Antithyroid Drug-induced Agranulocytosis: Report of 13 Cases

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Background: Antithyroid drug (ATD)-induced agranulocytosis is rare but may cause fatal complications in patients with thyrotoxicosis during treatment with thionamide-derived drugs. From our previous experience, we note that 2 of 11 such patients died in a 10-year retrospective study.

Methods: We reviewed thirteen patients who developed agranulocytosis from 7,466 patients with hyperthyroidism while they were being treated with ATD from July 1989 to November 2003.

Results: The incidence of ATD-induced agranulocytosis (absolute neutrophil counts $< 500/mm^3$) was 0.17%. The age of the 13 patients (female: male = 10:3) was 28 to 61 years (mean $\pm$SD: 39.6 $\pm$10.0 years). The most common clinical manifestations were fever (100%), sore throat (76.9%) and chills (46.1%). At the time of agranulocytosis attack, ATD had been administered for 12 to 66 days (mean $\pm$ SD: 36.4 $\pm$ 18.7 days) and the duration of symptoms was 1 to 14 days (mean $\pm$ SD: 4.6 $\pm$ 3.7 days). Intravenous infusion of 300 μg granulocyte colony-stimulating factor (G-CSF) per day was administered to 3 patients simultaneously with intravenous empirical broad-spectrum antibiotics. After intensive and supportive treatment in hospital, all the patients recovered with absolute neutrophil counts of more than $500/mm^3$ in 2 to 13 days (mean $\pm$ SD: 7.6 $\pm$ 3.4 days).

Conclusions: In our 25-year clinical experience, the most cost-effective method of managing agranulocytosis induced by thionamide-derived ATD is that all patients with thyrotoxicosis must be warned that their white blood cells and differential counts should be checked immediately whenever the "common cold" symptoms occur during treatment, especially within the first 3 months of medication.

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Key words: Graves' hyperthyroidism, antithyroid drugs, agranulocytosis

Graves' disease is an organ-specific autoimmune disease. The hypersecretion of thyroid hormone from the thyroid gland is mainly mediated by circulating thyrotropin (TSH) receptor antibodies. Although the mechanisms of this pathological immune process have been much explored, the ideal treatment to correct this autoimmune disorder remains unclear, both in clinical practice and basic research.[1,2] Thionamide-derived antithyroid drugs (ATD), radioactive iodine and surgery are currently

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the treatments for patients with Graves' hyperthyroidism. Except in North America where radioactive iodine is preferred as the treatment for those with Graves' hyperthyroidism, ATD are used nearly everywhere else, including Taiwan.[3]

In the treatment of thyrotoxicosis, the most serious adverse effect of ATD, which may lead to fatal complications, is agranulocytosis. Its incidence was reported to be less than 1% and the estimated risk was 3 per 10,000 patients per year.[1,4-6] In our previous ten-year retrospective study (January 1979 to June 1989), we found that among 11 patients with ATD-induced agranulocytosis, the mortality rate was 18%.[7] In this study, we report on a further 13 patients with ATD-induced agranulocytosis from July 1989 to November 2003.

METHODS

Based on the computerized data of 7,466 patients with a discharge diagnosis of hyperthyroidism (ICD code 288), 31 patients were simultaneously associated with agranulocytosis/leukopenia (ICD code 242) from July 1989 to November 2003. Among these, 13 patients with ATD-induced agranulocytosis were documented while they were hospitalized in Chang Gung Memorial Hospital (Linkou). All the patients with hyperthyroidism and agranulocytosis/leukopenia were reviewed. Agranulocytosis was defined as an absolute neutrophil count of $< 500/mm^3$. Among these 13 patients, thyrotropin-binding inhibitory immunoglobulin was recorded as positive (> 15%) in 6 patients.

As soon as agranulocytosis was diagnosed, ATD was discontinued. After blood samples for bacterial culture were obtained, all patients were treated intensively with parenteral antibiotics. Three patients were administered intravenous granulocyte-colony stimulating factor (G-CSF), 300 μg per day, for 5 days. White blood cells and differential counts were checked every day in the first week and then every two days, whilst in hospital, if the absolute neutrophil count was still $< 500/mm^3$. After discharge from hospital, all patients with ATD-induced agranulocytosis were followed up monthly for at least 6 months.

Bone marrow examinations were performed on five patients (patient no. 3, 6, 7, 8 and 12) because other hematological disorders needed to be excluded, such as unexplained cytopenia, leukemia and myeloproliferative disorder etc.

The results were expressed as mean ± SD. Mann-Whitney U test was used to compare the outcomes of the patients who received G-CSF intravenously with those who did not receive it. A p value < 0.05 was considered to be statistically significant.

RESULTS

The incidence of ATD-induced agranulocytosis in patients with hyperthyroidism was 0.17% (95% CI = 0.08% - 0.26%) in this study. The clinical characteristics of 13 patients with ATD-induced agranulocytosis are depicted in Table 1. The age of the 13 patients was 28 to 61 years (mean ± SD: 39.6 ± 10.0 years). Ten patients were female (mean ± SD: 39.9 ± 11.1 years) and three were male (mean ± SD: 38.7 ± 6.5 years). Four patients were treated with propylthiouracil, 6 patients with methimazole and 3 patients with carbimazole. When agranulocytosis was detected, ATD had been administered for 12 to 66 days (mean ± SD: 36.4 ± 18.7 days) and the duration from the onset of symptoms to laboratory confirmation of agranulocytosis was 1 to 14 days (mean ± SD: 4.6 ± 3.7 days). One patient with methimazole-induced agranulocytosis (patient no. 10), was unfortunately prescribed carbimazole 2 months later and a similar episode of agranulocytosis subsequently developed. She was admitted to hospital for intensive treatment again and discharged without any complications.

Among these 13 patients with ATD-induced agranulocytosis, three patients had a history of drug-induced allergic reaction. One patient (patient no. 11) had skin rashes induced by carbimazole and she was then treated with methimazole. Another two patients had a history of skin itching due to oral medication of penicillin-V (patient no. 1) and propranolol (patient no. 4).

The major complaints that caused patients to visit the outpatient clinic or emergency unit for medical help were fever (100%), sore throat (76.9%), chills (46.1%), cough (30.8%) and rhinorrhea (30.8%). Other symptoms (7% to 14%) were general malaise, oral ulcer, skin rashes, headache, palpitations and dysphagia (Table 2).

At the onset of agranulocytosis, the blood leukocyte counts were 0.1 to 2.3 x $10^3/mm^3$ (mean ± SD:

Table 1. The Clinical Characteristics of 13 Hyperthyroidism Patients Treated with Antithyroid Drugs at Onset of Agranulocytosis

Case no.	Gender	Age (yr)	Medication	Dose (mg/day)	Treatment duration (days)	Symptom duration (days)†
1*	F	28	Propylthiouracil	100 mg bid	26	6
2	F	61	Methimazole	5 mg tid	31	7
3	M	45	Methimazole	5 mg tid	60	14
4*	F	47	Methimazole	10 mg tid	30	7
5	F	33	Propylthiouracil	100 mg tid	28	5
6	F	29	Carbimazole	20 mg tid	31	6
7	M	39	Carbimazole	10 mg tid	57	2
8	F	42	Propylthiouracil	100 mg tid	13	2
9	M	32	Propylthiouracil	100 mg bid	60	1
10	F	34	Methimazole	10 mg bid	21	1
11*	F	32	Methimazole	10 mg tid	12	2
12	F	54	Carbimazole	10 mg bid	66	6
13	F	39	Methimazole	5 mg tid	18	1
Mean ±SD		39.6 ±10.0			36.4 ±18.7	4.6 ± 3.7

*: History of drug-induced allergic reaction such as skin rashes or itching; †: Time from the onset of symptoms to laboratory data confirmation of agranulocytosis

Table 2. Major Complaints of 13 Patients with Antithyroid Drug-induced Agranulocytosis

Symptoms	Number of patients	%
Fever	13	100
Sore throat	10	76.9
Chills	6	46.1
Cough	4	30.8
Rhinorrhea	4	30.8
Malaise	2	13.8
Oral ulcer	2	13.8
Rash	1	7.7
Headache	1	7.7
Palpitations	1	7.7
Dysphagia	1	7.7

$1.05 \pm 0.64 \times 10^3/mm^3$) and absolute neutrophil counts were 5 to 400/mm^3 (mean ± SD: 125.00 ± 140.50/mm^3) (Table 3). Furthermore, according to thyroid function tests, 9 patients were still in a hyperthyroid state, 7 patients with T4 13.6-21.6 μg/dL (normal range 5.0-12.4 μg/dL), TSH 0.001-0.2 uIU/mL (normal range 0.4-4.5 uIU/mL); 2 patients with free T4 1.92-2.71 ng/dL (normal range 0.85-1.86 ng/dL). The other 4 patients were in a euthyroid state with T4 5.06-12.05 μg/dL (normal range 5.0-12.4 μg/dL), TSH 0.003-1.2 uIU/mL (normal range 0.4-4.5 uIU/mL). The recovery time for absolute neutrophil counts of more than 500/mm^3 was 2 to 13 days (mean ± SD: 7.6 ± 3.4 days) after intensive and supportive treatment in hospital. Three patients (patient no. 3, 6 and 8) were administered intravenous G-CSF 300 μg per day during admission but did not show significant benefit based on the time of recovery (mean ± SD: 9.0 ± 3.6 days) for absolute neutrophil counts above 500/mm^3 when compared with the other 10 patients who did not receive G-CSF (mean ± SD: 7.0 ± 3.3 days) (p = 0.31; statistical power of 13%).

Bone marrow studies were performed in five patients (patient no. 3, 6, 7, 8 and 12) at the time of agranulocytosis. Four of them (patient no. 3, 6, 7 and 8) showed myeloid hypoplasia. Erythroid series slightly increased in one patient (patient no. 8). Infiltration of plasma cells was found in two patients (patient no. 8 and 12) and many vacuolated macrophages in one patient (patient no. 6).

Four of the thirteen patients had positive blood cultures (31%), including Enterobacter agglomerans (patient no. 7), Streptococcus species (patient no. 10), methicillin-resistant Staphylococcus epidermidis (patient no. 12) and Klebsiella pneumoniae (patient no. 13). The bacterial culture of a peri-anal abscess

Table 3. Blood Leukocyte Counts in Patients with Antithyroid Drug-induced Agranulocytosis

Patient no.	At onset of agranulocytosis		On recovery		
	Leukocyte (1000/mm^3)	Absolute neutrophil count (/mm^3)	Leukocyte (1000/mm^3)	Absolute neutrophil count (/mm^3)	Period (days)
1	2.3	208	3.6	1584	6
2	2.2	374	4.9	2450	5
3*	0.6	12	2.0	720	8
4	0.5	220	5.4	3996	5
5	1.4	126	3.8	1520	5
6*	1.4	0	8.2	4059	6
7	0.7	140	3.6	576	2
8*	1.2	11	2.2	748	13
9	0.8	112	7.1	3124	12
10	0.8	8	3.1	1023	7
11	0.1	5	2.9	667	13
12	0.9	9	2	860	10
13	0.8	400	2.1	609	7
Mean	1.05	125.00	3.92	1498.92	7.6
± SD	± 0.64	± 140.50	± 1.98	± 1348.64	± 3.4

*: Granulocyte colony stimulating factor (G-CSF) 300 μg per day was administered intravenously for 5 days during admission; when compared with after patients who did not receive G-CSF, the p value = 0.31.

revealed the same organism in patient no. 7. Septic shock was diagnosed in one patient (patient no. 13). Broad-spectrum antibiotics were administered intravenously to all patients. After hospitalization with intensive parenteral broad-spectrum antibiotic treatment and supportive care, all 13 patients were discharged without any complications or mortality.

DISCUSSION

ATD-induced agranulocytosis is rare but it may lead to mortality, mainly due to severe systemic infection, if appropriate medical intervention is not given immediately. The incidence of ATD-induced agranulocytosis in patients with hyperthyroidism has been reported to be less than 1%.[1] In this study, the incidence of this complication was 0.17% (95% CI = 0.08% - 0.26%), similar to a study with an incidence of 0.23% reported by Sheng et al. in Taiwan.[8] It is worth paying attention to because three quarters of patients with thyrotoxicosis are initially treated with ATD worldwide, except in North America where radioactive iodine is favored.[3]

In 1983, Cooper et al. concluded that higher doses of methimazole, greater than 30 mg/day, and/or age over 40 years caused higher risk of development of agranulocytosis, which usually occurred within the first 2 months of ATD therapy.[4] In the present study, the doses of methimazole or carbimazole of 15 to 30 mg/day (mean ± SD: 22.78 ± 7.12 mg/day) for 9 patients (69%) were significantly lower than reported by Cooper et al. in which that 57% were treated with methimazole 30 to 60 mg/day (mean ± SD: 49.4 ± 16.13 mg/day) (p = 0.000; Mann-Whitney U test).[4] Although a higher dose of ATD and a longer drug treatment period might cause greater probability of agranulocytosis, this serious complication can occur at any time, and even a lower dose of ATD cannot protect the patient from agranulocytosis.[6,7,9] McGavack and Chevalley reported that granulocytopenia rarely appeared before the tenth day of ATD treatment. This might be due to slow accumulation of enough ATD to induce a reaction in bone marrow tissue.[10] On the other hand, the majority of ATD-induced agranulocytosis usually occurs within 2 months of treatment.[4,6-8] In our study, the onset of agranulocytosis was between 12 and 66 days after treatment with ATD. In additional four previous

studies on 56 Chinese patients with ATD-induced agranulocytosis, 53 patients (95%) were reported to have a duration of ATD-induced agranulocytosis of about 12 days to 2 months, whereas the other 3 patients (5%) had a duration of up to 5 months.[7,8,11,12]

A previous course of ATD treatment without the occurrence of agranulocytosis should not be considered to suggest that it will not occur during a second exposure to ATD.[1,4,6,7] In a 10-year retrospective study, we reported that three patients with Graves' hyperthyroidism who did not suffer from ATD-induced agranulocytosis in the first treatment course went on to suffer from this serious adverse event during treatment with ATD for recurrent hyperthyroidism.[7] In terms of the pharmacological mechanism, carbimazole is identical to methimazole because carbimazole is rapidly metabolized to methimazole in the liver after absorption.[13] Therefore, a patient (patient no. 10 in this study) who has developed methimazole-induced agranulocytosis in the past should not be prescribed carbimazole subsequently. Furthermore, the alternative of propylthiouracil should also be avoided because of the possibility of immunological cross-reactivity.[6,14] All of the patients with hyperthyroidism in this study were treated with radioactive iodine later, except one patient (no. 11) who underwent bilateral subtotal thyroidectomy. Replacement therapy with thyroxine was given to all of these patients as a hypothyroid state developed subsequently.

The mechanism of ATD-induced agranulocytosis in patients with hyperthyroidism was demonstrated in vitro to be a drug-induced immune-mediated process rather than a direct toxic effect of ATD.[6,14-18] In those study, Wall et al. reported that in vitro peripheral lymphocyte transformation in response to ATD and circulating antibodies against neutrophils were significantly demonstrated in the patients with ATD-induced agranulocytosis when compared with control patients.[14] Using direct immunofluorescence tests, a transient autoantibody responsible from patients with agranulocytosis might be induced by propylthiouracil.[15] This ATD-induced specific immune-mediated process reacted not only with mature granulocytes but also affected both mature blood cells and myeloid progenitor cell growth.[16-18] In this study, of the 5 patients who underwent bone marrow examination at the time of agranulocytosis, 4 patients (patient no. 3, 6, 7 and 8) showed myeloid hypoplasia. The erythroid series slightly increased in one patient (patient no. 8). This situation was similar to the rats intoxicated with thiouracil, resulting in a decrease in the myeloid: erythroid ratio in the bone marrow.[10]

Although the risk of life-threatening bacterial infection was considered to be the main cause of death in patients with ATD-induced agranulocytosis, the bacterial cultures from blood samples were reported as "no growth to date" among more than half of such patients.[7,8] As for the available data of ATD-induced agranulocytosis in Taiwan, including this study, the mortality rates of the patients with positive bacterial blood culture (one of 14 patients) and those with negative culture (3 of 24 patients) was not significant (p value = 1, Fisher's exact test).[7,8,11] Although Pseudomonas aeruginosa and Klebsiella pneumoniae were reviewed as the most common causes of bacteremia in this critical condition, empirical broad-spectrum intravenous antibiotics should be initiated to cover both aerobic, including Gram-positive and Gram-negative, and anaerobic bacterial infection as soon as possible until the results of bacterial blood cultures are available.[8]

Although G-CSF was touted as an effective treatment for ATD-induced agranulocytosis, the benefit of G-CSF in such patients has not yet been documented, including a prospective randomized trial.[8,19,20] In this study, we demonstrated that the administration of G-CSF to 3 patients did not shorten their time of recovery when compared with the other 10 patients who did not receive it (p = 0.31). However, only 13 patients were included in this study with a statistical power of 0.13, which is far too low to make any conclusive remarks.

In this study, no mortality was noted in contrast to our previous report when 2 patients died in hospital.[7] In our 25 years clinical experience, the routine monitoring of white blood cells and differential counts has been not a cost-effective method. Early detection of the onset of this fatal complication induced by ATD is the key factor in rescuing patients in such critical conditions. The most common clinical symptoms of agranulocytosis were similar to those caused by upper respiratory tract infection or the so-called "common cold". Thus we also agree that all patients with thyrotoxicosis must be warned to return to the emergency unit or contact a physician immediately to have white blood cells and differen-

tial counts measurement whenever fever, sore throat and chills occur during treatment with ATD.

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REFERENCES

1. Weetman AP. Graves' disease. N Engl J Med 2000;343:1236-48.
2. Steinman L. Immune therapy for autoimmune diseases. Science 2004;305:212-6.
3. Wartofsky L, Glinoer D, Solomon B, Nagataki S, Lagasse R, Nagayama Y, Izumi M. Differences and similarities in the diagnosis and treatment of Graves' disease in Europe, Japan, and the United States. Thyroid 1991;1:129-35.
4. Cooper DS, Goldminz D, Levin AA, Ladenson PW, Daniels GH, Molitch ME, Ridgway EC. Agranulocytosis associated with antithyroid drugs. Effects of patient age and drug dose. Ann Intern Med 1983;98:26-9.
5. Davies TF, Larsen PR. Thyrotoxicosis. In: Larsen PR, Kronenberg HM, Melmed S, Polonsky KS, eds. Williams Textbook of Endocrinology. 10th ed. Philadelphia: WB Saunders, 2003:374-421.
6. Cooper DS. Antithyroid drugs. N Engl J Med 2005;352: 905-17.
7. Li KL, Huang HS, Wang PW, Lin JD, Juang JH, Liu RT, Huang BY, Huang MJ. Agranulocytosis associated with anti-thyroid drug in patients with Graves' thyrotoxicosis--report of 11 patients. Chang Gung Med J 1991;14:168-73.
8. Sheng WH, Hung CC, Chen YC, Fang CT, Hsieh SM, Chang SC, Hsieh WC. Antithyroid-drug-induced agranulocytosis complicated by life-threatening infections. QJM 1999;92:455-61.
9. Cooper DS, Daniels GH, Ridgeway EC. Agranulocytosis and dose of methimazole. Ann Intern Med 1984;101:283.
10. McGavack TH, Chevalley J. Untoward hematologic responses to the antithyroid compounds. Am J Med 1954;17:36-40.
11. Hou GL, Tsai CC. Oral manifestations of agranulocytosis associated with methimazole therapy. J Periodontol 1988;59:244-8.
12. Dai WX, Zhang JD, Zhan SW, Xu BZ, Jin H, Yao Y, Xin WC, Bai Y. Retrospective analysis of 18 cases of antithyroid drug (ATD)-induced agranulocytosis. Endocr J 2002;49:29-33.
13. Nakashima T, Taurog A. Rapid conversion of carbimazole to methimazole in serum; evidence for an enzymatic mechanism. Clin Endocrinol (Oxf) 1979;10:637-48.
14. Wall JR, Fang SL, Kuroki T, Ingbar SH, Braverman LE. In vitro immunoreactivity to propylthiouracil, methimazole, and carbimazole in patients with Graves' disease: a possible cause of antithyroid drug-induced agranulocytosis. J Clin Endocrinol Metab 1984;58:868-72.
15. Toth EL, Mant MJ, Shivji S, Ginsberg J. Propylthiouracil-induced agranulocytosis: an unusual presentation and a possible mechanism. Am J Med 1988;85:725-7
16. Douer D, Eisenstein Z. Methimazole-induced agranulocytosis: growth inhibition of myeloid progenitor cells by the patient's serum. Eur J Haematol 1988;40:91-4.
17. Fibbe WE, Claas FH, Van der Star-Dijkstra W, Schaafsma MR, Meyboom RH, Falkenburg JH. Agranulocytosis induced by propylthiouracil: evidence of a drug dependent antibody reacting with granulocytes, monocytes and haematopoietic progenitor cells. Br J Haematol 1986;64:363-73.
18. Salama A, Northoff H, Burkhardt H, Mueller-Eckhardt C. Carbimazole-induced immune haemolytic anaemia: role of drug-red blood cell complexes for immunization. Br J Haematol 1988;68:479-82.
19. Tajiri J, Noguchi S, Okamura S, Morita M, Tamaru M, Murakami N, Niho Y. Granulocyte colony-stimulating factor treatment of antithyroid drug-induced granulocytopenia. Arch Intern Med 1993;153:509-14.
20. Fukata S, Kuma K, Sugawara M. Granulocyte colony-stimulating factor (G-CSF) does not improve recovery from antithyroid drug-induced agranulocytosis: a prospective study. Thyroid 1999;9:29-31.
21. Tajiri J, Noguchi S, Murakami T, Murakami N. Antithyroid drug-induced agranulocytosis. The usefulness of routine white blood cell count monitoring. Arch Intern Med 1990;150:621-4.
22. Hanna FW, Lazarus JH, Scanlon MF. Controversial aspects of thyroid disease. BMJ 1999;319:894-9.
23. Toft AD, Weetman AP. Screening for agranulocytosis in patients treated with antithyroid drugs. Clin Endocrinol (Oxf) 1998;49:271.

抗甲狀腺藥物在甲狀腺高能症病患引起之無嗜中性白血球症：13病例報告

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背 景： 抗甲狀腺藥物引起的無嗜中性白血球症很少見，但對正在接受抗甲狀腺藥物治療的甲狀腺高能症病患而言，它有可能會引起潛在致命的併發症。在我們之前的 10 年研究，本院回顧分析報告的 11 位類似病例中有 2 位死亡。

方 法： 在西元 1989 年 7 月到 2003 年 11 月這段期間，本院的出院診斷含有甲狀腺高能症患者共計 7,466 位，我們統計並分析其中 13 位甲狀腺高能症病患合併發生抗甲狀腺藥物引起的無嗜中性白血球症的臨床結果。

結 果： 抗甲狀腺藥物引起的無嗜中性白血球症 (嗜中性白血球 < 500/mm^3) 發生率爲 0.17%。13 位病患年齡平均值爲 39.6 ± 10.0 歲，女與男的比例是 10：3。臨床最常見的徵狀是發燒 (100%)、喉嚨痛 (76.9%)、及發冷 (46.1%)。發生無嗜中性白血球症前服用抗甲狀腺藥物天數平均爲 36.4 ± 18.7 天，從徵狀發生到確定診斷是無嗜中性白血球症平均 4.6 ±3.7 天。確定診斷後，除了立刻停用抗甲狀腺藥物及給與靜脈注射廣效的抗生素藥物治療外，另有 3 位病患接受白血球生成因子 (G-CSF) 每天 300 μg 的輸注，但對絕對嗜中性白血球數加速回復所需的時間並沒有統計學上顯著的意義 (p = 0.31)。13 位病患的絕對嗜中性白血球數回升至 ≥ 500/mm^3 平均所需的時間爲 7.6 ± 3.4 天。病人皆康復出院。

結 論： 臨床上，要預防抗甲狀腺藥物引起的無嗜中性白血球症，最佳的方法是明確告知正在接受抗甲狀腺藥物治療的甲狀腺高能症病患提高警覺，尤其在投予抗甲狀腺藥物的初始三個月內，一旦發生發燒、喉嚨痛等類似感冒症狀時，要立刻回診或至附近醫療院所就醫，並同時檢驗白血球及絕對顆粒球數。

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關鍵詞：甲狀腺高能症，抗甲狀腺藥物，無嗜中性白血球症

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