Mesalazine-induced Churg-Strauss syndrome in a patient with Crohn's disease and sclerosing cholangitis

Sirs,

Churg-Strauss syndrome (CSS) is a rare disorder characterized by asthma, eosinophilia and systemic vasculitis (1). Three different phases can usually be recognized in CSS: asthma and atopic allergies such as rhinitis may precede of months, and sometimes of several years, the development of an eosinophilic infiltrative disease with eosinophilic pneumonia or gastro-enteritis followed by the vasculitic phase (1). The etiology of CSS is unknown but putative triggering factors have been identified, including desensitization, vaccination, rapid discontinuation of oral corticosteroids and, more recently, some drugs such as macrolide antibiotics and leukotriene receptor antagonists (2,3).

We report a case of Churg-Strauss syndrome in a patient with Crohn's disease associated with use of mesalazine, a compound known to induce rarely eosinophilic pneumonia (4).

A 39-year-old man with a 10-year history of atopic rhinitis, nasal polyposis, and asthma presented with weakness, fever, weight loss, arthralgias, vertigo, and paresthesias. He was on salbutamol, mesalazine and Ursodeoxycholic acid. Mesalazine had been started 10 months before presentation for Crohn's disease and sclerosing cholangitis, both histologically proven.

At presentation, his eosinophil count was 12124 x mm$^{-3}$ (56% of total); erythrocyte sedimentation rate 41 and C reactive protein 7 mg/L (3.5 < 5). A urine specimen revealed haematuria (1 plus).

Antineutrophil cytoplasmatic antibody (ANCA), antinuclear antibodies (ANA), and rheumatoid factor were negative. A nuclear magnetic resonance of the skull showed pansinusitis, whereas a computed tomography of the lung showed initial central tuberculosis of the aorta and its main branches. The pulmonary arteries can also be involved. The inflammation is caused by infiltration of inflammatory granulomatous vasculopathy (1). Since no reports on the association of Churg-Strauss syndrome with Crohn's disease were found in a literature search, and based on the well-known recognition that drugs can act as triggering factors in Churg-Strauss vasculitis (2, 3), mesalazine was stopped.

Eight months after diagnosis the patient is well under treatment with prednisone 15 mg/day. His eosinophil count is normal as well as his erythrocyte sedimentation rate and C reactive protein.

The cause(s) of Churg-Strauss syndrome is usually not known, but among putative triggering factors vaccinations, desensitization, antibiotics and, more recently, leukotriene receptor antagonists have been described (2-3, 5). Mesalazine is known to induce eosinophilic pneumonia and can cause activation of eosinophil (4, 6). More rarely, it has been associated with vasculitis-like syndromes and, in a single case, with Churg-Strauss syndrome in a patient with uveitis and ulcerative colitis (4, 6-10). In most cases blood eosinophilia was present (6-8).

To our knowledge this is the first report of a case of Churg-Strauss syndrome in a patient with Crohn's disease and sclerosing cholangitis. Even though we could not demonstrate a cause-effect relationship between mesalazine and Churg-Strauss syndrome, we believe that our patient's illness was probably caused by this drug because of its capacity to induce eosinophil activation and hypersensitivity reactions.

We suggest that mesalazine should be used with caution in patient with asthma.

R. A. SINFO
E. SABADINI
A. M. MARESCA


A retrospective review of medical records of 36 patients with TA has shown an association of other inflammatory autoimmune diseases such as, rheumatoid arthritis, systemic lupus erythematosus, spondyloarthropathy, Crohn's disease, ulcerative colitis, coeliac disease and chronic thyroiditis (2).

We described an unusual association of TA in a young woman with a medical history of coeliac disease and idiopathic retroperitoneal fibrosis.

In May 2005 a 34 year-old woman was admitted to the Vascular Surgical Unit of our Hospital with sub-nail necrotic lesions on her right hand. The patient reported episodes of claudication in the last six months, fatigue and discomfort in the muscles of her upper right arm, after minor efforts.

Remote anamnesis showed recurrent episodes of monoligotartis of knee and ankles since the age of six.

In 2000 as a result of persistent episodes of diarrhoea, progressive weight loss and iron deficiency anaemia she was admitted to the Internal Medicine Unit where positivity of Antinididgin antibodies IgA, Antidomysial antibodies IgA and Anti-Tissue transplantiguaninase IgA was demonstrated. A jejunal
bovine showed absence or reduced height of villi, increased crypt cell proliferation and increased lymphocytes and plasma cells in the lamina propria. A seronegative arthritis in coeliac sprue was diagnosed and therefore the patient started a gluten free diet with a good serological and clinical response.

In 2003 due to persistent episodes of low back pain followed by pain in the left flank, the patient was admitted to the Urology Unit where an echography showed bilateral hydronephrosis with acute renal failure. A pig-tail stent was introduced. After one week, an abdomen CT showed bilateral ureteral stenosis with hydronephrosis and the patient underwent surgical ureterolysis with aspiration of the adherent tissue. The histological findings confirmed the diagnosis of an idiopathic retroperitoneal fibrosis without secondary diseases.

During the period in our hospital in May 2005 the objective examinations showed absence of pulse in the right radial artery. Blood examinations showed: ESR 17 mm/h, CRP 0.88 mg/dl, negative Lupus Anti coagulant, Anti-cardiolipin, Antiβ2 glycoprotein I, ANA and ANCA antibodies. Study of cytokine serum levels showed normal range (4.16 pg/ml) and IL-8 (50 pg/ml). Study of circulating mononuclear cells showed a reduction of lymphocytes in the profile of our patient’s cytokines showed normal serum levels of TNF-α but IL-6 and IL-8 levels out of normal range with high serum level of IL-6 (4.16 pg/ml) and IL-8 (50 pg/ml). Study of circulating mononuclear cells showed a reduction of lymphocytes CD8 (244 cells/μl), CD19 (125 cells/μl), and CD56 (71 cells/μl) but CD4 were in the normal range.

Fig. 1.

Angio-Magnetic Resonance and Aortography confirmed the diagnosis of an idiopathic retroperitoneal fibrosis without secondary diseases. The patient fullfilled ACR criteria for Takayasu’s arteritis (3) and was referred to the Vasculitis Center where she started therapy with methylprednisolone 16 mg/day and low molecular weight heparin. To the best of our knowledge, this case report is the first showing an association between TA, idiopathic retroperitoneal fibrosis (IRF) and coeliac disease (CD). All three diseases have an autoimmune pathogenesis. An association between TA and coeliac disease was reported in literature in two case reports which showed an improvement in coeliac activity but with progressive renal vascular hypertension treated by angiotensin with stent implantation (4-5). Also an association between TA and idiopathic retroperitoneal fibrosis was described in two case reports (6-7) but recent advances showed morphological findings which would justify the separation between the two diseases. Idiopathic retroperitoneal fibrosis is a systemic disorder under the general heading of Chronic Perniaortitis (CP). The clinical history, angiography non-MRI and ¹⁸F-FDG positron emission tomography have allowed a definite diagnosis, leading to an understanding of the disease activity in our patient.

¹⁸F-FDG positron emission tomography show in patients with CP the presence of large-vessel vasculitis involving abdominal aorta and common iliac arteries and the vascular uptake in lumbosacral arteries was seen in 43% of patients (8).

With regards to the immunological study, the profile of our patient’s cytokines showed normal serum levels of TNF-α but IL-6 and IL-8 levels out of normal range with normal levels of ESR and CRP. Some studies have found that ESR and CRP are not able to differentiate patients with clinically active and inactive TA while IL-6 and IL-8 could be promising markers of disease activity (9). Moreover IL-8 shows a normalization in most follow-up patients after immunosuppressive therapy (10).

The study of the subsets of lymphocytes population by flow cytometric analysis in our patient showed a reduction of CD8, CD19, CD16/56. However these findings, such as autoantibody production, do not appear in many other papers and is still under dispute. It will be interesting to have more reports on these data in order to achieve correct interpretation (11).

The study of the genes of major histocompatibility complex showed important data about a possible link between the diseases. Our patient showed a double association with alleles for coeliac disease DQB1*0202, DQA1*0201, DQA1*0501 linked to DRB1*03 DRB1*07, but DRB1*07, DQB1*0202 also showed an association with Takayasu arteritis in a report on Korean patients (12). No other typical association with other alleles of TA, which had been shown in a large series of patients, or with alleles of IRF was detected in our patient.

This is the first case report of TA in association with both IRF and CD, but our study failed to find a genetic link between the three diseases.

M. BENUCI, A. BERTELLI, M. MANFREDI, E. CANTINI, S. MICHELAGNOLI

Section of Rheumatology; Section of Immunology and Allergology; Arthropathy Unit, Nuovo Ospedale S. Giovanni di Dio, Florence; Section of Immunohaematology Ospedale SS. Annunziata Florence; Internal Medicine Unit and Section of Rheumatology, Sector Vasculitis Center Ospedale M. Severino e Dolce, Porto, Pisa.

Address correspondence to: Maurizio Benuci, MB: Rheumatology Unit ASL 10, Nuovo Ospedale S. Giovanni di Dio, via di Forregalli 5, 50143 Firenze, Italy. E-mail: mbenuci@tiscali.it

References


Acknowledgements

A special thanks to Miss Patricia Manfredi for her precious help in the English revision.
