

Fig.1

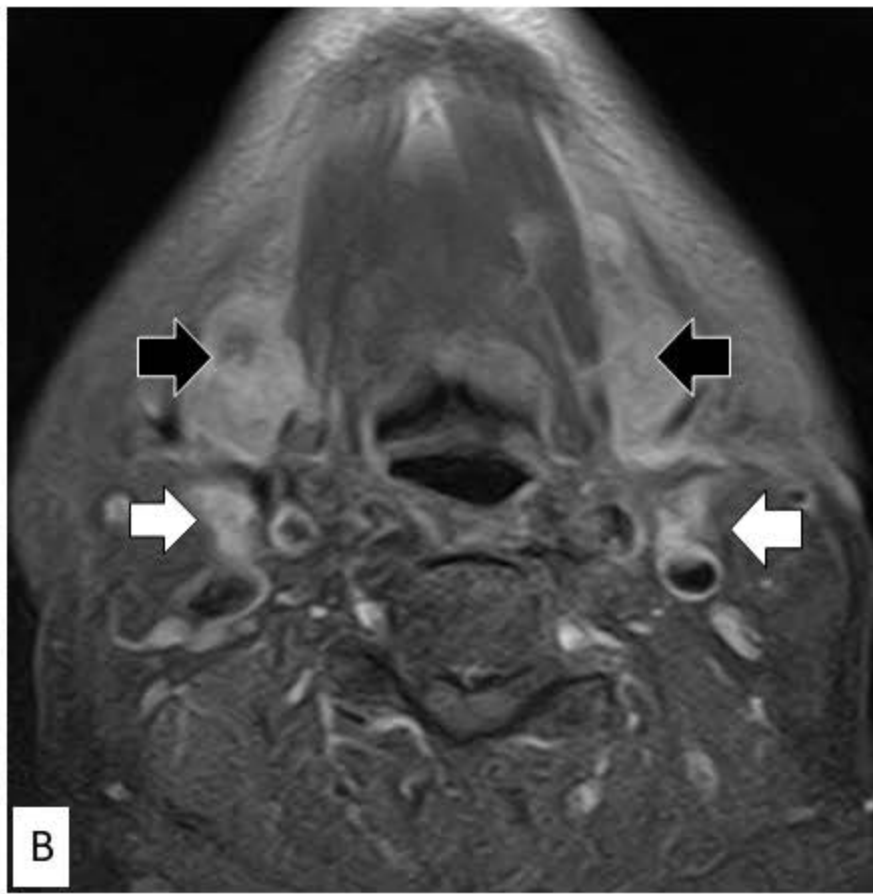
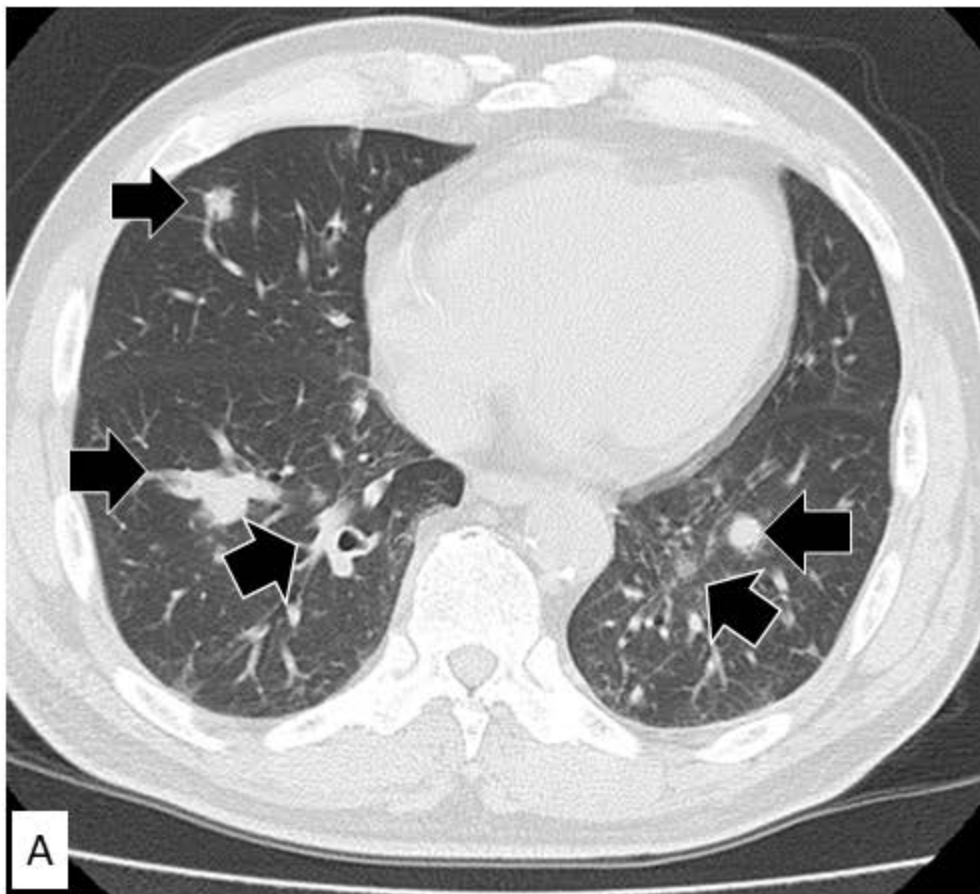


Fig.2

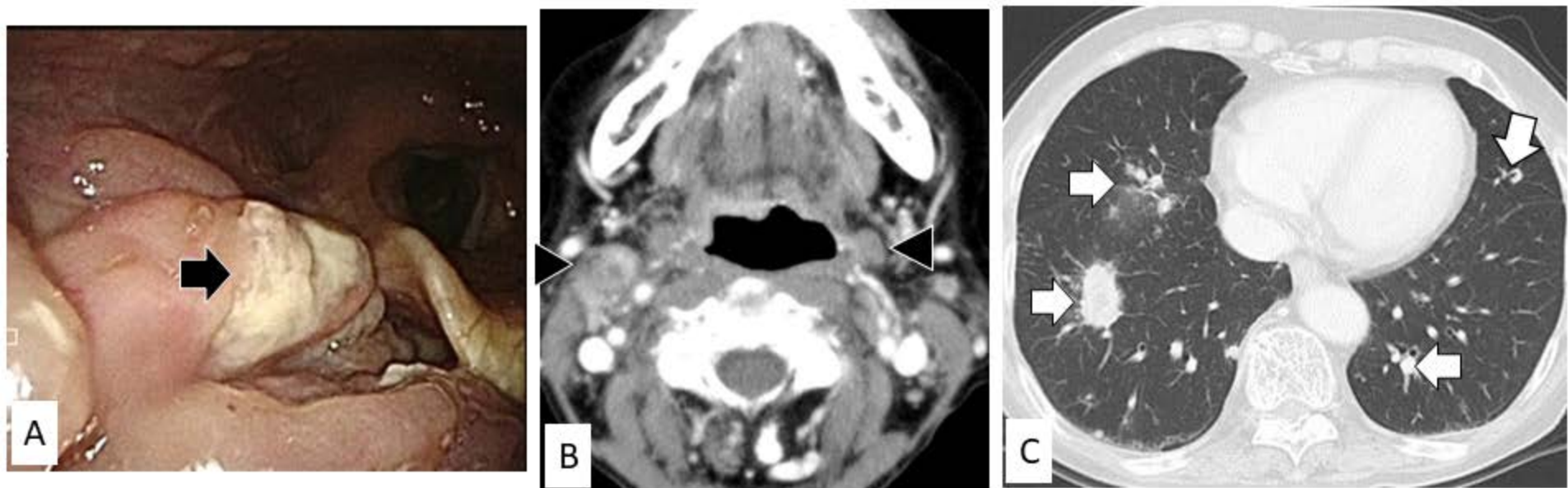


Fig.3

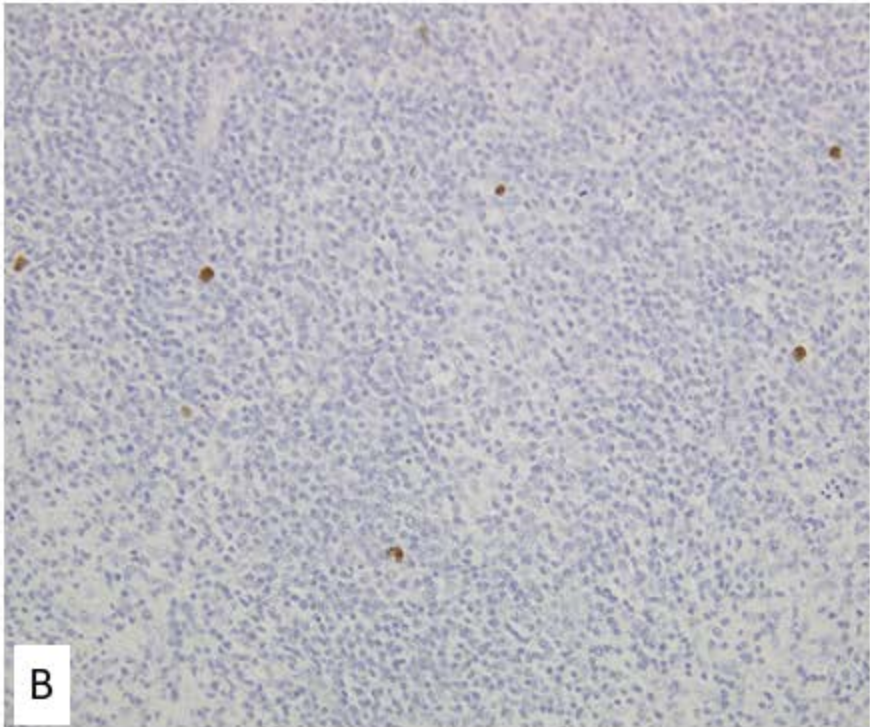
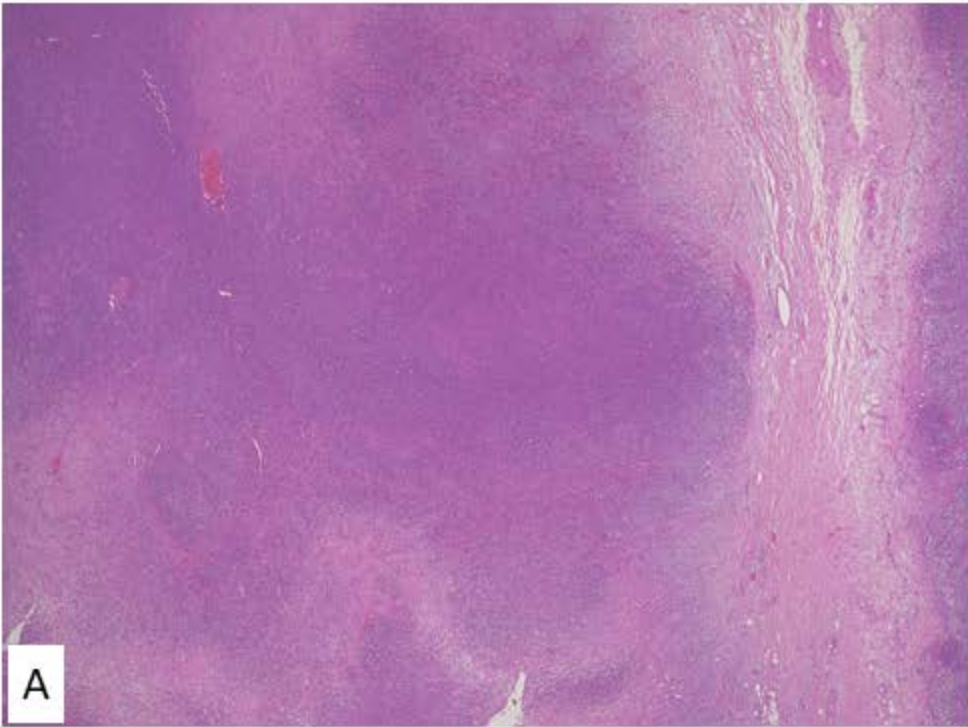


Table 1: Clinicopathological features of the current cases, and reports of MTX-associated LPD with lung involvement during MTX therapy

Ref.	Age/ Gen der	Complaint	Characteristics of lung involvement by CT scan	Lymph node swelling	Extranodal LPD lesions	MTX medication (mg/week)	MTX intake duration	Histopathology	EBV	Additional therapy	Prognosis
Current Case 1	67/M	Bilateral parotid swelling	Multiple tumors in both lungs	Neck, mediastinal, and left hilar lymph nodes	Lung, parotid gland, and submandibula r gland	14	10 yrs	Infiltration of atypical small lymphocytes, which were positive for CD3, and necrotizing lesions, which have possibility of subsiding	-	-	Alive
Current Case 2	74/F	Pharyngeal discomfort	Multiple tumors in both lungs	Neck lymph nodes	Lung and posterior part of tongue	14	15 yrs	Diffuse infiltration of atypical small lymphocytes, which were positive for CD3	+	-	Alive
Suemori K, et al. Intern Med 2015;54:1421-5.	79/F	Fever and fatigue	Multiple tumors in both lungs	None	Lung	8	5 yrs	Diffuse infiltration of monotonous lymphoid cells, which were predominantly positive for CD20	+	-	Alive
Tajima S, et al. Pathol Int 2015;65:661-5.	64/F	Cough and expectoration	Multiple tumors in both lungs	None	Lung	4–6	11 yrs, 10 mos	Extranodal NK/T-cell lymphoma	+	Chemotherapy with SMILE regimen	Alive

Lai WF, et al. BMJ Case Rep 2017;2017.	62/F	Fever, oral ulcers, and cough	Multiple tumors in both lungs	Mediastinal and axillary lymph nodes	Lung	15	Several weeks	Infiltration of abnormally enlarged CD20 positive lymphoid cells	+	-	Alive
Kudoh M, et al. Oral Surg Oral Med Oral Pathol Oral Radiol 2014;118:e105-10.	75/F	Occlusal pain and swollen gingiva	One tumor	Accessory and inguinal lymph nodes	Lung and retromolar triangle	8	5 yrs	Diffuse large B-cell lymphoma	+	Chemotherapy with R-CHOP	Alive
Kobayashi S, et al. Ann Hematol 2013;92:1561-4.	71/M	General malaise	Multiple tumors in both lungs	Neck, axillary, mediastinal, para-aortic, mesenteric, splenic hilar, and inguinal lymph nodes	Lung, liver, spleen, and ileum	10	5 yrs	LYG	+	-	Alive
Shimada K, et al. Scand J Rheumatol 2007;36:64-7.	54/F	Chest pain	Multiple tumors in both lungs	None	Lung, liver, and spleen	7.5	10 yrs	LYG	-	-	Alive
Oiwa H, et al. Intern Med 2014;53:1873-5.	65/F	Weight loss, appetite loss, and pruritic eruption on leg	Multiple tumors in both lungs	None	Lung, skin, and CNS	6	17 yrs	LYG	+	-	Alive

Jois RN, et al. Histopathology 2007;51:709-12.	48/F	Fatigue, cough, and weight loss	Bi-basal ground-glass shadowing	Mediastinal lymph nodes	Lung	10–25	1 yr, 4 mos	Diffuse large B-cell lymphoma	+	-	Alive
Kameda H, et al. Clin Rheumatol 2007;26:1585-9.	71/M	Axillary mass and dyspnea	Diffuse infiltration in both lungs (by X-ray)	Neck and axillary lymph nodes	Lung, spleen, and adrenal gland	6–8	2 yrs, 5 mos	LYG	+	Chemotherapy with CHOP regimen	Death
Ebeo CT, et al. Chest 2003;123:2150-3.	54/M	None	One tumor	None	Lung	7.5–20	5 yrs	Diffuse large B-cell lymphoma	-	Left upper lobectomy	Alive
Tokuyama K, et al. Jpn J Radiol 2014;32:183-7.	68/F	Fatigue, fever, and weight loss	One tumor	Mediastinal and left hilar lymph nodes	Lung	14	4 mos	Diffuse large B-cell lymphoma	+	-	Alive
Suzuki M, et al. Respirology 2007;12:774-6.	42/M	Fever and cough	One tumor	None	Lung	2.5–5	15 yrs	Diffuse large B-cell lymphoma	+	Right upper lobectomy	Alive
Koji H, et al. Mod Rheumatol 2016;26:271-5.	48/F	Bilateral cervical masses, fever, fatigue, and cough	Multiple tumors in both lungs	Mediastinal and para-aortic lymph nodes	Lung, liver, kidney, and spleen	4–8	11 yrs	CD8-positive T-cell LPD	+	-	Alive

Yamakawa H, et al. Mod Rheumatol 2016;26:441-4.	78/M	Fatigue and appetite loss	Multiple tumors in both lungs	None	Lung and retroperitonea l lesions	6	4 yrs	Diffuse infiltration of atypical small lymphocytes and plasma cells which were positive for CD20, CD79a, and bcl-2	+	-	Alive
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MTX: methotrexate; yr/yrs: year/years; mos: months; LPD: lymphoproliferative disorder; M: male; F: female; CNS: central nervous system; LYG: lymphomatoid granulomatosis; SMILE: steroid (dexamethasone), methotrexate, ifosfamide, L-asparaginase, and etoposide; CHOP: cyclophosphamide, doxorubicin, vincristine, and prednisone; R-CHOP: rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone