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Two patients with chronic hepatitis C who displayed a hypothyroidism during peginterferon therapy without clinical manifestations : Significance of negativity for thyroid-stimulation blocking antibody

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Abstract

Patient 1 was a 43-year-old woman on combined treatment with peginterferon-α 2a and ribavirin. Before starting treatment, TgAb and TPOAb were slightly positive. At 20 weeks after starting treatment, hypothyroidism developed, and treatment was discontinued. At 4 weeks after treatment discontinuation, TSH had worsened to 142.7 μIU/mL, FT3 to 0.8 pg/mL, and FT4 to 0.3 ng/dL. The patient had no overt clinical manifestations, and was thus followed up without specific therapy. At 22 weeks after treatment discontinuation, her thyroid function normalized. This was regarded as the natural course for painless thyroiditis. During the clinical course, TRAb, TSAb and TSBAb were negative. Patient 2 was a 45-year-old man who was started on peginterferon-α 2a, followed 3 weeks later with combined ribavirin. Before onset, TgAb, TPOAb and TRAb were positive. At 28 weeks after starting treatment, hypothyroidism developed, and treatment was discontinued. At 8 weeks after treatment discontinuation, TSH had worsened to 207.1 μIU/mL, FT3 to 1.3 pg/mL, and FT4 to 0.2 ng/dL. Although the patient had no overt clinical manifestations, Thyradin S 100 μg/day was started. Subsequently, laboratory values improved gradually, and by 17 weeks after treatment discontinuation, they had normalized. During the clinical course, TSBAb was negative. This case was regarded as a combination of latent hypothyroidism and painless thyroiditis. In both cases, TSBAb was not detected, thus suggesting a relationship with the absence of overt clinical manifestations.

Key words : peginterferon, hypothyroidism, painless thyroiditis, latent thyroid dysfunction, thyroid autoantibody

Introduction

In Japan, peginterferon is widely used as treatment in cases of chronic hepatitis C, serogroup 1, with high viral loads, and this has contributed to improved cure rates. The combination of peginterferon and ribavirin is known to enhance these antiviral effects, and consequently, even greater caution is necessary than with conventional interferon therapy, and adverse effects must be closely monitored [1, 2)]. We have reported that when using peginterferon in chronic hepatitis C patients, prior to starting treatment, antithyroid antibodies are detected at high rates; thus, the appearance of thyroid dysfunction, including latent thyroid dysfunction, must be carefully monitored [3)]. In addition, we reported a case in which Graves' disease developed during peginterferon monotherapy, followed by transition to hypothyroidism after treatment, and subsequently requiring thyroid hormone replacement therapy [4)].

In this report, we present 2 patients on peginterferon treatment who clearly developed laboratory evidence of hypothyroidism, but without any overt clinical symptoms. Based on our experiences with these cases, we herein report on the propriety of continuing peginterferon in such patients and whether symptomatic therapy is needed.

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Case reports

Patient 1

This 43-year-old woman had a height of 167.5 cm, weight of 68.3 kg, and a past history of intravenous drug use. She had been followed up for chronic hepatitis C over a 2-year period at Hospital A, her ALT was almost normal, and she had no subjective symptoms. Her physical examination was unremarkable, including no thyroid goiter. On August 15, 2009, at the patient's request, subcutaneous peginterferon-α 2a (Pegasys®) 90 μg/week and oral ribavirin 400 mg/day were started. Laboratory data when treatment was started are shown in Table 1. HCV-RNA load was 5.8 log/mL, serogroup 1. TSH, free T3 (FT3), and free T4 (FT4) were within normal limits, but antithyroglobulin antibody (TgAb) and antithyroid peroxidase antibody (TPOAb) were slightly positive at 1.0 U/mL and 0.3 U/mL, respectively. During the subsequent treatment course, HCV-RNA did not decrease, and thus, starting on September 19, ribavirin was increased to 600 mg/day, and starting on October 9, peginterferon-α 2a was increased to 180 μg/week.

Table1. Laboratory data at the start of therapy (patient 1)

Hematology		Virus and other markers	
WBC	5,530/μL	HBsAg	(−)
RBC	442x10⁴/μL	HBsAb	(−)
Hb	12.9g/dL	HBcAb	(−)
Ht	41.1%	HCV core Ab	109.2U
Platelet	204,000/μL	HCV-RNA	5.8(log)/mL
		serogroup	1
Electrolytes and renal function		AFP	1.8ng/mL
Na	136mEq/L		
K	4.1mEq/L	Blood chemistry	
Cl	102mEq/L	AST	22IU/L
UN	10.2mg/dL	ALT	20IU/L
CRNN	0.58mg/dL	LDH	137IU/L
		γ GTP	30IU/L
Thyroid function		Al-P	181IU/L
TSH	2.1μIU/mL	T.Chol	159mg/dL
FT3	2.8pg/mL	TG	67mg/dL
FT4	0.9ng/dL	TP	7.4g/dL
TPOAb	0.3U/mL	IgG	1,708mg/dL
TgAb	1.0U/mL	IgA	203mg/dL
TRAb	10%>	IgM	208mg/dL
		CRP	0.3>mg/dL

The patient had no subjective symptoms, but on January 4, 2010, 20 weeks after starting treatment, the laboratory data indicated hypothyroidism, showing TSH levels of 68.1 μIU/mL, FT3 levels of 1.3 pg/mL, and FT4 levels of 0.4 ng/dL; thus, peginterferon-α 2a and ribavirin were discontinued (Table 2).
The laboratory data continued to worsen, with values on February 6, 4 weeks after treatment discontinuation, showing TSH of 142.7 μIU/mL, FT3 of 0.8 pg/mL, and FT4 of 0.3 ng/dL. The patient had no subjective symptoms and no goiter, so follow-up was continued, without specific therapy. Subsequently, laboratory data improved gradually, and by June 5, 22 weeks after treatment discontinuation, values normalized to 1.2 μIU/mL, 2.7 pg/mL and 1.0 ng/dL for TSH, FT3 and FT4, respectively. HCV-RNA was persistently positive; thus, no virological response was achieved (Table 3).

When we pay attention to the serial changes in TSH, FT3 and FT4 during the clinical course (Figure 1), just before the onset of hypothyroidism, TSH decreased, with the appearance of transient latent hyperthyroidism. Similarly, we noticed the changes in TgAb and TPOAb antibody titers during the clinical course, at the time of hypothyroidism onset, as

Table2. Laboratory data 20 weeks after the start of therapy (patient 1)

Hematology		Virus and other markers	
WBC	2,010/μL	HCV core Ab	66.6U
RBC	359x10⁴/μL	HCV-RNA	3.1(log)/mL
Hb	11.4g/dL	AFP	2.4ng/mL
Ht	35.8%		
Platelet	124,000/μL	Blood chemistry	
		AST	22U/L
Electrolytes and renal function		ALT	14IU/L
Na	136mEq/L	LDH	149IU/L
K	3.9mEq/L	γ GTP	26IU/L
Cl	102mEq/L	Al-P	208IU/L
UN	9.9mg/dL	T.Chol	180mg/dL
CRNN	0.56mg/dL	TG	165mg/dL
		TP	7.5g/dL
Thyroid function			
TSH	68.1μIU/mL		
FT3	1.3pg/mL		
FT4	0.4ng/dL		

compared to before treatment, both antibody titers were elevated, but with normalization of thyroid function, both antibody titers gradually decreased. During this time, TSH receptor antibody (TRAb), thyroid stimulating antibody (TSAb), and thyroid-stimulation blocking antibody (TSBAb) remained negative (Figure 2).

Table3. Laboatory data 22 weeks after the stop of therapy (patient 1)

Hematology		Virus and other markers	
WBC	6,600/μL	HCV-RNA	6.1(log)/mL
RBC	422x10⁴/μL		
Hb	11.2g/dL	Blood chemistry	
Ht	35.6%	AST	47IU/L
Platelet	186,000/μL	ALT	44IU/L
		LDH	160IU/L
Electrolytes and renal function		γ GTP	79IU/L
Na	134mEq/L	Al-P	171IU/L
K	4.1mEq/L	T.Chol	174mg/dL
Cl	104mEq/L	TG	133mg/dL
UN	12.9g/dL	TP	7.1g/dL
CRNN	0.50mg/dL		
Thyroid function			
TSH	1.2μIU/mL		
FT3	2.7pg/mL		
FT4	1.0ng/dL		
TPOAb	39.3IU/mL		
TgAb	248.5IU/mL		

HCV-RNA did not disappear even during treatment, whereas ALT was normal, becoming slightly elevated after onset of hypothyroidism, before returning to its previous value with normalization of laboratory data. Total cholesterol also transiently increased with the onset of hypothyroidism, but returned to its previous values with improvement of the laboratory data (Figure 3).

Patient 2

This 45 year-old-man had a height of 180.0 cm, weight of 75 kg, and a history of diabetes mellitus. His other past medical history was unremarkable. He had a 20-year history of alcohol use equivalent to 70 g/day of ethanol. He had no subjective symptoms, and physical examination was unremarkable, including no thyroid goiter. Because of persistent ALT fluctuations, subcutaneous peginterferon-α 2a (Pegasys®) 90 μg/week was started on July 24, 2009, at Hospital B. However, the HCV-RNA load did not decrease, and on August 18, oral ribavirin 400 mg/day was added. On October 16, 12 weeks after starting treatment, he was transferred to Hospital A. Laboratory data when treatment was started at Hospital B

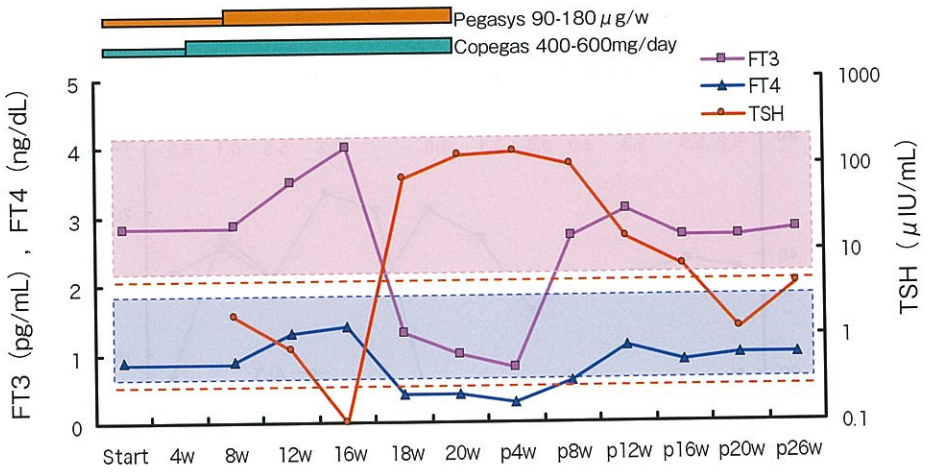

Figure 1. Serial changes of FT3, FT4 and TSH level in a 43-year-old female treated with peginterferon monotherapy. Netted background represents the range of each normal value of FT3 and FT4. Broken lines show upper and lower limit of normal level of TSH.

showed an HCV-RNA load of 4.1 log/mL, serogroup 2, ALT of 256 IU/L, and HbA1c of 7.7% (Table 4) . Laboratory data at the time of transfer to Hospital A showed persistently abnormal ALT levels of 223 IU/L, but HCV-RNA had become negative. A slightly elevated TSH of 4.3 U/mL was noted, and TgAb, TPOAb and TRAb were all positive at 11.1 U/mL, 52.1 U/mL and 55.9%, respectively (Table 5) .

On February 12, 2010, 28 weeks after starting treatment, laboratory data indicated hypothyroidism, with TSH of 13.0 μIU/mL and FT4 of 0.8 ng/dL; thus, peginterferon and ribavirin were discontinued. Subsequently, the laboratory data continued to worsen, with values on April 9, 8 weeks after treatment discontinuation, of TSH 207.1 μIU/mL, FT3 1.3 pg/mL, and FT4 0.2 ng/dL. Thyradin S® 100 μg/day was therefore started (Table 6) . During this time, the patient had no subjective symptoms, and there was no new appearance of goiter. Subsequent laboratory data improved gradually, and by June 12, 17 weeks after treatment discontinuation, TSH had almost normalized, and further clinical course was stable.

When we pay attention to the serial changes

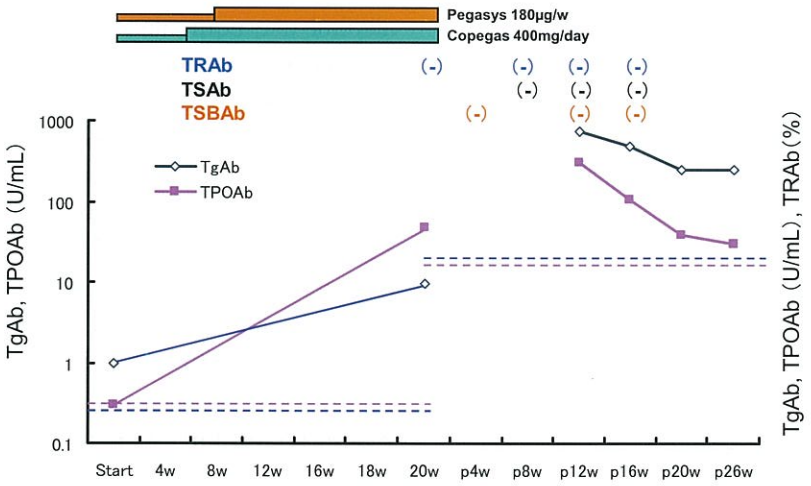

Figure 2. Serial changes of TPOAb , TgAb, TRAb, TSAb and TSBAb level in a 43-year-old female treated with peginterferon. Broken lines show upper limit of normal level of each TPOAb and TgAb.

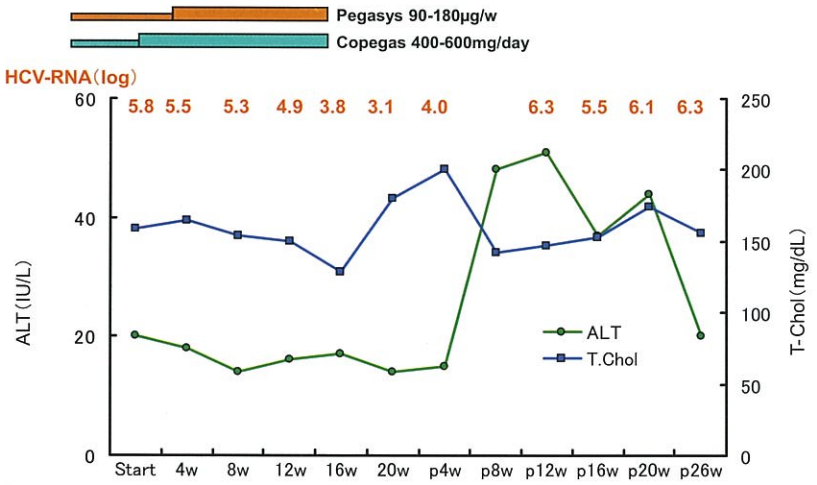

Figure 3. Serial changes of ALT, T-Chol and HCV-RNA level in a 43-year-old female treated with peginterferon monotherapy.

in TSH, FT3, and FT4 during the clinical course, as in patient 1, just before the onset of hypothyroidism, TSH decreased, with the appearance of transient latent hyperthyroidism (Figure 4). When we noticed the serial changes in TgAb and TPOAb antibody titers during the clinical course, as in patient 1, at the time of hypothyroidism onset, as compared to before treatment, both antibody titers were elevated, but with normalization of thyroid function, both antibody titers gradually decreased (Figure 5). If we examine the trends in TRAb, TSAb, and TSBAb during this time, TRAb was positive from before the onset of hypothyroidism, but as the laboratory data improved, this antibody titer decreased. TSAb was also positive at the onset of hypothyroidism, this antibody titer gradually decreased, and by July 7, 21 weeks after treatment discontinuation, it had become negative. TSBAb remained negative throughout the clinical course, before and after the onset of hypothyroidism (Figure 6).

HCV-RNA remained negative from 12 weeks after the start of treatment, thus a virological response was achieved. However, ALT was persistently abnormal even after HCV-RNA had disappeared. This improved after treatment discontinuation. Total cholesterol increased transiently at the onset of hypothyroidism, but with improvement in laboratory data due to Thyradin S® administration, total cholesterol returned to its previous value (Figure 7).

Table4. Laboratory data at the start of therapy (patient 2)

Hematology		Blood chemistry	
WBC	5,960/μL	AST	139IU/L
RBC	545x10⁴/μL	ALT	256IU/L
Hb	16.4g/dL	LDH	214IU/L
Ht	50.5%	γ GTP	212IU/L
Platelet	193,000/μL	Al-P	515IU/L
		TG	73mg/dL
Electrolytes and renal function		TP	8.4g/dL
Na	139mEq/L	PG	194mg/dL
K	4.5mEq/L	HbA1c	7.7%
Cl	102mEq/L		
UN	14.8mg/dL		
CRNN	0.61mg/dL		
Virus and other markers			
HBsAg	(−)		
HBsAb	(−)		
HBcAb	(−)		
HCV-RNA	4.1(log)/mL		
Sero group	2		
AFP	7.7ng/mL		

Table5. Laboratoryb dadta 12 weeks after the start of therapy (patient 2)

Hematology		Virus and other markers	
WBC	3,500/μL	HCV core Ab	191.1U
RBC	546x10⁴/μL	HCV-RNA	(−)
Hb	17.0g/dL	AFP	7.1ng/mL
Platelet	116,000/μL		
		Blood chemistry	
Electrolytes and renal function		AST	126IU/L
Na	137mEq/L	ALT	223U/L
K	4.0mEq/L	LDH	203IU/L
Cl	99mEq/L	γ GTP	299U/L
UN	13.5mg/dL	Al-P	202IU/L
CRNN	0.59mg/dL	T.Chol	152mg/dL
		TG	194mg/dL
Thyroid function		TP	7.8g/dL
TSH	4.3μU/mL	Alb	4.6g/dL
FT3	3.2pg/mL	IgG	1,534g/dL
FT4	0.9ng/dL	IgA	442mg/dL
TPOAb	52.1U/mL	IgM	55mg/dL
TgAb	11.1U/mL		
TRAb	55.9%		
TSBAb	45.1%		

Table6. Laboratory data 8 weeks after the stop of therapy (patient 2)

Hematology		Virus and other markers	
WBC	5,210/μL	HCV-RNA	(−)
RBC	531x10⁴/μL	AFP	11.0ng/mL
Hb	16.4g/dL		
Platelet	163,000/μL	Blood chemistry	
		AST	102U/L
Electrolytes and renal function		ALT	144U/L
Na	136mEq/L	LDH	217IU/L
K	3.8mEq/L	γ GTP	272U/L
Cl	99mEq/L	Al-P	372IU/L
UN	12.7mg/dL	T.Chol	198mg/dL
CRNN	0.70mg/dL	TG	121mg/dL
		TP	8.1g/dL
		Alb	4.6g/dL
Thyroid function		PG	224mg/dL
TSH	207.1μU/mL	HbA1c	7.3%
FT3	1.3pg/mL		
FT4	0.2ng/dL		
TPOAb	437.4IU/mL		
TgAb	801.0IU/mL		
TRAb	60.7%		
TSBAb	44.5%		
TSAb	325%		

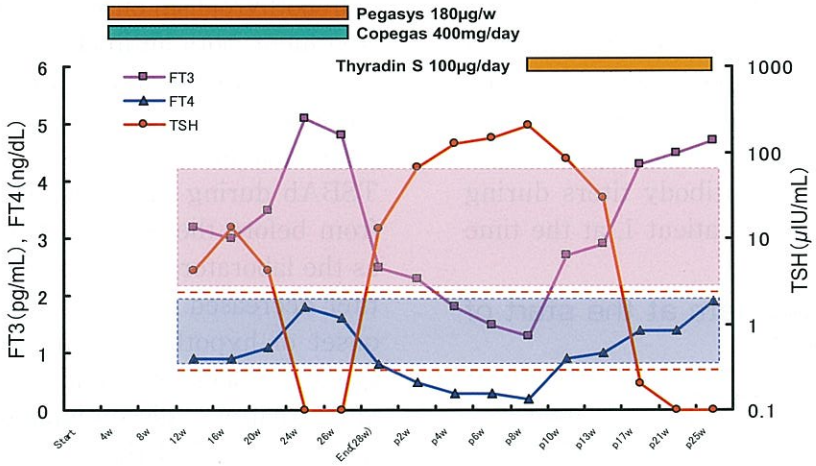

Figure 4. Serial changes of FT3, FT4 and TSH level in a 45-year-old male treated with peginterferon and ribavirin. Netted background represents the range of each normal value of FT3 and FT4. Broken lines show upper and lower limit of normal level of TSH.

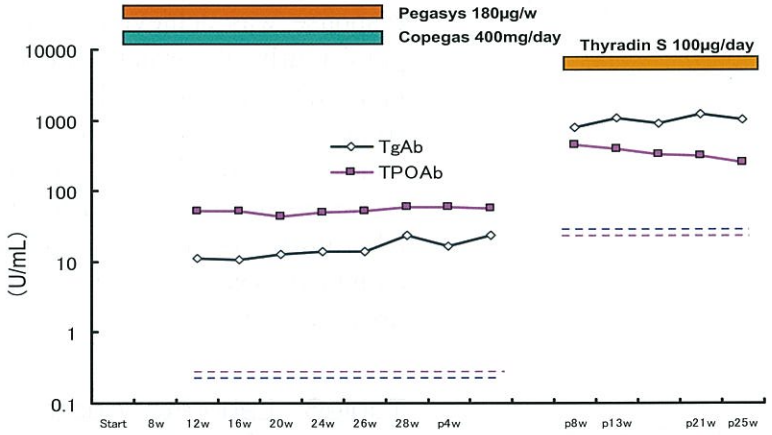

Figure 5. Serial changes of TPOAb and TgAb level in a 45-year-old male treated with peginterferon and ribavirin. Broken lines show upper limit of normal level of each TPOAb and TgAb.

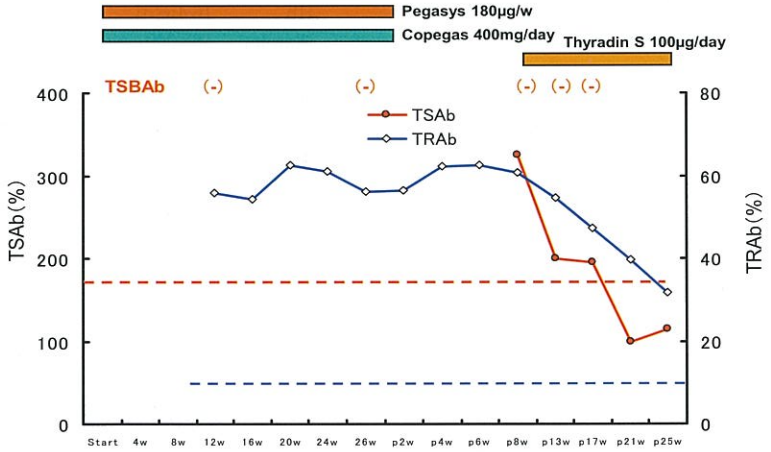

Figure 6. Serial changes of TRAb, TSAb and TSBAb in a 45-year-old male treated with peginterferon and ribavirin. Broken line shows upper limit of normal level of each TRAb and TSAb.

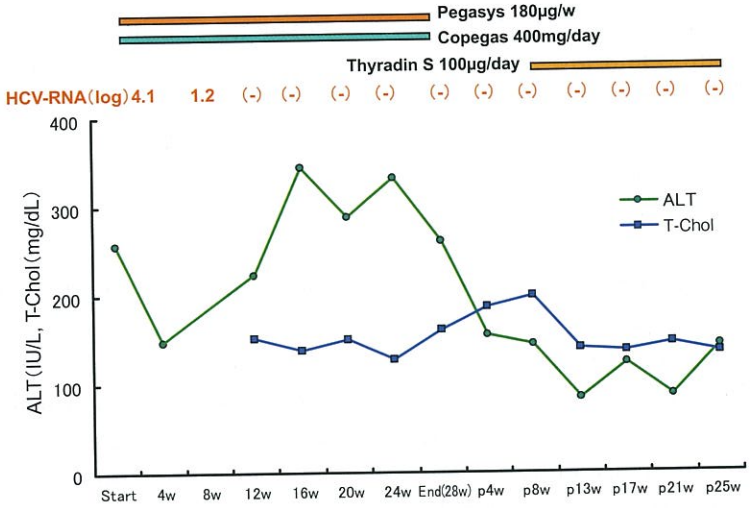

Figure 7. Serial changes of ALT, T-Chol and HCV-RNA level in a 45-year-old male treated with peginterferon and ribavirin.

Discussion

We found that in approximately 30% of chronic hepatitis C patients, at least one value among TSH, FT3, TRAb, TgAb and TPOAb will be abnormal or positive [3]. In such patients, when using interferon (IFN) therapy, careful monitoring for thyroid dysfunction is necessary, and about once monthly, thyroid hormone and thyroid autoantibodies should be checked.

Interferon, in addition to antiviral activity, has immunomodulatory functions, including inhibition of B cell activation, enhancement of T-cell mediated antibody production, and enhancement of natural killer activity; and it is known to act as a so-called biochemical response modifier (BRM). When IFN, with these various actions, is administered for therapeutic purposes, adverse effects on the host and onset or worsening of autoimmune diseases such as thyroid dysfunction must be anticipated [5, 6].

Peginterferon is usually administered for 24 weeks as monotherapy for low viral load; and for 48 weeks, in combination therapy with ribavirin, for moderate or high viral load. With peginterferon, based on its pharmacological characteristics, because continuous effective blood concentrations are maintained early after starting treatment, this leads to a sustained viral response (SVR). In patients with an early viral response (EVR), in whom HCV-RNA disappears within 1 month of starting treatment, to avoid unnecessary adverse effects, shortened treatment duration should be given consideration. In fact, in a case we previously reported [4], with a low viral load and TgAb positivity before treatment, EVR was seen. However, due to the onset of Graves' disease, peginterferon had to be discontinued 20 weeks after treatment was started; yet as a result, SVR was achieved. In that case, if peginterferon had been discontinued at an earlier stage after starting treatment, the onset of thyroid dysfunction might have been prevented beforehand.

Both of the patients in this report developed hypothyroidism due to peginterferon, yet there were no subjective or objective symptoms, and no goiter was present. Patient 1, with serogroup 1 and high viral load, was positive for TPOAb and TgAb before treatment. These antibody titers increased and decreased in parallel with a decrease and improvement in thyroid function. Peginterferon was discontinued, the patient was followed without therapy, and 20 weeks after discontinuation, thyroid function returned to normal. During the clinical course, TRAb, TSAb and TSBAb were not detected, and this was regarded as

the natural course for painless thyroiditis. In patient 2, with serogroup 2 and low viral load, thyroid autoantibodies were not measured before PEG-IFN treatment, but at 12 weeks after starting treatment, TRAb, TPOAb and TgAb were positive, and TSH was slightly elevated. The TRAb, TPOAb and TgAb titers increased in parallel with a decrease in thyroid function; and they decreased with an improvement in thyroid function with Thyradin S® administration, including negative conversion of TSAb. This patient had a clear transition from latent hypothyroidism to hypothyroidism. TSBAb was persistently negative, thus suggesting that this might have been related to the absence of overt clinical manifestations.

In various reports to date, in patients who develop Graves' disease with IFN treatment, TRAb and TSAb usually become positive [7, 8]. When painless (or silent) thyroiditis develops, in patients with positive thyroid autoantibodies before treatment, although antibody titers rise, TRAb, TSAb and TSBAb are not detected [9, 10]. In addition, Morita et al. [11] reported a case with serial progression from painless thyroiditis to Graves' disease, and during Graves' disease, TRAb and TSAb were detected. This case corresponds exactly to our previously reported case [4].

Here, patient 1 had findings consistent with painless thyroiditis, and transient hypothyroidism, followed by spontaneous resolution. In general, in painless thyroiditis, thyrotoxicosis for about 1 month is followed by transient hypothyroidism, which may continue for several months, and this is followed by resolution. Goiter is usually palpable, but in a patient, like ours, without thyroid goiter, if the onset is missed and sequential disease develops, then accurate recognition of the transition in pathology becomes difficult; thus, caution is required.

In the pathogenesis of painless thyroiditis, transient thyrotoxicosis occurs due to destructive thyroiditis in which an autoimmune mechanism plays a role. Because new thyroid hormone synthesis is inhibited due to tissue destruction, there is transition to a state of transient hypothyroidism [12]. In these cases, whether peginterferon should be continued or discontinued is debatable. However, as mentioned previously, patients with subsequent onset of Graves' disease have been reported [4, 11]. In a pathologic condition in which immune responses continue to change greatly, the possibility of new induction of TRAb, TSAb and TSBAb, and a transition to a subsequent pathologic condition, cannot be excluded. Therefore, discontinuation of peginterferon was considered appropriate.

In patient 2, the serial changes in TSH, FT3 and FT4 showed a similar pattern as in patient 1. Thus, in patient 2, with a background of latent hypothyroidism, transient painless thyroiditis followed by and hypothyroidism, similar to patient 1, presumably occurred. Interestingly, by discontinuing peginterferon and ribavirin, in conjunction with improved thyroid function with Thyradin S®, a decrease in TRAb titer and negative conversion of TSAb were observed. With regard to the finding that although TRAb was positive, TSBAb was persistently negative, TRAb assay measured both TSAb and TSBAb, and the results for TSAb and TSBAb may have reflected the respective predominant phases due to immune response changes. Improvement in ALT after discontinuation of peginterferon may reflect improvement in hepatic dysfunction by an autoimmune mechanism due to peginterferon administration. Despite the absence of overt clinical manifestations, thyroid hormone replacement therapy with Thyradin S® was successful. Therefore, in cases with a background similar to that of patient 2, this method of treatment should be considered.

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References

1) Jamil KM., Leedman PJ., et al.：Interferon-induced thyroid dysfunction in chronic hepatitis C. ：Gastroenterol Hepatol 24, 1017-

1023, 2009
2) Galossi A., Guarisco R., et al. : Extrahepatic manifestation of chronic HCV infection. J Gastrointestin Liver Dis 26, 65-73, 2007
3) Ishikawa K., Nitatori T., et al. : Latent thyroid dysfunction in patients with chronic hepatitis C virus infection and its relevance to emergence of symptoms after peg-interferon treatment. Journal of the Faculty of Nursing, Iwate Prefectural University 10, 23-36, 2008
4) Ishikawa K., Nitatori T., et al. : A case with hepatitis C who displayed hyperthyroidism followed by hypothyroidism during the course of peg-interferon monotherapy : relevance to changes in thyroid autoantibodies titer.
5) Marcellin P., Pouteau M., et al : Hepatitis C virus infection, alpha interferon therapy and thyroid dysfunction. J Hepatol 22, 364-369, 1995
6) Iino S. : Bibliographical consideration of peg-interferon alpha-2a or peg-interferon alpha-2b with ribavirin therapy for chronic hepatitis C. Prog Med 27, 1389-1396, 2007
7) Bohbot NL., Young J., et al. : Interferon-alpha-induced hyperthyroidism: a three-stage evolution from silent thyroiditis towards Graves' disease. Eur J Endocrinol 154, 367-372, 2006
8) Kitahara S., Uehara Y. et al. : Thyrotoxicosis caused by treatment with interferon-α for chronic hepatitis C : case report. Sogorinsho 49 2330-2333, 2000
9) Kamikubo K., Takami R. et al. : Case report: Silent thyroiditis developed during alpha-interferon therapy. Am J Med Sci 306, 174-176, 1993
10) Uchida K., Matsui A. et al. : Painless thyroiditis occurring during long-term treatment with interferon alfa in a patient with chronic active hepatitis C. South Med J 89, 81-83, 1996
11) Morita S., Honda T., et al. : A case of Graves' disease following painless thyroiditis induced by pegylated-interferon and ribavirin therapy to a patient with chronic hepatitis C. Kanzo 51, 300-304, 2010
12) Kubota K. : A clinical status that needs differential diagnosis with Basedow's disease:diagnosis and treatment of painless thyroiditis and subacute thyroiditis. Current Therapy 27, 127-131, 2009

和文要旨

症例 1。43 歳女性。peginterferon-α 2A および ribavirin の併用療法を行った。治療開始前甲状腺機能は正常で、TgAb,TPOAb は弱陽性であった。治療開始 20 週後、甲状腺機能低下を示し、治療を中止した。治療中止 4 週後には、TSH 142.7 μIU/mL、FT3 0.8pg/mL 、FT4 0.3ng/dL まで悪化した。自他覚症状、甲状腺腫も無かったので、無処置で経過観察を行ったところ、治療中止 22 週後甲状腺機能は正常化した。無痛性甲状腺炎の自然経過と考えられた。経過中 TRAb, TSAb, TSBAb は陰性であった。

症例 2。45 歳男性。2009 年 7 月 24 日、peginterferon-α 2a の投与を開始。治療開始 28 週後、甲状腺機能低下を示し治療を中止した。治療中止 8 週後には、TSH 207.1 μIU/mL、FT3 1.3pg/mL 、FT4 0.2ng/dL まで悪化し、ThyradinS100 μg/day の投与を開始した。その後検査値は漸次改善し、治療中止 17 週後にはほぼ正常化した。経過中 TSBAb,は陰性であった。潜在性甲状腺機能障害に無痛性甲状腺炎を合併した症例と考えられた。両例とも TSBAb が陰性で、自他覚症状の欠如との関連が示唆された。

キーワード：ペグインターフェロン，甲状腺機能低下症，無痛性甲状腺炎，潜在性甲状腺障害，甲状腺自己抗体