

The results of the present study suggest that the hypoxic conditions induced by severe asthma attacks do not induce axonal damage and neurodegeneration in children and that the use of appropriate treatments for asthma attacks in accordance with the JPGL criteria can help prevent neuronal damage.

Ethical disclosures

Patient's data protection

Confidentiality of data. We have followed the protocols of our work centre on the publication of patient data and that all the patients included in the study have received sufficient information and have given their informed consent in writing to participate in that study.

Right to privacy and informed consent. Right to privacy and informed consent. We have obtained the informed consent of the patients and/or subjects mentioned in the article. The author for correspondence is in possession of this document.

Protection of human subjects and animals in research. The procedures followed were in accordance with the regulations of the responsible Clinical Research Ethics Committee and in accordance with those of the World Medical Association and the Helsinki Declaration.

Conflicts of interest

None of the authors have conflicts of interest to disclose.

References

1. Robert M, Mathuranath PS. Tau and taupathies. *Neurol India*. 2007;55:11–6.
2. Japanese Society of Allergy and Clinical Immunology. Japanese pediatric guidelines for the treatment and management of asthma 2008. 1st ed. Tokyo: Kyowa Kikaku; 2008.
3. Morikawa A, Nishima S. New Japanese pediatric guidelines for the treatment and management of bronchial asthma. *Pediatr Int*. 2007;49:1023–31.
4. Kosik KS, Finch EA. MAP2 and Tau segregate into dendritic and axonal domains after the elaboration of morphologically distinct neuritis: an immunocytochemical study of cultured rat cerebrum. *J Neurosci*. 1987;7:3142–53.
5. Sjögren M, Davidsson P, Tullberg M, Minthon L, Wallin A, Wikkelso C, et al. Both total and phosphorylated tau are increased in Alzheimer's disease. *J Neurol Neurosurg Psychiatry*. 2001;70:624–30.
6. Hesse C, Rosengren L, Andreasen N, Davidsson P, Vanderstichele H, Vanmechelen E, et al. Transient increase in total tau but not phospho-tau in human cerebrospinal fluid after acute stroke. *Neurosci Lett*. 2001;297:187–90.
7. Noguchi-Shinohara M, Hamaguchi T, Nozaki I, Sakai K, Yamada M. Serum tau protein as a marker for the diagnosis of Creutzfeldt-Jakob disease. *J Neurol*. 2011;258:1464–8.
8. Wunderlich MT, Lins H, Skalej M, Wallesch CW, Goertler M. Neuron-specific enolase and tau protein as neurobiochemical markers of neuronal damage are related to early clinical course and long-term outcome in acute ischemic stroke. *Clin Neurol Neurosurg*. 2006;108:558–63.
9. Sjögren M, Vanderstichele H, Agren H, Zachrisson O, Edsbacke M, Wikkelso C, et al. Tau and A β 42 in cerebrospinal fluid from healthy adults 21–93 years of age: establishment of reference values. *Clin Chem*. 2001;47:1776–81.
10. S. Hasegawa*, H. Wakiguchi, R. Hirano, F. Okazaki, K. Kudo, T. Ichiyama

Department of Pediatrics, Yamaguchi University Graduate School of Medicine, Yamaguchi 755-8505, Japan

*Corresponding author.

E-mail address: shunji@yamaguchi-u.ac.jp (S. Hasegawa).

<http://dx.doi.org/10.1016/j.aller.2012.10.012>

Multiple cancers in a patient with common variable immunodeficiency

To the Editor,

Common variable immunodeficiency (CVID) is the most common symptomatic primary immunodeficiency.^{1,2} Recurrent bacterial infections are considered as the main clinical manifestations of CVID, while patients also have a predisposition to a number of complications, including autoimmunity, granulomatous disease and malignancy.^{1,3,4} CVID is characterised by low concentration of IgG in combination with low IgA and/or IgM, despite normal to low number of B-cell and variable T-cell abnormalities.^{1,2}

Herein an adult woman with CVID is presented who suffered from cancers in different organs.

The patient was a 61-year-old woman with a medically uneventful teenage and adulthood since onset of persistent

gastrointestinal (GI) problems, including diarrhoea, abdominal pain, gastro-oesophageal reflux at the age of 45 years. Work up for celiac disease, inflammatory bowel disease, vasculitides and infections were all negative, but she was treated for colitis according to colonoscopy findings for five years with intermittent use of different medications, such as asacol, steroids, and metronidazole and also combination drugs to eradicate *H. pylori* infection without any significant improvement.

At 50 years of age, she was admitted to hospital because of severe pneumonia, which was treated with intravenous antibiotics; however, the GI and lung problems remained unresponsive to treatments. Subsequently, immunological work up was done for the patient, based on her history of persistent diarrhoea and pneumonia. Quantitative immunoglobulin measurement revealed an IgG: 17 mg/dL, IgA <5 mg/dL, IgM <10 mg/dL, while lymphocyte enumeration showed normal number of B- and T-cells (Table 1).

Table 1 Laboratory data of the patients with CVID.

Parameter	Result	Normal range
Serum IgG	17 mg/dL	750–1560 mg/dL
Serum IgM	<10 mg/dL	46–453 mg/dL
Serum IgA	<5 mg/dL	46–304 mg/dL
CD3+ T-cells	80.6%	68–82%
CD3+ CD4+ T-cells	22.5%	35–55%
CD3+ CD8+ T-cells	55.6%	19–37%
CD19+ B-cells	10.1%	5–15%

Further and detailed immunological studies revealed impaired antibody function and absent iso-haemagglutinin titres; hence the diagnosis of CVID was made and monthly intravenous immunoglobulin (IVIG) replacement therapy and prophylactic antibiotics were started for the patient, which led to improvement of respiratory and GI symptoms.

Four years later, at the age of 54 years, she revealed a mass in her right breast, which was removed by total mastectomy, whereas histopathological report showed stage I–II invasive ductal carcinoma. All tumour markers such as AFP, CA-125, CA19-9 and CEA were negative. One year later, she developed continues vaginal spotting, which resulted in total hysterectomy, while histopathological report was compatible with benign endometrial polyp and right ovarian cyst without any malignancy or metastatic lesion. One year later, she developed a thyroid mass and multinodular goitre, which led to hypothyroidism and high anti TPO titre (20 IU/mL, with normal range of: 1–16 IU/mL) and high TSH: 8.3 mIU/mL (normal: 0.3–4 mIU/mL). Because of enlarging mass and extension to hyoid bone and compression of beneath structures, thyroid gland was removed at 57 years of age with final diagnosis of adenoma with microfollicular intercapsular invasion.

Meantime taking biopsy specimens via endoscopic examination was performed regularly and serially, which showed chronic active inflammation in duodenal and gastric mucosal. At 58 years of age, GI symptoms recurred, while studies revealed severe gastritis and nodular duodenitis, unresponsive to treatment. Gastroduodenectomy was performed with post operation report of adenocarcinoma and high grade dysplasia with in situ carcinoma. All tumour markers were normal again.

She is not well without any either GI problem or serious bacterial infection, over two years of follow-up. She is still under regular IVIG therapy. It has been estimated that the patients with CVID have an increased rate of malignancies, about 1.8–13 fold in all types of cancers, compared to the normal population.⁵ Surveys of CVID patients have consistently shown a raised incidence of carcinoma of the stomach and lymphoma in CVID patients.^{6–8}

Although the exact reasons of increased prevalence of cancers in CVID is unknown, immune dysregulation, recurrent infections with pathogens involved in carcinogenesis, and chromosomal instability could be some causes of

malignancies in immunodeficiencies.^{8,9} The presented case is a unique one, since the patient experienced cancers in at least three organs. Malignancy is one of the important complications of CVID, which could lead to co-morbidity and mortality in the affected patients, especially in elderly ones.

Ethical disclosures

Confidentiality of data. The authors declare that no experiments were performed on humans or animals for this investigation.

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this investigation.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

Conflict of interest

The authors have no conflicts of interest and no funding was received.

References

1. Cunningham-Rundles C, Maglione P. Common variable immunodeficiency. *J Allergy Clin Immunol.* 2012;129, 1425–1426.e2.
2. Aghamohammadi A, Parvaneh N, Rezaei N. Common variable immunodeficiency: a heterogeneous group needs further subclassification. *Exp Rev Clin Immunol.* 2009;5:629–31.
3. Aghamohammadi A, Farhoudi A, Moïn M, Rezaei N, Kouhi A, Pourpak Z, et al. Clinical and immunological features of 65 Iranian patients with common variable immunodeficiency. *Clin Diagn Lab Immunol.* 2005;12:825–32.
4. Aghamohammadi A, Abolhassani H, Moazzami K, Parvaneh N, Rezaei N. Correlation between common variable immunodeficiency clinical phenotypes and parental consanguinity in children and adults. *J Investig Allergol Clin Immunol.* 2010;20:372–9.
5. Mellemkjaer L, Hammarstrom L, Andersen V, Yuen J, Heilmann C, Barington T, et al. Cancer risk among patients with IgA deficiency or common variable immunodeficiency and their relatives: a combined Danish and Swedish study. *Clin Exp Immunol.* 2002;130:495–500.
6. Aghamohammadi A, Pouladi N, Parvaneh N, Yeganeh M, Movahedi M, Gharagolou M, et al. Mortality and morbidity in common variable immunodeficiency. *J Trop Pediatr.* 2007;53:32–8.
7. Abolhassani A, Aghamohammadi A, Imanzadeh A, Mohammadinejad P, Sadeghi B, Rezaei N. Malignancy phenotype in common variable immunodeficiency. *J Investig Allergol Clin Immunol.* 2012;22:133–4.
8. Cunningham-Rundles C, Siegal FP, Cunningham-Rundles S, Lieberman P. Incidence of cancer in 98 patients with common varied immunodeficiency. *J Clin Immunol.* 1987;7:294–9.
9. Rezaei N, Hedayat M, Aghamohammadi A, Nichols KE. Primary immunodeficiency diseases associated with increased susceptibility to viral infections and malignancies. *J Allergy Clin Immunol.* 2011;127:1329–41.

M. Nabavi^a, H. Esmailzadeh^{a,*}, S. Arshi^a, M. Fallahpour^a,
N. Rezaei^{b,c}

^a *Department of Allergy and Immunology, Rasool e Akram Hospital, Tehran University of Medical Sciences, Tehran, Iran*

^b *Research Center for Immunodeficiencies, Pediatrics Center of Excellence, Children's Medical Center, Tehran University of Medical Sciences, Tehran, Iran*

^c *Molecular Immunology Research Center; and Department of Immunology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran*

* Corresponding author.

E-mail address: esmailzadeh.ho@yahoo.com

(H. Esmailzadeh).

<http://dx.doi.org/10.1016/j.j.aller.2012.10.003>