PERKEMBANGAN PATOGENESIS DAN TATA LAKSANA *SYSTEMIC LUPUS ERYTHEMATOSUS*

YULIASIH

2020

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Penulis
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Setting,lay out dan desain cover
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PRAKATA

Alhamdulillah penulis mengucapkan puji syukur ke hadirat Allah Swt. atas selesainya penyusunan buku referensi ini. Buku ini disusun untuk para klinisi dan para peneliti yang ingin memperluas pengetahuan tentang "Perkembangan Patogenesis dan Tata Laksana Systemic Lupus Erythematosus (SLE)". SLE merupakan penyakit autoimun yang banyak dijumpai di bidang Ilmu Penyakit Dalam khususnya bidang Reumatologi. Penyakit ini di klinik masih menjadi tantangan tersendiri dalam hal menegakkan diagnosis dan pelaksanaan terapi. Diagnosis menjadi masalah besar di klinik karena manifestasinya yang luas menyerupai penyakit sistemik yang lain. Keterlambatan diagnosis dapat mempersulit perawatan dan dapat mengakibatkan kematian. Penulis mencoba mengurai dalam buku ini tentang patogenesis, manifestasi klinik dan contoh-contoh kasus yang berat yang telah dianalisis, serta pengobatan yang harus dilakukan.

Dalam buku ini dijelaskan tentang patogenesis SLE yang terkait dengan faktor genetik. Seberapa besar faktor genetik memengaruhi respons imun. Diketahui bahwa respons imun yang terjadi pada SLE tidak disebabkan oleh satu gen namun banyak gen yang terlibat di dalam patogenesis, sehingga masih banyak peluang bagi para peneliti dalam mengungkap misteri gen-gen yang kemungkinan memiliki korelasi dalam menimbulkan respons imun yang tidak terkendali. Selain peran gen, peneliti juga mengungkap peran sel-sel imun terutama sel T dalam mencetuskan inflamasi sistemik yang ditangkap oleh klinisi sebagai gejala klinik. Sel T yang aktif mensekresi berbagai sitokin yang berperan dalam memicu manifestasi klinik dan terkait dengan aktivitas penyakit. Untuk menilai aktivitas penyakit klinisi tidak hanya berpedoman pada gejala klinis namun juga dievalusi peranan komplemen dalam menilai aktivitas penyakit. Berpedoman dengan tata laksana yang benar maka akan menurunkan angka kematian SLE yang menurut penulis sangat penting mengingat angka kematian SLE di RSUD Dr. Soetomo masih relatif tinggi dibandingkan dengan negara-negara yang sudah cukup maju dalam penyelenggaraan pelayanan kesehatan.

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Penulisan buku ini tidak menutup kemungkinan masih terdapat kekurangan dalam mengungkap bab demi bab mengingat penyakit SLE sedemikian luasnya dan pesatnya perkembangan penelitian. Harapan penulis buku ini dapat bermanfaat dan memberikan informasi bagi para pembaca tentang penyakit SLE.

Penulis

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RANGKUMAN

Systemic Lupus Erythematosus (SLE) tidak hanya penyakit autoimun sistemik prototipikal, tetapi juga salah satu penyakit paling heterogen yang harus dikenali oleh para dokter, ahli genetika, dan peneliti klinis. Dalam hal ini, sifat heterogen pada SLE menyangkut dalam bidang patogenesis, yang mana banyak gen yang terlibat di dalamnya dan masing-masing orang diperkirakan berbeda-beda karena manifestasi klinisnya yang berbeda. Dari beberapa laporan studi banyak gen yang terlibat tidak hanya HLA, tetapi gen-gen lain juga ikut berperan. Studi-studi selama dekade ini banyak difokuskan pada *single point* mutasi atau lebih dikenal dengan *single nucleotide polymorphism* (SNP). Beberapa studi melaporkan bahwa terjadinya SNP pada sitokin yang menyebabkan penyakit SLE bermanifestasi berat (Tsokos, 2011). Selain itu, adanya beragam abnormalitas fenotipe dan fungsi sel-sel imun antara lain sel dendritik, sel T, sel B, serta adanya gangguan keseimbangan Treg dan Th17 yang menyebabkan gangguan keseimbangan sitokin. Dalam patogenesis SLE tidak hanya sel-sel imun yang mengalami kelainan namun terbentuknya autoantibodi yang bervariasi juga ikut menentukan manifesatsi klinik. Pada populasi SLE yang dirawat di RSUD Soetomo Surabaya, pasien-pasien yang manifestasi klinik berat tidak semuanya menunjukkan ANA atau dsDNA yang positif besar. Padahal berdasarkan literatur kadar dsDNA dapat untuk menilai aktivitas penyakit serta prognosis.

Mortalitas SLE telah menurun dari 50% di era pre-kortikosteroid (sekitar tahun 1948) menjadi 15 tahun bertahan hidup 85–95% di era modern (Simard & Costenbrader, 2011). Prevalensi SLE telah diperkirakan 30–50 per 100.000, yang setara dengan sekitar 500.000 pasien di Eropa dan 250.000 di AS. Analisis yang memberikan bukti bahwa keturunan, ras, dan etnis memiliki dampak besar pada manifestasi dan keparahan SLE. Insiden dan prevalensi SLE lebih tinggi pada pasien kulit hitam, Asia, dan Hispanik yang cenderung lupus lebih awal (usia sangat muda) dan memiliki penyakit yang lebih parah dan lebih aktif dengan kronisitas penyakit lebih panjang serta risiko kematian yang tinggi. Hal ini diduga terkait dengan perbedaan genetik dan paparan lingkungan lokal. SLE pada umumnya terjadi pada wanita hampir 90%, tetapi perbandingan jumlah penderita laki-laki dan perempuan pada populasi Dr. Soetomo agak ekstrem dengan perbandingan jumlah pasien wanita dan laki-laki 40:1, sedangkan negara lain ada yang melaporkan penderita wanita banding laki yaitu 9:1.

Manifestasi klinik SLE berbeda-beda pada masing-masing individu apakah terkait dengan autoantibodi masih kurang jelas sehingga klinisi tidak bisa memprediksi manifestasi klinik tentu serta memperkirakan perjalanan penyakit. Ada beberapa tipe perjalanan penyakit yaitu *relapsing remitting*, persisten aktif, secara klinik tenang namun secara serologi aktif, dan remisi yang panjang. Manifestasi klinik yang heterogen tersebut menimbulkan tantangan besar dalam mendiagnosis serta pengobatan. Dibutuhkan tenaga ahli yang sangat berpengalaman dalam merawat pasien SLE khususnya yang berat dan mengancam jiwa. Atas dasar laporan studi-studi klinik, dilakukan pengembangan terapi yang berbasis molekuler. Pendekatan '*treat-to-target*' yang baru-baru ini diperkenalkan dalam merawat SLE dapat menekankan aktivitas penyakit sebagai tujuan utama terapi; namun, respons yang bervariasi pada berbagai organ hal ini masih menjadi kendala besar dalam merawat pasien SLE dan menjaga kualitas hidup pasien.

hormonal umumnya aman untuk sebagian besar pasien SLE dengan aktivitas penyakit stabil atau *quiescent* (Bertsias, 2017).

KESIMPULAN

Dalam beberapa dekade terakhir ini, telah banyak kemajuan besar di bidang SLE, seperti penentuan faktor risiko dan fenotipe, patogenesis, dan metode-metode pengobatan SLE. Penemuan peran faktor-faktor yang dapat meningkatkan produksi interferon tipe I melalui *Toll-like receptor* (TLR) telah menumbuhkan ide-ide baru dalam target terapi SLE selain melibatkan sel B dan sel T. Penemuan faktor-faktor genetik dan lingkungan yang dapat menyebabkan kerentanan terhadap terjadinya autoimunitas pada akhirnya dapat memudahkan identifikasi individu-individu yang berisiko terhadap SLE. Obat-obatan baru telah ditambahkan ke dalam strategi terapi baru yang ditujukan untuk mempercepat tercapainya remisi dan pencegahan *flare* dengan terapi yang lebih intens namun tetap aman. Strategi pencapaian remisi, terapi rumatan, dan manajemen komorbiditas menjadi kunci penting dalam perawatan pasien SLE. Maka dari itu, manajemen penyakit SLE sangat menekankan perlunya pendekatan multidisiplin ilmu dan keahlian dalam bidang penyakit dalam, khususnya rematologi.

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