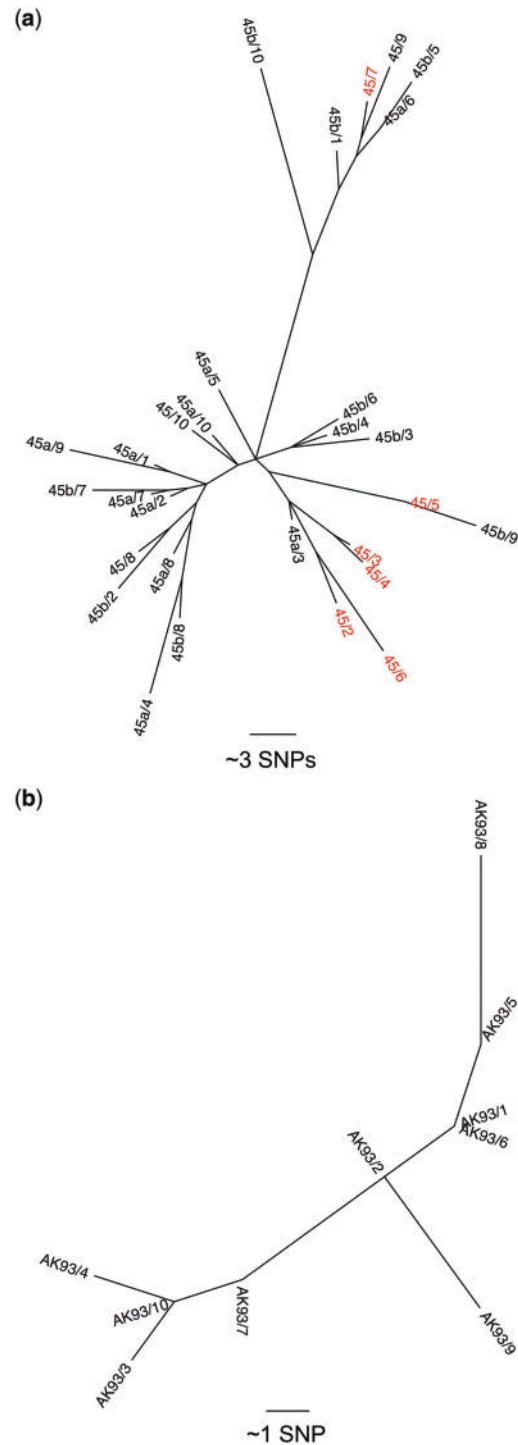
We undertook a study to investigate the bacterial species carried by 69 patients with a diagnosis of GPA and ENT involvement. This work was approved by the National Research Ethics Service (NRES) Committee East of England – Cambridge Central (REC reference: 08/H0308/176). Informed consent was obtained before sample collection. Nasal swabs (1–3 swabs per patient) were inoculated into high-salt (7.5%) nutrient broths and incubated statically at 37°C overnight; from this culture, 100 µl was inoculated onto Brilliance Staph 24 Agar (all

media sourced from Oxoid, UK). Representative blue single colonies (putative *S. aureus*) were picked and streaked to purity on Columbia blood agar for further analysis. We noted that swabs from two patients (referred to as 0045 and 0093, neither with active disease in the ENT tract when sampled) grew blue colonies (see Supplementary Fig. S1A–D, available at *Rheumatology* online) identified as *Staphylococcus pseudintermedius* by matrix-assisted laser desorption ionization–time of flight mass spectrometry (MALDI-TOF MS, Bruker, Germany). Both were on immunosuppression (mycophenolate mofetil and rituximab alongside steroids, respectively) at the time of sampling (Supplementary Table S1, available at *Rheumatology* online). Patient 0045 was positive for *S. pseudintermedius* on three occasions spaced 6 weeks apart (confirming persistent carriage), but we only obtained a single swab from patient 0093.

Ten colonies from each of the primary culture plates positive for *S. pseudintermedius* (30 colonies total for 0045 and 10 for 0093) were submitted for whole-genome sequencing (Supplementary Table S2, available at *Rheumatology* online). Ten colonies were picked from each sample to determine whether the two participants carried single or multiple *S. pseudintermedius* clones, as previously reported for *S. aureus* [3]. Whole-genome sequence data confirmed the species identification. Multilocus sequence typing derived from the sequence data indicated that patient 0045 carried sequence type (ST) 155 strain in all three samples (see Fig. 1a), and generation of a core genome phylogeny revealed that the 30 isolates differed by a total of 138 single-nucleotide polymorphisms across the core genome. Patient 0093 carried a novel ST that was subsequently assigned as ST1025; the 10 isolates from this patient differed by a total of 13 single-nucleotide polymorphisms (see Fig. 1b). All isolates were genotypically methicillin susceptible on the basis of being *mecA* negative. Isolates from patient 0045 contained genes mediating resistance to penicillin (*blaZ*), tetracycline (*tetM*) and aminoglycosides (*aacA*-aphD), and 6 of 30 isolates tested from this case carried the trimethoprim-resistance gene *dfpG* (Fig. 1a). Isolates from patient 0093 were positive for *blaZ* (penicillin resistance) alone (Supplementary Table S2, available at *Rheumatology* online).

*S. pseudintermedius* is a commensal and opportunistic pathogen of cats and dogs, in which it causes skin and soft tissue infections [4]. Increasingly, *S. pseudintermedius* is recognized as a zoonosis in humans [5, 6]. Re-analysis of isolates reported as *S. aureus* by clinical microbiology laboratories may identify *S. pseudintermedius* in a small proportion of patients [7]. A recent observational study at a large regional microbiology laboratory over a 2-year period reported the clinical characteristics of 24 patients who were culture-positive for *S. pseudintermedius* [5]. Most cases had severe co-morbidities and had contact with dogs at the time of infection (92.1%). Isolates were associated with skin and soft tissue infections in most cases (75%), although two patients had invasive disease [5]. This suggests that acquisition may occur from dogs,

Fig. 1 Multilocus sequence typing of both patients



Patient 0045 carried the ST155 strain in all three samples (see Fig. 1a), and generation of a core genome phylogeny revealed that the 30 isolates differed by a total of 138 SNPs across the core genome. Patient 0093 carried a novel ST that was subsequently assigned as ST1025; the 10 isolates from this patient differed by a total of 13 SNPs (see Fig. 1b). ST: sequence type; SNP: single nucleotide polymorphisms.

although a study that investigated the presence of *Staphylococcus* spp. in 119 dogs and their 107 owners found only one dog–owner pair that both carried *S. pseudintermedius* [8]. Neither patient in the present study had a history of contact with dogs, and thus it remains unclear which factors determine colonization with *S. pseudintermedius*.

To the best of our knowledge, this is the first evidence of persistent nasal carriage of *S. pseudintermedius* in humans. The detection of two distinct lineages demonstrates that colonization is not limited to a specific clone. Transmission and factors leading to persistent carriage are not known, but local damage relating to vasculitis and pharmacological immune suppression may make GPA patients more prone to colonization. It remains unclear whether *S. pseudintermedius* has any impact on relapse risk or is directly involved in the etiopathogenesis of GPA.

## Acknowledgements

We thank the library construction, sequencing and core informatics teams from the Wellcome Trust Sanger Institute. AK was supported by the ERA-EDTA with a long-term fellowship (12 months) from August 2014 to August 2015. EMH is supported by a UK Research and Innovation (UKRI) Fellowship: MR/S00291X/1.

**Funding:** This work was supported by a National Institute for Health Research Biomedical Research Centre (NIHR BRC) Immunity, Infection and Inflammation pump-priming grant.

**Disclosure statement:** The authors have declared no conflicts of interest.

## Supplementary data

Supplementary data are available at *Rheumatology online*.

**Andreas Kronbichler** <sup>1,2</sup>, **Beth Blane**<sup>3</sup>, **Mark A. Holmes**<sup>4</sup>, **Josef Wagner**<sup>5</sup>, **Julian Parkhill**<sup>5</sup>, **Sharon J. Peacock**<sup>3,5,6</sup>, **David R. W. Jayne**<sup>1,4</sup> and **Ewan M. Harrison**<sup>3,5</sup>

<sup>1</sup>*Vasculitis and Lupus Clinic, Addenbrooke's Hospital, Cambridge, UK*, <sup>2</sup>*Department of Internal Medicine IV (Nephrology and Hypertension), Medical University Innsbruck, Innsbruck, Austria*, <sup>3</sup>*Department of Medicine, University of Cambridge, Addenbrooke's Hospital*, <sup>4</sup>*Department of Veterinary Medicine, University of Cambridge, Cambridge*, <sup>5</sup>*Wellcome Trust Sanger Institute, Wellcome Genome Campus, Hinxton* and <sup>6</sup>*Department of Pathogen Molecular Biology, London School of Hygiene and Tropical Medicine, London, UK*

Accepted 6 September 2018

Correspondence to: Andreas Kronbichler, Vasculitis and Lupus Clinic, Box 57, Addenbrooke's Hospital, Hills Road, CB2 0QQ, Cambridge, UK.

E-mail: andreas.kronbichler@i-med.ac.at

## References

- 1 Yates M, Watts R. ANCA-associated vasculitis. *Clin Med* 2017;17:60–4.
- 2 Cohen Tervaert JW. Trimethoprim-sulfamethoxazole and antineutrophil cytoplasmic antibodies-associated vasculitis. *Curr Opin Rheumatol* 2018;30:388–94.
- 3 Paterson GK, Harrison EM, Murray GG. Capturing the cloud of diversity reveals complexity and heterogeneity of MRSA carriage, infection and transmission. *Nat Commun* 2015;6:6560.
- 4 Moodley A, Damborg P, Nielsen SS. Antimicrobial resistance in methicillin susceptible and methicillin resistant *Staphylococcus pseudintermedius* of canine origin: literature review from 1980 to 2013. *Vet Microbiol* 2014;171:337–41.
- 5 Somayaji R, Priyantha MA, Rubin JE, Church D. Human infections due to *Staphylococcus pseudintermedius*, an emerging zoonosis of canine origin: report of 24 cases. *Diagn Microbiol Infect Dis* 2016;85:471–6.
- 6 Yarbrough ML, Lainhart W, Burnham CA. Epidemiology, clinical characteristics, and antimicrobial susceptibility profiles of human clinical isolates of *Staphylococcus intermedius* group. *J Clin Microbiol* 2018;56:e01788–17.
- 7 Börjesson S, Gómez-Sanz E, Ekström K, Torres C, Grönlund U. *Staphylococcus pseudintermedius* can be misdiagnosed as *Staphylococcus aureus* in humans with dog bite wounds. *Eur J Clin Microbiol Infect Dis* 2015;34:839–44.
- 8 Han JI, Yang CH, Park HM. Prevalence and risk factors of *Staphylococcus* spp. carriage among dogs and their owners: a cross-sectional study. *Vet J* 2016;212:15–21.

*Rheumatology* 2019;58:550–553

doi:10.1093/rheumatology/key353

Advance Access publication 5 December 2018

## Coexistence of systemic lupus erythematosus with Kikuchi-Fujimoto disease involving the salivary gland, initially disguised as lymphoma

### Rheumatology key message

- Kikuchi-Fujimoto disease associated with lupus can mimic lymphoma due to nodal and extra-nodal involvement.

SIR, Kikuchi-Fujimoto disease (KFD) is a histiocytic necrotizing lymphadenitis, which predominantly affects woman of Japanese or other Asiatic descent aged  $\leq 40$  years [1]. The aetiology of KFD is not well established, but it is suspected to be triggered by a virus or a hyper-autoimmune response [2, 3]. It is a rare benign disease, characterized by localized lymphadenopathy with fever and night sweats. KFD is an important differential diagnosis for malignant lymphoma and other infectious conditions because it mimics their clinical presentation and laboratory findings. Herein, we present the case of a male patient with KFD showing salivary gland involvement, coexisting with lupus, where lymphoproliferative disease was initially suspected.

A 42-year-old otherwise healthy male presented to our clinic with complaints of fever up to 38°C for 3 weeks, weight loss and night sweats. His medical history was