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RESEARCH LETTER

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).

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 continuous 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,

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%

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.

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