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Dear Editor

A Case of Streptomycin-Induced Pneumonitis

Antituberculosis drugs are associated with predictable incidences of adverse effects such as fever, skin rash, and hepatitis.[1] First-line agents such as isoniazid (INH), rifampicin (RFP), and ethambutol (EB) are sometimes reported to cause drug induced pneumonitis.[2] In contrast, although pyrazinamide (PZA) and streptomycin (SM) have side effects including hepatotoxicity and ototoxicity, respectively,[1] to our knowledge, pneumonitis induced by these drugs has not been reported.

We report a case of SM-induced pneumonitis diagnosed by the drug lymphocyte stimulation test (DLST).

CASE REPORT

An 89-year-old man was admitted for abnormal lung shadow. His chest radiograph showed consolidation in the upper side of the right lung. Physical examination was unremarkable without fever and cough. Laboratory data revealed anemia and thrombocytopenia with mild renal dysfunction (Table 1). *Mycobacterium tuberculosis* infection was confirmed by gas-

Table 1 Laboratory data on admission

WBC	4700 /μl	AST	21 IU/l	PT	12.7 S
Neut.	45.6 %	ALT	11 IU/l	PT	90 %
Lymp.	36.6 %	ALP	149 IU/l	PT-INR	1.06
Mono.	7.2 %	γGTP	14 IU/l	APTT	29.2 S
Eosi.	10.0 %	LDH	187 IU/l	Fib	337 mg/dl
Baso.	0.6 %	T-Bil	0.40 IU/l	HCV Ab	(-)
RBC	304 × 10^4 /μl	BUN	34.6 mg/dl	HBs AG	(-)
Ht	28.2 %	Cre	2.02 mg/dl	DLST	
Hb	9.8 g/dl	Na	140 mEq/l	PZA	711 cpm
MCV	92.8 fl	K	4.4 mEq/l	S.I.	98 % (<180%: negative)
MCH	32.2 pg	Cl	108 mEq/l	SM	908 cpm
MCHC	34.8 g/dl	TP	6.5 g/dl	S.I.	488 % (>199%: positive)
Plt	11.1 × 10^4 /μl	CRP	0.18 mg/dl		

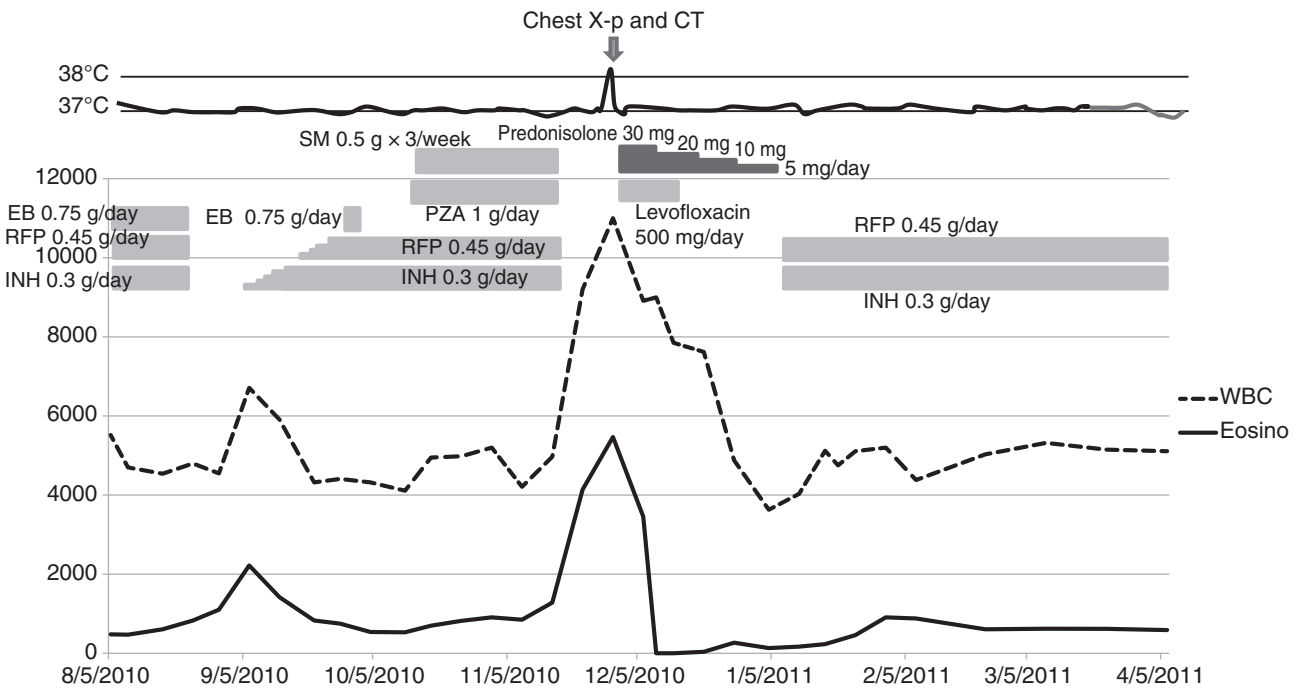

Fig. 1 Clinical course of fever, WBC, esinocyte and medication.

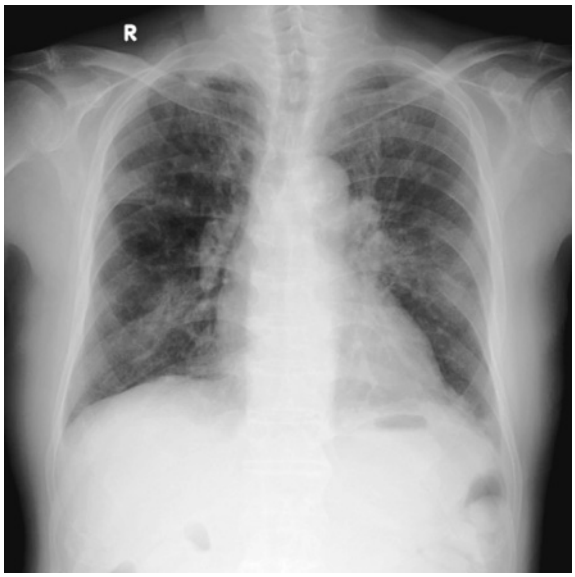

Fig. 2a Chest X-ray at onset of dyspnea showed bilateral spotty consolidation in the lungs.

tric fluid culture and PCR. Sputum was not examined as sample could not be obtained.

Antituberculosis drugs were started as follows, INH (0.3 g/day), RFP (0.45 g/day), and EB (0.75 g/day). Because he developed skin rash with itching and eosinophilia after two weeks, these drugs were all ceased and symptoms improved within ten days. Although INH and RFP were re-admitted without side effects, after EB was re-started, skin eruption with itching was seen again after a few days. Therefore, EB was stopped. As its back up, PZA (1.0 g/day) and SM (0.5 g × 2 days/week) were started. However, about a month after beginning these drugs, skin eruption with itching was seen again and blood examination revealed eosinophilia (Fig. 1). Although we stopped all drugs immediately, skin rash continued for two weeks, and then the patients developed high fever with dyspnea. Differential cell count of sputum revealed 60% lymphocytes and 40% neutrophils. DLST of SM was positive, but that of PZA was negative (Table 1). Because chest X ray films showed bilateral spotty consolidation (Fig. 2a) and chest CT indicated membranous shadows, with small reticular shadows which were consistent with a nonspecific interstitial pneumonia (NSIP) pattern (Fig. 2b), we suspected drug induced pneumonitis. Prednisolone (30 mg) was administered orally. With this therapy, pneumonitis and skin rash improved in a short time and eosinophilia returned to normal ranges rapidly. After a while, we re-tried INH and RFP at a regular dose because the susceptibility test of these two drugs for tuberculosis was sensitive. Thereafter, the patient experienced no difficulties with these drugs.

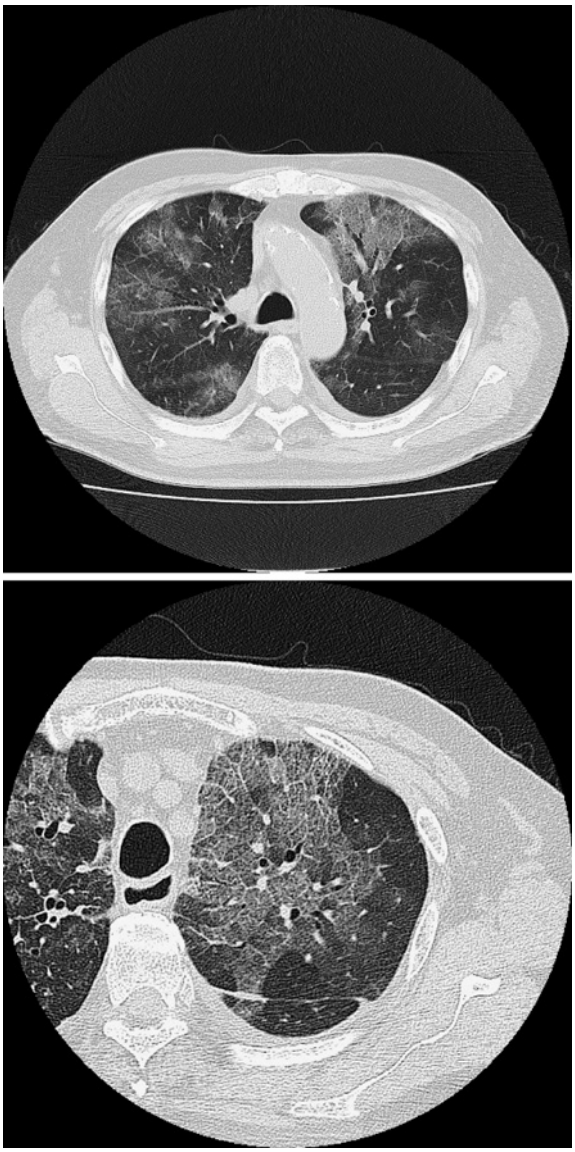

Fig. 2b Chest CT at onset of dyspnea indicated membranous shadow with small reticulous shadow.

DISCUSSION

Adverse drug reaction (ADR) is commonly explained by pharmacological actions of a drug. However, ADR occurs unpredictably as an idiosyncratic reaction in a few patients.[3] According to Suzuki *et al.*, the drug provocation test (DPT), controlled administration of a suspected drug,[4] is recommended in order to diagnose antituberculosis drug induced hypersensitivity reactions, because DPT for antituberculosis drugs was more sensitive than DLST.[5] In this case, EB was confirmed to induce skin rash by DPT. The skin rash was seen by re-exposure to EB and disappeared when EB was stopped. However, concerning interstitial pneumonia following additional medication by PZA and SM, we did not try DPT or desensitizing therapy because they may have induced a life-

threatening side effect such as respiratory failure. Instead of DPT, we examined DLST for PZA and SM.

DLST is performed to examine the sensitivity of T cells to a suspected drug by measuring the proliferation of the cells exposed to the drug in vitro. Although the sensitivity of DLST is not enough, a positive result often contributes to the diagnosis of drug induced hypersensitivity reaction.[6] In this case, DLST of SM was positive, but that of PZA, which has been associated with dose-dependent pharmacological hepatotoxicity, was negative.

Unfortunately, due to the patient's poor condition and old age, we could not perform bronchoalveolar lavage or transbronchial lung biopsy. However, differential cell count of sputum did not show the increase of eosinophils, suggesting that this case was not eosinophilic pneumonia.[7] Lung damage induced by cytotoxic drugs is generally irreversible.[8] On the other hand, interstitial pneumonia caused by immunological drug reactions usually responds to steroid therapy.[9] Based on the good response to steroid therapy, the increase of blood eosinophils, and the positive result of DLST, we diagnosed this case as allergic drug induced pneumonitis due to SM.

Interstitial pneumonia induced by a drug is often serious and can result in death without early diagnosis and management. Although SM-induced pneumonitis is extremely rare, we have to recognize that this drug can cause such a life-threatening ADR.

Hisanori Machida[1], Tsutomu Shinohara[2],
Yoshio Okano[1] and Fumitaka Ogushi[1]

[1]Division of Pulmonary Medicine and [2]Department of Clinical Investigation, National Hospital Organization National Kochi Hospital, Kochi, Japan
Email: machidah@kochi2.hosp.go.jp
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