

## Ticlopidine에 의한 중증 호중구 감소증 2예

가

김성태 · 이정구 · 서찬종 · 신익균

## Two Cases of Severe Neutropenia Associated with Ticlopidine

Seong Tae Kim, MD, Jung Gu Lee, MD, Chan Jong Seo, MD and Eak Kyun Shin, MD

Department of Internal Medicine, Gachon Medical School, Gil Medical Center, Incheon, Korea

## ABSTRACT

Ticlopidine is a powerful inhibitor of platelet aggregation which is induced by adenosine diphosphate. Ticlopidine has been shown to be effective in reducing combined stroke, myocardial infarction, reocclusion of coronary stent. The principal side effects of ticlopidine are severe neutropenia, rash and gastrointestinal upset. Recently, we experienced two cases of severe neutropenia associated with ticlopidine. One was administered ticlopidine to prevent subacute thrombosis after intracoronary stent implantation in unstable angina pectoris. Thirty days of therapy, her absolute neutrophil count (ANC) had dropped to  $14/\text{mm}^3$ . The other patient was presented with recurrent episodes of cerebral infarction, for which he had undergone right carotid angiogram. The carotid angiogram demonstrated tight stenosis of right internal carotid artery. Carotid artery stenting was performed at right internal carotid artery without any complications. Twenty seven days of ticlopidine therapy, his ANC had dropped to  $111/\text{mm}^3$ . The ticlopidine was stopped, and they were given granulocyte-colony stimulating factor  $250 \mu\text{g/day}$  subcutaneous injection until their ANC was up to  $1000/\text{mm}^3$ . They were discharged with normal neutrophil count and no other complications. (Korean Circulation J 1999;29(7):746-750)

**KEY WORDS :** Ticlopidine · Neutropenia · Stent reocclusion · G-CSF.

## 서 론

ticlopidine thienopyridine  
가  $1,500/\text{mm}^3$  . 1984 Bruno  
adenosine diphosphate  
가 . Tic-  
10 30% lopidine  
2)3)  
: 1999 3 2  
: 1999 6 9  
: , 405 - 760 1198 . 4)5) Ticlopidine  
가  
: (032) 460 - 3204 · : (032) 469 - 4320 glycoprotein  
E - mail : EKShin@Ghil.com IIb/IIIa

Bleeding time

ticlopidine

증례

증례 1 :

: , 63 .

: , .

: 25 5

5 10

3.5 mm × 20 mm(JoMED™ Heparin bonded surface) stent ticlopidine 500 mg

2 30

2 ,

가 :

: 100/60 mmHg, 96

/ , 37.8 , 24 / ,

: Ticlopidine

12.9g/dl, 38.9%, 9,830/mm<sup>3</sup>  
( 61%, 29.8%, 5.4%,  
2.9%), 270,000/mm<sup>3</sup>

10.7 g/dl, 31.5%,  
111/mm<sup>3</sup>( 13%, 85%, 2%)

280,000/mm<sup>3</sup>, ESR 15 mm/h, CRP 5 positive  
cholesterol 155 mg/dl,  
HDL - cholesterol 52 mg/dl, 114 mg/dl,

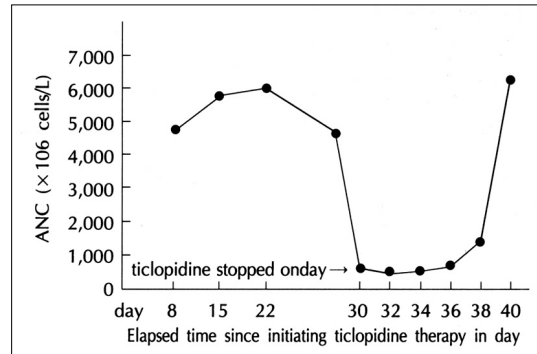


Fig. 1. Course of decline in absolute neutrophil count (ANC).

167 mg/dl,

Escheria coli

Fig. 1

: Ticlopidine

ticlopidine  
3 cephalosporin aminoglycoside  
granulocyte colony stimulating factor(G -  
CSF) 250 µg 1,000/mm<sup>3</sup>  
. 3 , 6  
300

mg 1

증례 2 :

: , 66 , .

: , 가 , , .

: 40 pack - years 가 3

, 8

300 mg 1

(transient  
ischemic attack)

95%

6 mm × 20 mm(PALMAZ™ balloon  
expandable) stent

ANC ( $\times 10^6$  cells/L)

ticlopidine stopped on day

day 8 15 22 27 29 31 33 35 42

Elapsed time since initiating ticlopidine therapy in day

Elapsed time (day)	ANC ( $\times 10^6$ cells/L)
0	4,800
8	6,500
15	7,000
22	6,100
27	500
29	400
31	500
33	800
35	2,100
42	5,900

Schomig<sup>10)</sup>  
ticlopidine 257  
phenprocoumon, 260  
82%, 78%  
가 0.8% 5.4%  
ticlopidine  
ticlopidine colony  
Ticlopidine  
Guillerno<sup>18)</sup> ticlopidine  
3 G-CSF 2 3  
1 10 가 2,000/  
Ticlopidine 10 15% mm<sup>3</sup>  
1 가  
(1%) , ticlopidine 2  
1989 x-ray  
ticlopidine  
G-CSF  
6 7  
가 가 3 1,000/mm<sup>3</sup>  
The Canadian G-CSF  
American Ticlopidine Study(CATS) Ticlopidine  
Aspirin Stroke Study(TASS) 0.9% 가  
(Absolute Neutrophil Count : ANC.  
450/mm<sup>3</sup>)  
(451-800/mm<sup>3</sup>)  
ticlopidine 1 3 dine  
, ticlopidine 3 ticlopidine  
. Ticlopidine 가  
2 1 가  
ANC가  
ticlopidine 30 27  
, ticlopidine  
G-CSF 6 7  
James<sup>15)</sup> Debrak<sup>16)</sup> 요 약  
ticlopidine Ticlopidine  
가

ticlopidine

가

ticlopidine

G - CSF

중심 단어 :

## REFERENCES

- 1) Rubidi R, Jelic S. *Haematological aspects of drug induced agranulocytosis. Scan J Haematol* 1972;9:18-27.
- 2) Weisberg LA, for the Ticlopidine Aspirin Stroke Study Group. *The efficacy and safety of ticlopidine and aspirin in non-whites; analysis of a patient subgroup from the Ticlopidine Aspirin Stroke Study. Neurology* 1993;43:27-31.
- 3) Gent M, Blakely JA, Easton JD, Ellis DJ, Hachinski VC, Harbison JW, et al. *The Canadian American Ticlopidine Study (CATS) in thromboembolic stroke. Lancet* 1989;1:1215-20.
- 4) Di Minno G, Cerbone AM, Mattioli PL, et al. *Functionally thrombosthenic state in normal platelets following the administration of ticlopidine. J Clin Invest* 1985;75:328-38.
- 5) Gachet C, Cazenove JP, Ohlmann P, et al. *The thienopyridine ticlopidine selectively prevents the inhibitory effects of ADP but not of adrenaline on cAMP levels raised by stimulation of the adenylate cyclase of human platelets by PGE. Biochem Pharmacol* 1990;40:2683-7.
- 6) Ito MK, Smith AR, Lee ML. *Ticlopidine: a new platelet aggregation inhibitor. Clin Pharm* 1992;11:603-17.
- 7) Cheong SS, Park SW, Park SJ, Suh DC, Lee MJ. *Percutaneous transluminal angioplasty with Palmaz-Schatz stent in the carotid artery stenosis. Korea Circulation J* 1996;26:921-5.
- 8) Julio C Palmaz, Jean C Laborde, Frank Rivera, Carlos E Encarnacion, et al. *Stenting of the iliac arteries with the Palmaz stent: Experience from a multicenter trial. Cardiovasc Intervent Radiol* 1992;15:291-7.
- 9) Balsano F, Rizzon P, Violi F, Scrutinio D, Cimminiello C, Aguglia F, et al. *Antiplatelet treatment with ticlopidine in unstable angina: A controlled multicenter clinical trial. Circulation* 1990;82:17-26.
- 10) Schomig A, Neumann FJ, Kastrati A, Schuhlen H, Blasini R, Hadamitzky M, et al. *A randomized comparison of antiplatelet and anticoagulant therapy after the placement of coronary artery stents. N Engl J Med* 1996;334:1084-9.
- 11) Balsano F, Rizzon P, Violi F, et al. *Antiplatelet treatment with ticlopidine in unstable angina: A controlled multicenter clinical trial. Circulation* 1990;82:17-26.
- 12) Hass WK, Easton JD, Adams HP, et al. *A randomized trial comparing ticlopidine hydrochloride with aspirin for the prevention of strokes in high risk patients. N Engl J Med* 1989;321:501-7.
- 13) Gent M, Easton JD, Hachinski VC, et al. *The Canadian American ticlopidine study (CATS) in thromboembolic stroke. Lancet*;1989. p.1215-20.
- 14) Haynes RB, Sandler RS, Larrons EB, Pater JL, Yatsu FM. *A critical appraisal of ticlopidine. A new antiplatelet agent. Arch Intern Med* 1992;152:1376-80.
- 15) James A Carlson, Jon E Maesner. *Fatal neutropenia and thrombocytopenia associated with ticlopidine: The annals of pharmacotherapy* 1994;28:1236.
- 16) Debrak Farver, Lori A Hansen. *Delayed Neutropenia with Ticlopidine: The Annals of pharmacotherapy* 1994;28:1344.
- 17) Ono K, Kurohara K, Yoshihara M, Shimamoto Y, Yamaguchi M. *Agranulocytosis caused by ticlopidine and its mechanism. Am J Hematol* 1991;37:239-42.
- 18) Guillermo R, Juan JA, Juan TJ, Ciraco A. *Granulocyte Colony-Stimulating Factor for Neuropenia Secondary to ticlopidine. Acta Haematol* 1994;91:106-7.
- 19) Gardner FH. *Ticlopidine-induced neutropenia; recognition and management. IM* 1989;12:35-8,41.
- 20) Lee SG, Ahn CW, Kim HS, Rim SJ, Cho SY, Min YH. *A case of ticlopidine-induced neutropenia treated with rhG-CSF. Korea Circulation J* 1998;28:118-22.