Case Report

Fluorine-18-Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography in Diagnosis and Assessment of Takayasu Arteritis and Ulcerative Colitis

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Takayasu arteritis (TA) and ulcerative colitis (UC), both immune-mediated inflammatory diseases, rarely occur together. This report describes TA in a 29-year old female patient who was being treated for UC for three years. As she had left-side neck pain and headache, she was diagnosed with TA and her response to tumor necrosis factor (TNF) inhibitor was assessed by fluorine-18-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography (PET)/computed tomography (CT). Positive responses to the TNF inhibitor were seen by PET/CT for the TA and by endoscopy for the UC. We conclude that TNF inhibitors are effective treatments for both TA and UC. We found that PET/CT is a useful for diagnosing and assessing TA. **(J Rheum Dis 2017;24:55-59)**

Key Words. Takayasu arteritis, Ulcerative colitis, Positron emission tomography

INTRODUCTION

Takayasu arteritis (TA) is a vasculitis involving medium and large arteries, while ulcerative colitis (UC) is an inflammatory bowel disease that affects the colon. The causes of these two auto-immune diseases are not yet clear [1]. However, since tumor necrosis factor (TNF), a pro-inflammatory cytokine, plays a key role in the inflammation caused by autoimmune reactions, TNF inhibitors can be regarded as potential treatments for both diseases. For the cases of UC or TA treatment, TNF inhibitors in particular infliximab have been used in patients who relapse or steroid dependence occurs [1,2].

Fluorine-18-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography (PET)/computed tomography (CT) has been used as a diagnostic and follow-up tool for TA [3-5]. Since it is an imaging modality that reflects metabolic status, it assesses TA activity in terms of vascular metabolic uptake.

We described a patient with TA already suffering from UC, and evaluated treatment responses by means of PET/CT.

CASE REPORT

A 29 year old female patient visited our hospital complaining of left neck pain, headache and claudication of the upper extremities over the previous 2 months. She had been treated for UC for 3 years by taking azathioprine (AZA) and 5-aminosalicylic acid (ASA). But she also developed diarrhea and intermittent hematochezia 2 months ago.

At the time of her visit, her heart rate was 95 beats/minute, body temperature was 36.9°C, and respiration rate was 20/minute. Reduced blood pressure was noted on her left arm (100/84 mmHg) compared to her right arm (124/85 mmHg). Arterial pulse was also diminished on the left brachial artery. Tenderness was observed at car-

otid artery of her left neck. There was no neurological abnormality.

Laboratory findings were as follow: white blood cell count, 9,900/mm^3 (4,000~10,000/mm^3); hemoglobin, 7.9 g/dL (13.0~17.0 g/dL); and platelet count, 610,000/mm^3 (150,000~400,000/mm^3). Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were elevated to 61 mm/hour (0~20 mm/hour) and 12 mg/dL (0~0.5 mg/dL), respectively. Other laboratory findings were within normal limits, including liver function and renal function. Anticardiolipin immunoglobulin M (IgM)/IgG, anti-beta-2-glycoprotein1 IgM/IgG and lupus anticoagulant were all negative. Complement (C) 3, C4, IgG, IgM, and IgA were all normal. However, a perinuclear anti-neutrophil cytoplasmic antibody (p-ANCA) was positive.

Contrast enhanced neck CT performed to evaluate the tenderness of the neck revealed that the bilateral common carotid arteries, subclavian arteries, and aortic arch were all surrounded by soft tissue densities with enhancement, with the left side of both common carotid arteries and subclavian arteries being more severely affected than the right sides (Figure 1A). In addition, angiography showed that parts of the vertebral artery as well as the bilateral common carotid arteries and subclavian arteries were abnormally narrowed (Figure 1B). No coronary artery lesion was observed.

Based on her age, the difference between right and left brachial blood pressure, the claudication of the upper ex-

tremities and arteriogram abnormalities (lesions of the common carotid artery, thoracic aorta and abdominal aorta), the patient was diagnosed as TA according to the diagnostic criteria of K. Ishikawa [6]. Since the disease had spread to all segments of the aorta including the abdominal aorta as well as the aortic arch, the TA was classified specifically as type V TA [7].

PET/CT performed to evaluate the inflammatory status of TA revealed increased uptake of FDG in the thoracic and abdominal aorta as well as in both common carotid arteries and subclavian arteries, suggesting active inflammation (Figure 2B). In addition to the increased FDG uptake, the contour of entire aorta was irregular and exit of inferior mesenteric artery was abnormally narrow, although that of celiac axis and superior mesenteric artery were normal. Meanwhile, there was no uptake on colon. Sigmoidoscopy was performed to evaluate the disease activity of UC and revealed a loss of vessel wall and redness of the mucosa between rectum and sigmoid colon (Figure 2A). Since the mucosa was friable, even a light touch caused membrane bleeding, with some spontaneous bleeding as well.

In order to treat her TA and UC, both of which were highly active, high dose steroid (1 mg/kg) was administered combined with AZA and 5-ASA. However, there were no improvement in symptoms and laboratory data, including ESR and CRP. Therefore, we decided to use infliximab to control these two diseases together. We ad-
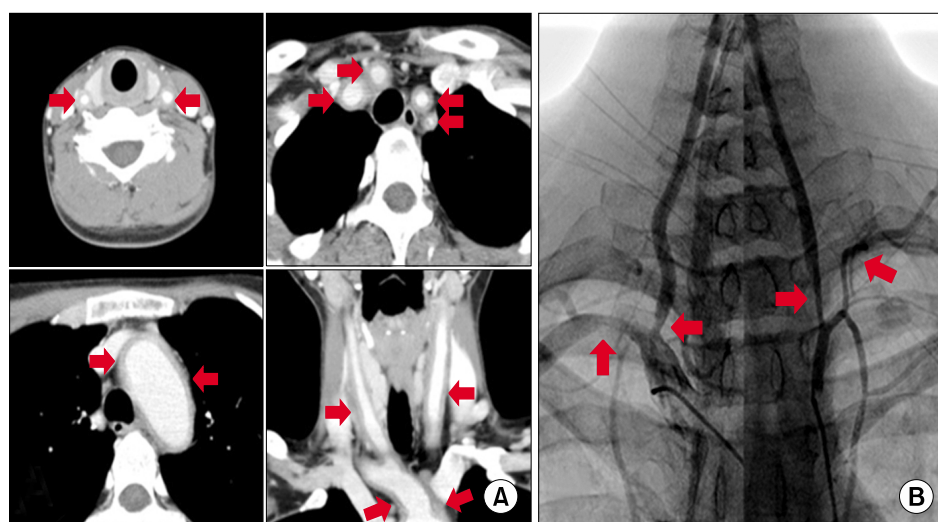

Figure 1. (A) Neck computed tomography images showing bilateral common carotid arteries, subclavian arteries, and aortic arch (arrows) surrounded by soft tissue density with enhancement, with left side of both common carotid arteries and subclavian arteries being more severe than the other side. (B) Angiographic images representing that the vertebral artery as well as the bilateral common carotid arteries and subclavian arteries were abnormally narrow as well (arrows).
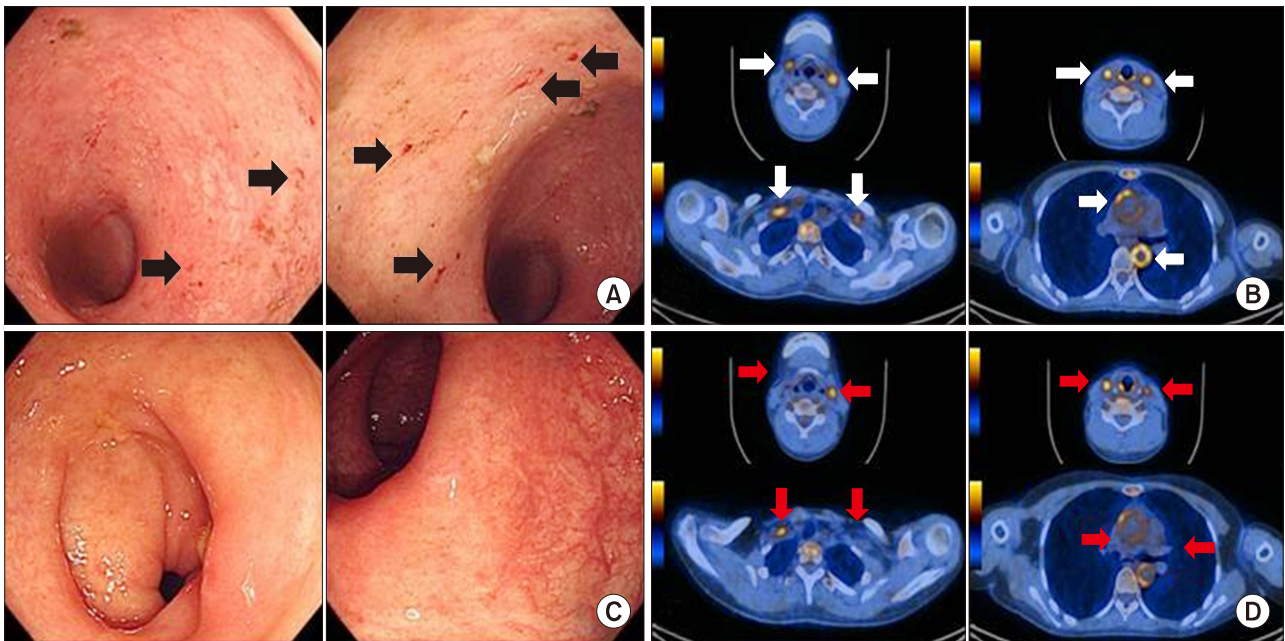
Figure 2. (A) Sigmoidoscopy which is done before the administration of the infliximab, representing a loss of vessel wall, redness of mucosa and spontaneous bleeding (black arrows). (B) Positron emission tomography (PET)/computed tomography (CT) before the administration of the infliximab. There is increase of uptake of fluorodeoxyglucose at both common carotid arteries, subclavian arteries and thoracic and abdominal aorta (white arrow). (C) Sigmoidoscopy after 3 months of the treatment, although the redness of mucosa was still left, the spontaneous bleeding disappeared. (D) PET/CT after 3 months of the treatment. The uptake of both common carotid arteries, subclavian artery and aorta baseline have been decreased (arrow).

Table 1. The table of cases with TA and UC in terms of diagnostic tool, treatment and follow up

Case [reference]	Diagnostic tool	Initial treatment	Biologic therapy	Other treatment	Follow up tool
Possemato et al. [4]	N/A	Mycophenolate	Infliximab, adalimumab, tocilizumab	None	Contract enhanced ultrasound, PET/CT
Pyo et al. [8]	CT, angiography, PET/CT	Prednisolone (50 mg/d), AZA (50 mg)	None	None	NA
Takahashi et al. [9]	CT, MRI	Prednisolone (20 mg/d), 5-ASA (2,250 mg/d)	None	None	NA
Sood et al. [12]	Angiography	Steroid, sulfasalazine	None	None	NA
Horai et al. [13]	CT	Prednisolone (30 mg/d)	None	None	NA
Sy et al. [14]	NA	5-ASA, prednisolone, 6-mercaptopurine	Adalimumab	None	NA
	NA	5-ASA, prednisolone, methotrexate	None	None	NA
	NA	5-ASA, prednisolone, 6-mercaptopurine	None	None	NA
	NA	Prednisolone	None	None	NA
Katsinelos et al. [15]	Angiography	Prednisolone (50 mg/d), 5-ASA, AZA	None	Ticlopidine hydrochloride 75 mg/d	NA
Horai et al. [10]	CT, Angiography	Prednisolone (30 mg/d)	None	Warfarin	NA

Note that we have utilized PET/CT as an assessment and follow up tool, for the co-existence of TA and UC. TA: Takayasu arteritis, UC: ulcerative colitis, NA: not available, PET/CT: positron emission tomography/computed tomography, AZA: azathioprine, ASA: amino salicylic acid.

ministered infliximab at a dose of 5 mg/kg, as induction therapy at 0, 2, and 6 weeks, and continued treatment every 8 weeks.

The clinical symptoms including neck pain, headache, claudication of upper extremities, hematochezia, and abdominal pain have been all improved after induction therapy of infliximab. Moreover, ESR and CRP fell from 61 mm/hour to 17 mm/hour and 12 mg/dL to 0.1 mg/dL, respectively after 3 months.

Follow-up PET/CT and sigmoidoscopy were performed 3 months after infliximab use. The increased FDG uptakes on both carotid arteries, subclavian arteries and the aorta seen on previous scan significantly decreased on the follow-up scan (Figure 2D). On the follow-up sigmoidoscopy, the friable, inflamed mucosa showed a significant improvement with no sign of spontaneous bleeding (Figure 2C).

In short, clinical symptoms, laboratory data, PET/CT and endoscopy are all improved. Up to the time of writing, the patient has been receiving infliximab every 8 weeks as maintenance dose, with no worsening of symptoms.

DISCUSSION

It has been well known that immunologic abnormalities are present in TA and UC [8]. In TA, natural killer-cell and T cells infiltrate the aorta, and the levels of several cytokines such as TNF, interleukin (IL)-6, or IL-18 increase. These cytokines also increase in UC patients, implying that UC is also associated with autoimmune phenomena [1]. Among that cytokines, TNF is targeted by TNF inhibitor. TNF inhibitor is known as an effective treatment for TA [1]. Also, it, particularly infliximab, can be used for treating the active or glucocorticoid-refractory UC [2]. In this case, the TA and UC were treated together, using infliximab.

UC can occur together with other autoimmune diseases, not only TA but also lupus erythematosus, autoimmune hemolytic anemia, chronic hepatitis and so on [9]. Hence we should approach UC patients systemically, not just concentrating on one part of the body [9]. Indeed the female patient described here was initially diagnosed as UC and only diagnosed as TA 3 years later on the basis of her neck pain and headache. At the time of diagnosis, the patient in this case was revealed to have positive P-ANCA. This result can be associated with UC [10,11]. High prevalence of P-ANCA about 40 to 60% in UC has been reported [11]. The cases about coexistence of TA and UC

are rarely reported over the world and most of them are Japanese. In Korea, there are only a few cases, including the case reported by Pyo et al. [8]. To the patient with both TA and UC, we used PET/CT for assessing not only the disease activity but also treatment response, which is the unique point of our report. Other cases are summarized at the Table 1 including diagnostic, treatment and follow up tool [4-10,12-15].

The disease activity of TA was evaluated from ^{18}F-FDG PET/CT, it showed good performance in the assessment of vessel inflammation.

We conclude that PET/CT can be a good tool for diagnosing and assessing the treatment response in TA patients.

SUMMARY

Biological treatments should be considered for UC and TA patients refractory to current immunosuppressive treatments. The PET/CT could be used to assess TA and its response to treatment.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

REFERENCES

1. Clifford A, Hoffman GS. Recent advances in the medical management of Takayasu arteritis: an update on use of biologic therapies. Curr Opin Rheumatol 2014;26:7-15.
2. Ford AC, Sandborn WJ, Khan KJ, Hanauer SB, Talley NJ, Moayyedi P. Efficacy of biological therapies in inflammatory bowel disease: systematic review and meta-analysis. Am J Gastroenterol 2011;106:644-59.
3. Alibaz-Oner F, Aydin SZ, Direskeneli H. Advances in the diagnosis, assessment and outcome of Takayasu's arteritis. Clin Rheumatol 2013;32:541-6.
4. Possemato N, Macchioni P, Germanò G, Pipitone N, Versari A, Salvarani C. Clinical images: PET-CT and contrast- enhanced ultrasound in Takayasu's arteritis. Rheumatology (Oxford) 2014;53:447.
5. Alibaz-Oner F, Dede F, Ones T, Turoglu HT, Direskeneli H. Patients with Takayasu's arteritis having persistent acute-phase response usually have an increased major vessel uptake by 18F-FDG-PET/CT. Mod Rheumatol 2015;25:752-5.
6. Arend WP, Michel BA, Bloch DA, Hunder GG, Calabrese LH, Edworthy SM, et al. The American College of Rheumatology 1990 criteria for the classification of Takayasu arteritis. Arthritis Rheum 1990;33:1129-34.
7. Mason JC. Takayasu arteritis--advances in diagnosis and management. Nat Rev Rheumatol 2010;6:406-15.

8. Pyo JY, Park JS, Song CH, Lee SW, Park YB, Lee SK. Takayasu arteritis associated with ulcerative colitis and optic neuritis: first case in Korea. Korean J Intern Med 2013; 28:491-6.
9. Takahashi N, Tanabe K, Sugamori T, Sato M, Kitamura J, Sato H, et al. Association between Takayasu arteritis and ulcerative colitis - case report and review of serological HLA analysis. Med Sci Monit 2011;17:CS81-4.
10. Horai Y, Miyamura T, Shimada K, Takahama S, Minami R, Yamamoto M, et al. A case of Takayasu's arteritis associated with human leukocyte antigen A24 and B52 following resolution of ulcerative colitis and subacute thyroiditis. Intern Med 2011;50:151-4.
11. Schulte-Pelkum J, Radice A, Norman GL, López Hoyos M, Lakos G, Buchner C, et al. Novel clinical and diagnostic aspects of antineutrophil cytoplasmic antibodies. J Immunol Res 2014;2014:185416.
12. Sood A, Midha V, Sood N, Bansal M. Coexistence of Takayasu's arteritis with ulcerative colitis. J Assoc Physicians India 2006;54:151-2.
13. Horai Y, Satoru O, Lapalme-Remis S, Sumiyoshi R, Nakashima Y, Suzuki T, et al. Takayasu arteritis developing during treatment of ulcerative colitis with infliximab. Mod Rheumatol 2013;23:572-6.
14. Sy A, Khalidi N, Dehghan N, Barra L, Carette S, Cuthbertson D, et al. Vasculitis in patients with inflammatory bowel diseases: A study of 32 patients and systematic review of the literature. Semin Arthritis Rheum 2016;45:475-82.
15. Katsinelos P, Tsolkas P, Beltsis A, Chatzimavroudis G, Papaziogas B, Kapelidis P, et al. Takayasu's arteritis and ulcerative colitis in a young non-Asian woman: a rare association. Vasa 2005;34:272-4.