



Title	Aseptic Meningitis with Relapsing Polychondritis Mimicking Bacterial Meningitis
Author(s)	Yaguchi, Hiroaki; Tsuzaka, Kazufumi; Niino, Masaaki; Yabe, Ichiro; Sasaki, Hidenao
Citation	Internal Medicine, 48(20), 1841-1844 https://doi.org/10.2169/internalmedicine.48.2173
Issue Date	2009
Doc URL	http://hdl.handle.net/2115/39596
Type	article (author version)
File Information	RP.pdf



[Instructions for use](#)

Aseptic meningitis with relapsing polychondritis mimicking bacterial meningitis

Hiroaki Yaguchi^{a),b)}, Kazufumi Tsuzaka^{a)}, Masaaki Niino^{b)}, Ichiro Yabe^{b)#},

Hidenao Sasaki^{b)}.

a) Department of Neurology, Kushiro Rosai Hospital, Kushiro, Japan

b) Department of Neurology, Hokkaido University Graduate School of Medicine,
Sapporo, Japan

#Correspondence to Ichiro Yabe

Department of Neurology, Hokkaido University Graduate School of Medicine, N15 W7,

Kita-ku, Sapporo 060-8638, Japan

e-mail; yabe@med.hokudai.ac.jp

Abstract

Relapsing polychondritis (RP) is a rare multisystem autoimmune disease. Though meningitis in RP is not common, some cases with cerebrospinal fluid (CSF) pleocytosis of lymphocyte cells have been reported. Of the 18 previously reported cases, two cases demonstrated pleocytosis of polymorphonuclear leukocytes (PMN) in the CSF. In addition, the cases whose glucose level in the CSF was decreased also were seen. Our case also demonstrated pleocytosis of PMN in CSF mimicking bacterial meningitis. In the clinical field, we cannot get the culture of CNF on the day. We regard the gulucose level and cellular fraction as impotant. Therefore, we must look upon meningitis in RP as a differential diagnosis of bacterial meningitis.

Key word: aseptic meningitis, relapsing polychondritis, polymorphonuclear leukocytes, cerebrospinal fluid (CSF), bacterial meningitis

Introduction

Relapsing polychondritis (RP) is an episodic and progressive inflammatory disease of cartilaginous structures, including the elastic cartilage of the ear and nose, hyaline cartilage of the peripheral joints, fibrocartilage at axial sites, and cartilage of the tracheobronchial tree [1]. Multiple neurological abnormalities including meningitis can occur during the course of RP [2,3]. Recently attracts attention of the neurologist and many meningitis patients had been reported. Some cases showed pleocytosis with a predominance of polyphonuclear leukocytes. We must look upon meningitis in RP as a differential diagnosis of bacterial meningitis .

Case report

A-56-old woman treated with the bronchodilating agent developed an acute onset of headache, followed by bilateral ear swelling and diplopia. On admission, the patient's body temperature was 38.8°C, blood pressure 109/60 mmHg, and respiratory rate 22/min. Her general examination revealed a saddle nose, bilateral ear swelling and a stenotic sound of the upper respiratory tract. Laryngotracheal stenosis was observed with a laryngoscope. Neurological examination revealed neck stiffness and left abducent nerve palsy. Consciousness disturbance and pathological reflexes were not detected. Deep tendon reflexes were present and symmetrical. Muscle tonus was normal. A superficial

and deep sensory disturbance was not detected. The patient's cerebellar function and gait were also normal. There was no muscular atrophy or involuntary movements.

The blood count showed 22,900 leukocytes with 92% polymorphonuclear leukocytes (PMN), 2,870,000 red cells and 413,000 platelets per cubic millimeter. Serum electrolytes, creatinine, glucose, coagulation tests, liver functional tests, lacticodehydrogenase, and creatine kinase were normal. C-reactive protein (CRP)(24.72 mg/dl) and the erythrocyte sedimentation rate (ESR) (160 mm/h) were elevated. Serum IgG was 1,685 mg/dl. Laboratory data associated with collagen disease were all within the normal range. Cultures of blood, urine and sputum were negative.

A CSF study showed 640 cells/mm³ with 94 % PMN, glucose 62 mg/dl (blood glucose 125 mg/dl), protein 114 mg/dl, and IgG index 0.47. The opening pressure was 200 mmH₂O. Adenosine deaminase (ADA) and angiotensin converting enzyme (ACE) were within the normal range. Smear for acid-fast bacilli, Gram stain and Indian ink were negative. In CSF cultures for bacteria, Mycobacterium tuberculosis and cytology were also negative. And the other 2 times of CSF studies before PSL therapy showed pleocytosis with a predominance of PML.

Brain MRI, MRA and Nerve conduction studies were normal. EEG demonstrated α -actives without a slow wave. A biopsy of the left ear cartilage before predonisone

therapy showed inflammation and infiltration of neutrophils, plasma cells and lymphocytes. (Fig. A,B)

We established a diagnosis of aseptic meningitis with RP. One thousand mg/day of methylprednisolone was given intravenously for three days as a steroid pulse therapy, followed by oral prednisolone (PSL) at 40 mg/day for four weeks (which was then tapered at rate of 10 mg every two weeks). After steroid therapy was initiated, her symptoms improved considerably.

Two months later, her physical and neurological symptoms had returned to normal. Serological data demonstrated that WBC, CRP and ESR also returned to normal. On CSF study, 4 cells/mm³, glucose 67 mg/dl and protein 37 mg/dl were detected.

Two years later following the attack, she was still medicated with oral PSL(7.5 mg/day) without recurrence.

Discussion

Relapsing polychondritis (RP) is a rare multisystem autoimmune disease of unknown origin characterized by recurrent episodes of inflammation and a progressive destruction of cartilaginous tissues. Elastic cartilage of the ears and nose, hyaline cartilage of the peripheral joints, vertebral fibrocartilage and tracheobronchial cartilage, as well as the proteoglycan-rich structures of the eye, heart, blood vessels or inner ear may all be

affected. In most patients RP manifests as a fluctuating but progressive course which eventually results in a significant shortening of life expectancy [3]. Central and peripheral nerve system involvement in RP occurs in approximately 3 % of patients [2]. Various cranial neuropathies as well as headaches, encephalopathy, seizures, hemiplegia, and cerebral aneurysms have been reported [2,3]. The diagnosis was usually established by clinical features, whose criteria are proposed by McAdam et al [1], Damiani et al [4], and Michet et al [5]. Modifications to the McAdam criteria were made by Damiani et al due to the variability of clinical manifestations during the course of this disease. This patient fulfilled both Damiani's and Michet's criteria.

In this case, the neurological symptoms were meningitis and abducens paralysis. Abducens paralysis seemed to have been a cranial neuropathy because it was improved by administration of PSL and there were no neurological sign of brain stem involvement or increased intracranial pressure.

Our case showed marked pleocytosis with a predominance of PMN in the CSF. The meningitis and encephalitis in patients with RP including our case has been noted in 17 cases previously reported in the literature (Table 1) [6-21]. In the initial reported cases, pleocytosis with a predominance of lymphocytosis in the CSF were described. But in more recent cases, pleocytosis with a predominance of PMN were reported. Eight cases

presented pleocytosis with a predominance of lymphocytosis in the CSF [6-16]. On the other hand, 3 cases including our case presented pleocytosis with a predominance of PMN leukocytes were reported [17,18]. In addition, in the 2 cases without our case the level of glucose in the CSF was decreased, and therapy by immunosuppressors including PSL made the level of glucose normalized. One case, at the first onset of meningitis, showed pleocytosis of mononuclear cells in the CSF, but the recurrence showed meningitis with pleocytosis of PMN in the CSF [19]. In the other case, PMN leukocytes were nearly half of leukocytes [20]. The efficiency of therapy by immunosuppressors, including PSL was good without one case[16]. In cases with more inflammation, a predominance of PMN is observed.

Although pleocytosis of mononuclear cells in the CSF can be seen in meningitis with most inflammatory diseases, patients with neuro-Behcet's disease have increased levels of PMN leukocytes in the CSF on acute exacerbation. In systemic lupus erythematosus (SLE) patients with aseptic meningitis, significantly higher cell counts with neutrophil predominance can occur rarely and suggests cerebral vasculitis with ischemia [22]. In addition, the level of glucose in the CSF is rarely decreased in the neuropsychiatric manifestation of SLE (NP-SLE), which has been reported at a low incidence between 3 % and 8 % of patients [22].

Thirty percent of RP patients have a complication of autoimmune diseases e.g. Behcet's disease, SLE [23]. We speculate that the increase of PMN in the CSF is caused by RP as well as other inflammatory diseases (e.g. neuro-Behcet's disease, SLE) .

One has to be aware that meningitis with RP can also be the differential diagnosis of bacterial meningitis.

References

- [1] McAdam LP, O'Hanlan MA, Bluestone R, Pearson CM. Relapsing polychondritis: prospective study of 23 patients and a review of the literature. *Medicine* 55: 193-215, 1976.
- [2] Letko E, Zafirakis P, Baltatzis S, Voudouri A, Livir-Rallatos C, Foster CS. Relapsing polychondritis: a clinical review. *Semin Arthritis Rheum* 31: 384-395, 2002
- [3] Gergely P Jr, Poor G. Relapsing polychondritis. *Best Pract Res Clin Rheumatol* 18: 723-738, 2004
- [4] Damiani JM, Levine HL. Relapsing polychondritis--report of ten cases. *Laryngoscope* 89: 929-946, 1979.
- [5] Michet CJ Jr, McKenna CH, Luthra HS, O'Fallon WM. Relapsing polychondritis. Survival and predictive role of early disease manifestations. *Ann Intern Med* 104: 74-78, 1986.
- [6] Nagashima T, Tanaka H, Ito M, Hirata K, Katayama S, Watanabe K. A case of aseptic meningitis caused by relapsing polychondritis. *Rinsho Shinkeigaku (Clin Neurol)* 46: 40-44, 2006. (in Japanese, Abstract in English)
- [7] Hsu KC, Wu YR, Lyu RK, Tang LM. Aseptic meningitis and ischemic stroke in relapsing polychondritis. *Clin Rheumatol* 25: 265-267, 2006.

- [8] Brod S, Booss J. Idiopathic CSF pleocytosis in relapsing polychondritis. *Neurology* 38: 322-323, 1988.
- [9] Stewart SS, Ashizawa T, Dudley AW Jr, Goldberg JW, Lidsky MD. Cerebral vasculitis in relapsing polychondritis. *Neurology* 38: 150-152, 1988.
- [10] Hanslik T, Wechsler B, Piette JC, Vidailhet M, Robin PM, Godeau P. Central nervous system involvement in relapsing polychondritis. *Clin Exp Rheumatol* 12: 539-541, 1994.
- [11] Ohta Y, Nagano I, Niiya D, Fujioka H, et al. Nonparaneoplastic limbic encephalitis with relapsing polychondritis. *J Neurol Sci* 220: 85-88, 2004.
- [12] Watanabe T, Yasuda Y, Tanaka H, Akiguchi I. Relapsing polychondritis with mental disorders: a case report. *Rinsho Shinkeigaku (Clin Neurol)* 37: 243-248, 1997. (in Japanese, Abstract in English)
- [13] Yang SM, Chou CT. Relapsing polychondritis with encephalitis. *J Clin Rheumatol* 10: 83-85, 2004.
- [14] Fujiki F, Tsuboi Y, Hashimoto K, Nakajima M, Yamada T. Non-herpetic limbic encephalitis associated with relapsing polychondritis. *J Neurol Neurosurg Psychiatry*. 75:1646-1647, 2004.
- [15] Kuwabara M, Shimono T, Toyomasu M, et al. "Prominent ear sign" on diffusion-weighted magnetic resonance imaging in relapsing polychondritis. *Radiat Med*.

26:438-441, 2008.

[16] Imamura E, Yamashita H, Fukuhara T, Nagashima K, Kohriyama T, Tokinobu H. An autopsy case of perivascularitic meningoencephalitis associated with relapsing polychondritis presenting with central nervous system manifestation. *Rinsho Shinkeigaku (Clin Neurol)* 49: 172-178, 2009. (in Japanese, Abstract in English)

[17] Ragnaud JM, Tahbaz A, Morlat P, Sire S, Gin H, Aubertin J. Recurrent aseptic purulent meningitis in a patient with relapsing polychondritis. *Clin Infect Dis* 22: 374-375, 1996.

[18] Wasserfallen JB, Schaller MD. Unusual rhombencephalitis in relapsing polychondritis. *Ann Rheum Dis* 51: 1184, 1992.

[19] Berg AM, Kasznica J, Hopkins P, Simms RW. Relapsing polychondritis and aseptic meningitis. *J Rheumatol* 23: 567-569, 1996.

[20] Kothare SV, Chu CC, VanLandingham K, Richards KC, Hosford DA, Radtke RA. Migratory leptomenigeal inflammation with relapsing polychondritis. *Neurology* 51: 614-617, 1998.

[21] Fujioka S, Tsuboi Y, Mikasa M, et al. A case of encephalitis lethargica associated with relapsing polychondritis. *Mov Disord* 23:2421-2423, 2008.

[22] West SG. Systemic lupus erythematosus and the nervous system. in: *Duboi's Lupus*

Erythematosis. 6th ed. Wallace DJ, Hahn BH Eds. Philadelphia, Lippincott Williams & Wilkins, 2001: 708-717.

[23] Gilliland BC. Relapsing polychondritis. in: Harrison's Principles of Internal Medicine. 16th ed. Kasper DL, Braunwald E, Fauci AS, Hauser SL, Longo D, Jameson JL Eds. New York, McGraw-Hill, 2004: 2015-2017.

Legends

Table

PMN; polymorphonuclear cells, M; monocytes, L; lymphocytes,

PSL; prednizolone, MTX; methotrexate, CyA; ciclosporin, AZP; azathioprine, CY;

cyclophosphamide, (-); not described

*no registry of cellular fraction

Figure

(A) Biopsy sample of the left ear cartilage shows perichondrial inflammation with neutrophils, plasma cells and lymphocytes (hematoxylin-eosin stain ×10)

(B) Neutrophils in the areas of cartilage destruction (hematoxylin-eosin stain ×40)

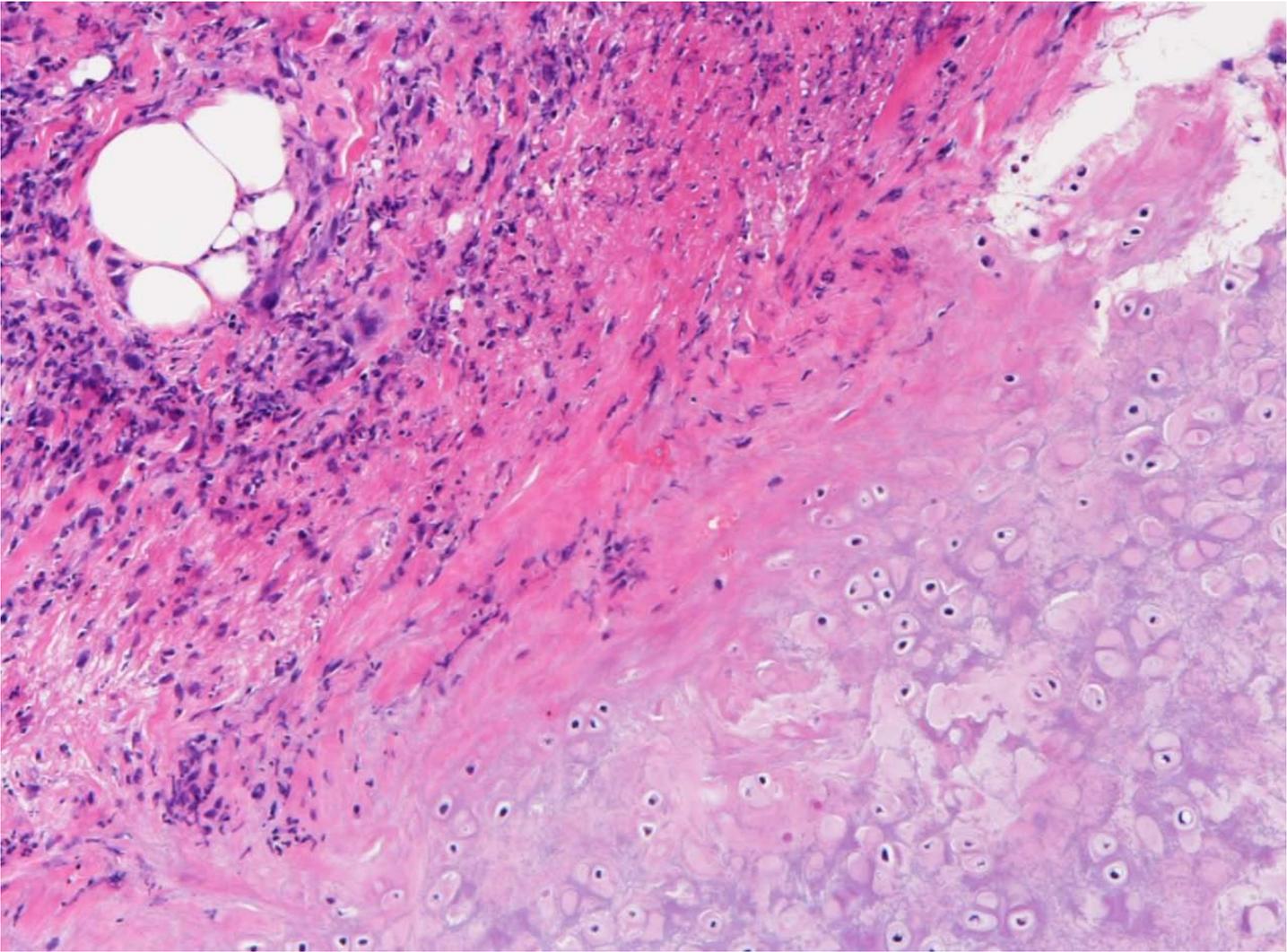
Table Summary of relapsing polychondritis cases with meningitis

References	Age (yrs) and gender	CSF profile			Serum glucose (mg/dl)	Treatment	Outcome
		Leucocytes (PMN/M/L) (per mm ³)	protein (mg/dl)	glucose (mg/dl)			
Nagashima et al [6]	65 M	302/ 450 (M+L)	79	65	179	PSL	improvement
Hsu et al [7]	71 F	0/ 110 (M+L)	116	57.6	(-)	PSL	improvement
Brod and Booss [8]	30 F	2/4/31	(-)	(-)	(-)	(-)	(-)
	75 F	40/0/90	98-140	(-)	(-)	PSL	improvement
Stewart et al [9]	52 M	140/0/200	176	normal	(-)	none	improvement
Hanslik et al [10]	70 F	5/10/22	(-)	(-)	(-)	PSL	improvement
Ohta et al [11]	57 M	10/0/58	57	86	(-)	PSL	improvement
Watanabe et al [12]	60 M	5/0/44	51	normal	(-)	PSL	improvement
Yang et al [13]	49 M	55/4/86	87	54	(-)	PSL	improvement
Fujiki et al[14]	45M	480(PMN+M)/7520	86	84	99	PSL	improvement
	62M	4080(PMN+M)/1992 0	46	77	107	PSL	improvement
Kuwabara et al[15]	61 M	13/299(M+L)	(-)	(-)	(-)	PSL	improvement
Imamura et al[16]	70 F	0/73(M)	123	(-)	(-)	PSL+MTX+ CyA	death
Ragnaud et al [17]	70 F	2340/ 260 (M+L)	40	37.2	(-)	PSL	improvement
Wasserfallen and Schaller [18]	73 F	646/0/304	100	39.6	165.6	PSL+CY	improvement
Berg et al [19]	60 M						
	onset	31/9/109	140	22	(-)	PSL+AZP	improvement
	recurrence	190/10 (M+L)	80	20	(-)	PSL	improvement
Kothare et al [20]	66 M	14/4/8	59	68	(-)	PSL	improvement
Fujioka et al[21]	66 F	90*	147	(-)	(-)	PSL	improvement
Our case	62 F	601/0/38	114	62	125	PSL	improvement

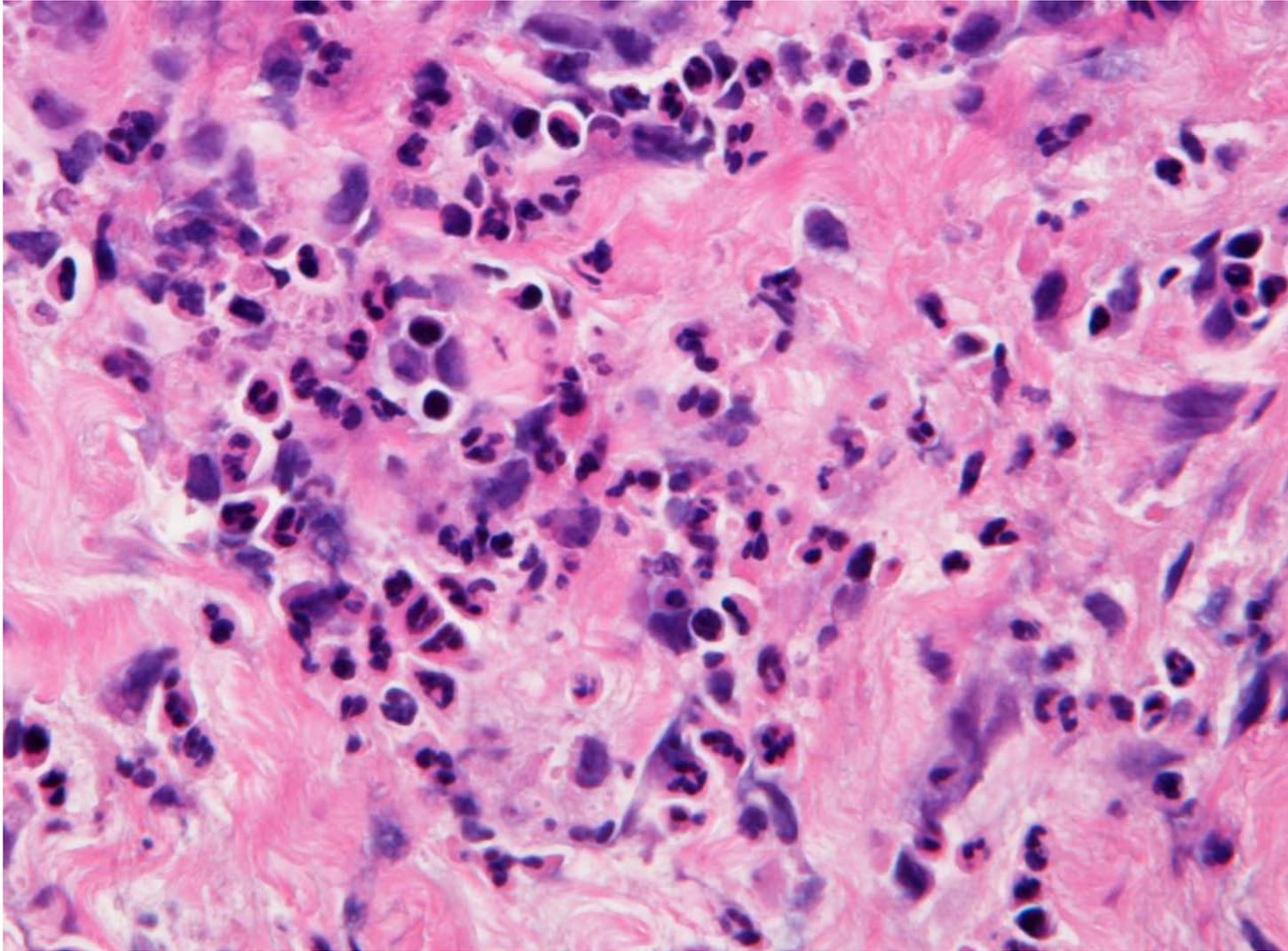
PMN; polymorphonuclear cells, M; monocytes, L; lymphocytes,

PSL; prednisolone, MTX; methotrexate, CyA; ciclosporin A, CY; cyclophosphamide, AZP;

azathioprine, (-); not describe * no registry of cellular fraction



A)



B)