Thrombocytosis in Infants with Congenital Cytomegalovirus Infection Being Treated with Valganciclovir

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Background

- Congenital CMV (cCMV) is associated with sensorineural hearing loss and neurodevelopmental disabilities.
- Infants with symptomatic cCMV infection benefit from 6 months of oral valganciclovir (vGCV) therapy.
- Neutropenia, thrombocytopenia, and hepatotoxicity are adverse effects vGCV, for which we monitor in our outpatient ID clinic.
- We observed a pattern that cCMV infants treated with vGCV developed an uptrend in platelets and/or thrombocytosis (platelet count >450,000/uL) while on therapy which has not been previously been reported.

Methods

- Medical records and laboratory results from our multi-disciplinary cCMV clinic led by Infectious Diseases at Lurie Children's Hospital were reviewed (2017-2020).
- Data included: cCMV signs/symptoms, cCMV treatment prescribed, indication for ganciclovir/vGCV treatment, and complete blood count prior to, during, and post- vGCV therapy.

Results

- Of 21 cCMV infants referred to clinic:
  - 14 received >1 month of vGCV for symptomatic disease
  - 1 discontinued vGCV <1 month due to perceived fussiness
  - 1 was part of a clinical trial
- Four infants were initially treated with ganciclovir for ≤1 month and then transitioned to vGCV.
- Of the 14 patients treated with vGCV:
  - 10 (71%) had sensorineural hearing loss (50% unilateral)
  - 12 (86%) had central nervous system abnormalities (including cystic lesions on head ultrasound)
  - 5 (36%) had thrombocytopenia
  - 7 (50%) were intrauterine growth restricted
- Eleven infants (79%) developed thrombocytosis.
- Thirteen infants (93%) had an uptrend in platelet count [not including normalization of initial thrombocytopenia (platelets <150,000/uL)].
- Neutropenia (absolute neutrophil count <500/uL) occurred in 1 patient and required temporary discontinuation of vGCV.

Conclusions

- We observed an interesting trend of rising platelet count and the development of thrombocytosis in the majority of our cCMV patients on vGCV, which has not been previously described.
- This observation is limited by small number of patients and thrombocytosis is not a definitive association/adverse effect.
- With increasing use of vGCV and interest in both its antiviral activity and effect on bone marrow function, this observation is notable and warrants further study.

References

1. American Academy of Pediatrics. Cytomegalovirus infection. In: Red Book: 2018 Report of the Committee on Infectious Diseases, 31st Ed, Kimberlin DW, Brady MT, Jackson MA, Long SS, American Academy of Pediatrics, Itasca, IL 2018. p.310.
2. Kimberlin DW, Jester PM, Sánchez PJ, et al. Valganciclovir for symptomatic congenital cytomegalovirus disease. N Engl J Med 2015; 372:933.

Table 1: Congenital CMV patients receiving vGCV: clinical features and platelet trends

Patient	Congenital CMV features	Age of CMV testing (day of life)	Age at start of treatment (day of life)	Duration of vGCV treatment (months)	Platelet uptrend while on vGCV	Thrombocytosis >450,000 while on vGCV	Platelets oscillated* while on vGCV	Sensorineural hearing loss (SNHL)
1	SNHL, CNS subependymal cystic lesions	2	19	6	Y	Y	N	unilateral
2	SNHL, CNS subependymal cystic lesions	2	12	6	Y	Y	Y	unilateral
3	SNHL	3	22	6	Y	Y	N	unilateral
4	thrombocytopenia, rash, ventriculomegaly, pneumonitis	2	2	6†	Y	Y	N	
5	IUGR, petechiae, CNS periventricular calcification, ventriculomegaly	1	1	7†	Y	Y	N	
6	SNHL, thrombocytopenia, CNS complex cystic lesions in germinal matrix regions	3	9	6	N	N	Y	bilateral
7	SNHL, CNS periventricular white matter changes	10	12	6	Y	Y	Y‡	bilateral
8	IUGR, thrombocytopenia, petechial rash, microcephaly, SNHL, CNS cortical malformation, ventriculomegaly	45	45	7†	Y	Y	Y	bilateral
9	thrombocytopenia, ventriculomegaly	2	24	5	Y	N	N	
10	IUGR, CNS intracranial calcifications, hyperbilirubinemia	9	14	6	Y	Y	Y	
11	IUGR, SNHL	3	31	6	Y	Y	Y	bilateral
12	IUGR, thrombocytopenia, CNS cerebral calcifications and cortical malformation, SNHL	2	7	6†	Y	N	N	unilateral
13	IUGR, SNHL, CNS periventricular cysts	4	12	6	Y	Y	N	bilateral
14	IUGR, SNHL, microcephaly, ventriculomegaly	1	35	6	Y	Y	N	bilateral

sensorineural hearing loss (SNHL); intrauterine growth restriction (IUGR); yes (Y); no (N)
*oscillated = both increased and decreased over time (as opposed to only trending upward)
†received IV ganciclovir initially and transitioned to vGCV
‡on numerous other medications, including antiepileptics

Figure 1: Platelet counts of cCMV infants treated with vGCV