Integrated Case Based Discussion

20-05-2015

History

2 years old child with

- Fever
- Recurrent infections
- Bleeding nose
- Poor weight gain
- Maculopapular rash.

Physical examination

- Pallor
- Lymphadenopathy
- Moderate hepatomegaly
- Massive splenomegaly
- Maculopapular rash
- Skin nodules
- Ophthalmoscopy:
  - ✓Optic disc changes
  - ✓Tinytan colored spots on the Iris.

Laboratory Findings

- Hb: 7gm%
- TWBC count: 1.1lakh/cumm
- Smear: WBC precursor cells with monocytosis

Questions

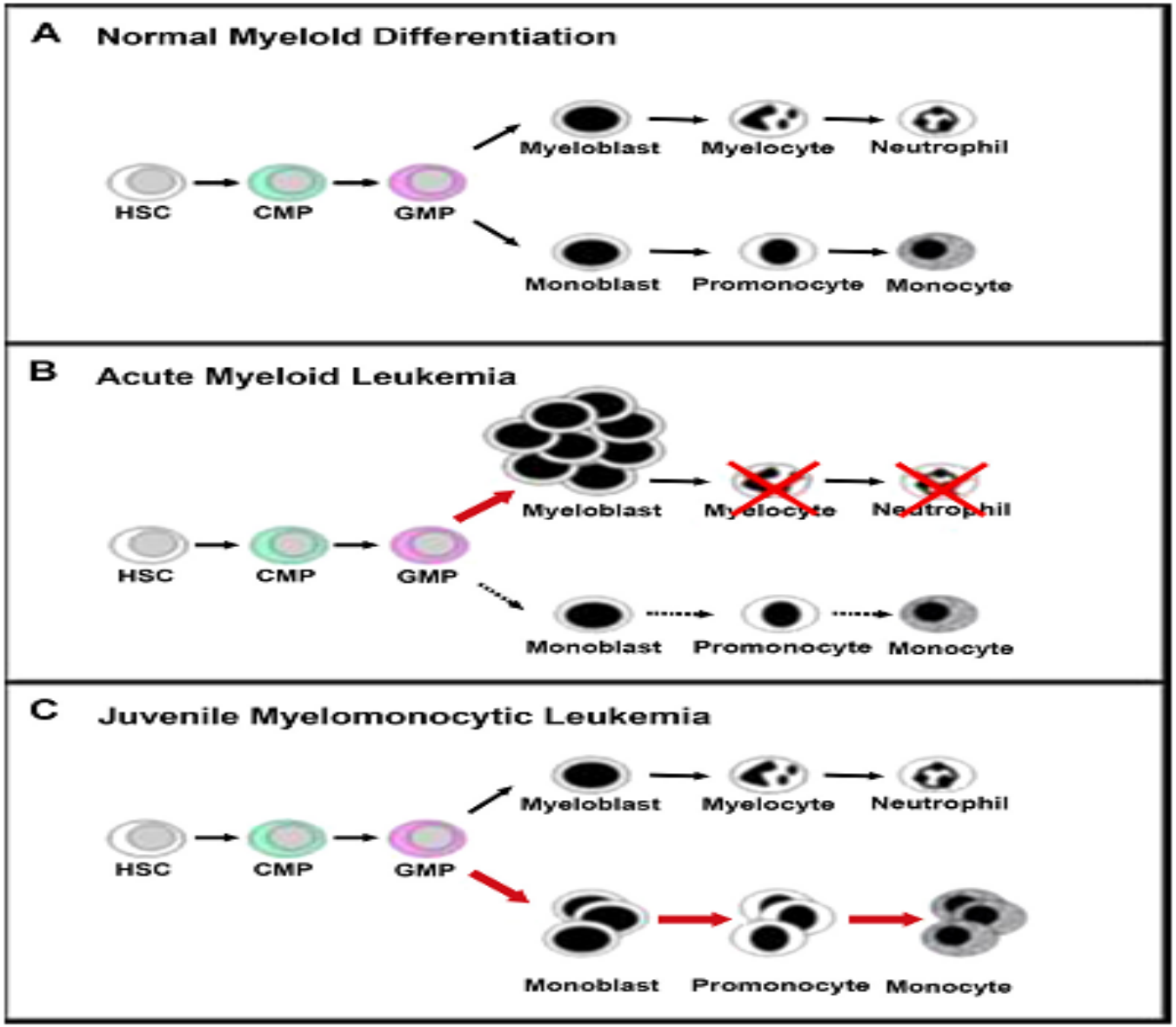

Fig. 1. Schematic diagram of (*A*) normal hematopoietic differentiation; (*B*) accumulation of undifferentiated myeloblasts representing acute myeloid leukemia; and (*C*) increased production of monocytic cells along the full spectrum of differentiation, including blast forms, promonocytes, monocytes, and macrophages, as observed in juvenile myelomonocytic leukemia. CMP, common myeloid progenitor; GMP, granulocyte monocyte progenitor; HSC, hematopoietic stem cell. (*From* Chan RJ, Cooper T, Kratz CP, et al. Juvenile myelomonocytic leukemia: a report from the 2nd International JMML Symposium. Leuk Res 2009;33(3):356; with permission.)

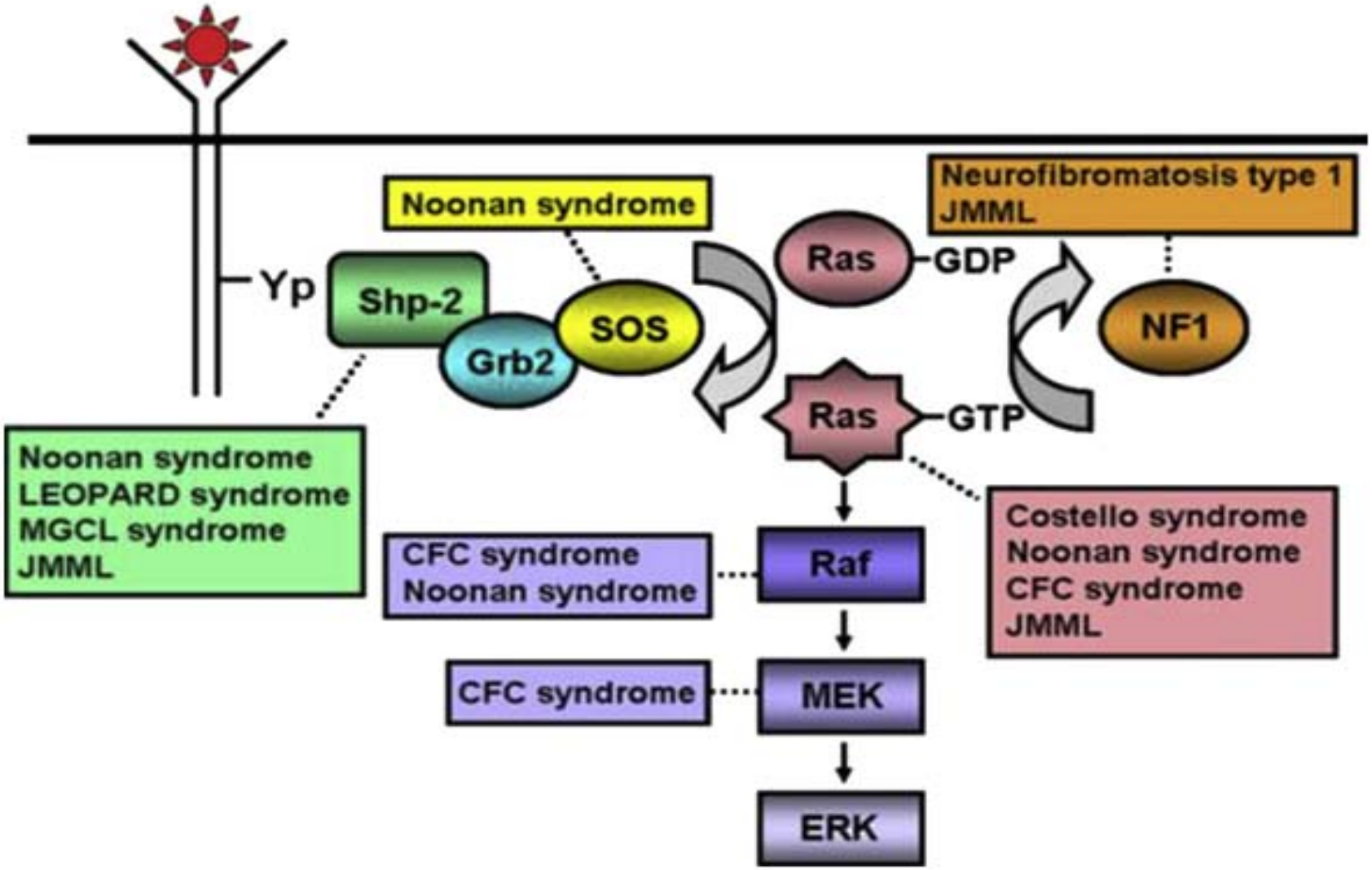

Fig. 2. Schematic diagram showing ligand-stimulated Ras activation, the Ras-Erk pathway, and the gene mutations found to date contributing to the neurocardio-facio-cutaneous congenital disorders and JMML. CFC, cardia-facio-cutaneous; NL/MGCL, Noonan-like/ multiple giant cell lesion. (*From* Chan RJ, Cooper T, Kratz CP, et al. Juvenile myelomonocytic leukemia: a report from the 2nd International JMML Symposium. Leuk Res 2009;33(3): 357; with permission.)

Table 1
Juvenile myelomonocytic leukemia diagnostic criteria

Category 1	Category 2	Category 3
All of the following	At least one of the following	At least two of the following
Splenomegaly[a]	Somatic mutation in *RAS* or *PTPN11*	circulating myeloid precursors
Absolute monocyte count >1000/μL	Clinical diagnosis of NF-1 or *NF1* gene mutation	White blood cells >10,000/μL
Blasts in peripheral blood/ bone marrow <20%	Homozygous mutation in *CBL*	Increased fetal hemoglobin for age
Absence of the t(9;22) *BCR/ ABL* fusion gene	Monosomy 7	Clonal cytogenetic abnormality excluding monosomy 7
		GM-CSF hypersensitivity

The diagnosis of JMML can be made if a patient meets all of the Category 1 criteria and one of the Category 2 criteria. If there are no Category 2 criteria met, then the Category 3 criteria must be met.

[a] For the 7% to 10% of patients without splenomegaly, the diagnostic criteria must include all other features in Category 1 plus either one of the parameters in Category 2 or two features in Category 3.

(*Modified from* Chan RJ, Cooper T, Kratz CP, et al. Juvenile myelomonocytic leukemia: a report from the 2nd International JMML Symposium. Leuk Res 2009;33(3):358; with permission.)