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【 EDITORIAL 】

Paraneoplastic Large-vessel Vasculitis Associated with Myelodysplastic Syndrome

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Key words: large-vessel vasculitis, myelodysplastic syndrome, giant cell arteritis, Takayasu arthritis, steroid, azacitidine

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I recently read a report of myelodysplastic syndrome (MDS) simultaneously accompanied by giant cell arteritis (GCA) (1). In this report, Senjo et al. demonstrated the importance of considering GCA as a cause of anemia of chronic disorder (ACD) in elderly patients with MDS, even in countries where the prevalence of GCA is low, and their patient was the first reported Japanese case of concurrent MDS and GCA diagnosed by a temporal artery biopsy (1). According to the revised 2012 Chapel Hill Consensus Conference (CHCC) nomenclature of vasculitis, GCA and Takayasu arthritis (TA) are classified as large-vessel vasculitis (LVV) (2). To my knowledge, there have only been 13 reported cases of MDS accompanied by LVV, including GCA or TA, except for refractory anemia with excess blasts in transformation (RAEB-t) and chronic myelomonocytic leukemia (CMML), which are not included in the WHO 2008 classification of MDS (Table) (1, 3-10). Since GCA usually shows a marked increase in inflammatory markers such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR), the author reviewed the levels of both inflammatory markers at the onset of LVV associated with MDS. In most cases, the levels of CRP and ESR were markedly elevated, suggesting that we should consider the possibility of underlying LVV in MDS cases, based on the findings of highly elevated inflammatory markers of unknown causes, as well as ACD.

Liozon et al. described a strong temporal association between MDS and temporal arteritis from the observation that only one of seven instances of MDS had been diagnosed more than six months before or after the onset of arteritis (6). Steurer et al. reported a 60-year-old patient who developed LVV along with the progression from refractory anemia with ringed sideroblasts to RAEB-1 (5), and 11 of the 13 cases with MDS developed LVV concurrently or within 6 months (Table). These findings suggest the possibility of paraneoplastic LVV associated with MDS. Despite good prognostic predictions, five patients developed acute myeloid leukemia (AML) at an early date (1, 5-8). In these cases, as Senjo et al. described, while the steroid therapy was effective in controlling the LVV, it had no effect on the progression of MDS. In addition, Espinosa et al. reported a patient who died from sepsis shortly after starting high-dose steroid therapy against GCA with MDS (4), and the 67-year-old patient of Steurer et al. also developed splenic abscess early after steroid treatment (5). These reports suggest that special caution should be practiced in cases of serious infection in patients receiving steroid therapy for LVV associated with MDS.

Most patients with both LVV and MDS receive high or medium doses of corticosteroids. Although evidence is insufficient at present to conclude that the progression to AML and the appearance of severe infections are caused by steroid therapy, the subsequent immunosuppression may have influenced the prognosis of MDS. On the other hand, Mishima et al. reported a case of MDS with LVV that showed a relatively good clinical course with the administration of azacitidine (9). More recently, Galland et al. described the importance of hematologic treatment based on their experience of a poor-prognosis MDS case accompanied by LVV (10). For the treatment of MDS with LVV, aggressive multidisciplinary treatments including new chemotherapies, such as azacitidine, may be considered under the supervision of hematologists and rheumatologists.

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Table. **Patients with MDS and Large Vessel Vasculitis.**

Case	Reference	Gender	Age	MDS Types	IPSS	ESR (mm/h)	CRP (mg/L)	Types of vasculitis	Time relation of vasculitis to MDS	Treatments	Outcomes
1	(3)	F	67	RA*	NA	NA	NA	GCA	-3 years	GC	Stable
2	(4)	F	75	RAEB-2**	Int-2	98	NA	GCA	0	GC	Dead for infection (one month)
3	(5)	M	67	RAEB-1**	Int-1	72	231	LVV	0	GC	Sepsis, Splenic abscess (5 days) ››› Stable
4	(5)	M	60	(RARS**›››) RAEB-1**	Int-1	88	291	LVV	+2 years	GC	AML (4 months)
5	(6)	F	76	RA*	NA	90	118	GCA	+6 months	GC	NA
6	(6)	F	73	RA*	NA	140	140	GCA	0	GC	NA
7	(6)	M	68	ASIA*	NA	92	94	GCA	0	GC	Early transformation into AML
8	(6)	F	87	RAEB*	NA	90	78	GCA	0	GC	NA
9	(7)	M	62	RCMD**	Low	96	172	TA	+2 months	GC/MTX	AML (12 months), Dead for infection
10	(8)	F	71	RCMD**	Int-1	NA	208	LVV	0	GC	AML (4 months), Dead for AML
11	(9)	M	66	RCMD**	Int-1	155	100	LVV	0	Azacitidine	Relapse of MDS (12 months)
12	(10)	M	55	RAEB-2**	Very high****	NA	333	LVV	0	GC/Azacitidine	Dead for deterioration of MDS (49 days)
13	(1)	M	81	MDS-SLD***	Low****	NA	84	GCA	0	GC	AML (5 months)

* RA, ASIA, RAEB [French-American-British (FAB) classification, Bennett et al. 1982], ** RAEB-1, RAEB-2, RCMD [WHO (World Health Organization) 2008 classification of MDS], *** MDS-SLD (WHO 2016 classification of MDS), **** Risk groups classified by IPSS-R (revised-IPSS)

IPSS: International prognosis scoring system, RA: refractory anemia, RAEB: refractory anemia with excess blasts, RARS: refractory anemia with ringed sideroblasts, ASIA: acquired sideroblastic idiopathic anemia, RCMD: refractory cytopenia with multilineage dysplasia, SLD: single lineage dysplasia, NA: not available, GCA: giant cell arteritis, LVV: large vessel vasculitis, TA: Takayasu arteritis, GC: glucocorticoids, MTX: methotrexate, AML: acute myeloid leukemia

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