Data collection and definitions

Demographic characteristics, comorbid conditions, time of antimicrobial therapy, and presence of a ventilator, central venous catheter, or Foley catheter at the time of bacteremia onset were recorded. Comorbidities at diagnosis were classified using the Charlson Comorbidity Index. The severity of illness was assessed using the Pitt bacteremia score [1] in all patients. Immunosuppressive therapy was defined as receipt of immunosuppressive agents within six weeks, or prednisolone ≥20 mg daily for two weeks, or 30 mg of prednisolone daily for at least one week before bacteremia onset. The primary infection source of bacteremia was determined according to the definitions of the Centers for Disease Control and Prevention [2]. If no infectious focus was identified, bacteremia was considered primary. Antimicrobial therapy was considered active if the drugs used at therapeutic doses had *in vitro* activity against the strain isolated after the onset of bacteremia (herein named "*in vitro* active antibiotic therapy"). Data on the 30-day mortality were also recorded.

WGS and analyses

Bacterial genomic DNA from representative isolates was extracted using the QIAamp PowerFecal Pro DNA Kit (Qiagen, Valencia, CA, USA) and sequenced using the MiSeq Illumina platform and/or Nanopore (Biotools Co., Ltd., New Taipei, Taiwan ROC). For nanopore sequencing, libraries of long-read sequencing were established via end-repair, A-tailing, barcoding, and adapter ligation using KAPA End Repair and A-Tailing reagent and KAPA HyperPlus Kit (KAPA Biosystems, Roche, Basel, Switzerland). The barcode ligation was performed using a Native Barcoding Expansion kit (EXP-NBD104; ONT, Oxford, UK), and adapter ligation was performed using the Oxford Nanopore Technologies (ONT) ligation library preparation kit (SQK-LSK109; ONT, Oxford, UK). Libraries were purified using KAPA Hyper Beads at a 0.4× ratio to enrich the

long-DNA fragments. The ONT PromethION 24 device was used to sequence DNA libraries with FLO-PRO002 flow cells (R9.4.1). Guppy (v4.0.11) was applied to decode the raw sequencing data with HighQuality basecalling mode. NanoPack (v1.1.0) was used to check the sequencing results and validate the read length profile [3]. Raw reads were assembled using FLYE (v2.8.3) to form primary contigs [4]. Racon (v1.4.22) was applied to polish primary contigs with the alignment results from Minimap2 (v2.17), followed by model correction using Medaka (v1.2.3) [5,6]. Finally, contigs were corrected for homologous sequences from related genomes using Homopolish (v0.2) [7]. Fully polished contigs were analyzed using QUAST (v5.0.2) and BUSCO (v5.0.0) to evaluate the quality of the assemblies and the completeness of the genome, respectively [8,9]. Antimicrobial resistance (AMR) genes were identified using a Resistance Gene Identifier (RGI). Kleborate [10] and Kaptive [11] were used to analyze and visualize the sequence (ST-type), capsular (K-type), lipopolysaccharide (O-type) types, and resistance and virulence patterns. PlasmidFinder and oriTfinder were used to identify the plasmid incompatibility (Inc.) group and a complete conjugation module (oriT, relaxase, type IV coupling protein, and T4SS gene cluster), respectively. A phylogenetic tree of *K. pneumoniae* was inferred from the SNPs identified using kSNP3 [12] and constructed using a maximum likelihood tree in FastTree 2.1.3 [13]. The kmer size was set to 19 for the whole genome and 31 for the plasmid, and the optimum size was estimated using the Kchooser available in the package. The resulting tree was visualized using iTOL (https://itol.embl.de/). Virulence genes in the bla_{KPC} plasmid were predicted using VFDB [14] and VirulenceFinder [15].

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