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Central nervous system involvement in granulomatous polyangiitis (GPA)

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Introduction.– Even though granulomatous polyangiitis (GPA) is a multisystem autoimmune disorder, the central nervous system (CNS) involvement is an uncommon manifestation. The aim of this study was to evaluate CNS involvements of patients with GPA.

Patients.– The hospital files of the patients with the diagnosis of GPA who were followed up between the years 2005 and 2012 in Hacettepe University Hospital were retrospectively evaluated.

Results.– Totally 48 patients (M/F: 27/21) were evaluated. Mean ages and disease duration was 42.6 ± 10.4 and 4.2 ± 3.3 years. CNS involvement was seen in three (6.3%) patients. First case was a 67 years old female presented with constitutional symptoms, anemia and headache. Multiple parachymal metastasis were found in Torax CT and brain MRI (cerebellar and left temporal region). PET-BT revealed lesions in thoracic, sinonasal and cranial regions. Malignancy was not detected in tru-cut lung biopsy. cANCA and MPO were positive. After pulse therapy (MP and CYC) [1] symptoms regressed.

Second case was a 55 years old female presented as pitosis and sinonasal symptoms. Brain MR revealed a frontal mass involving bilaterally olfactory bulb. Imaging and pathologic evaluation of para-nasal region was consisted with GPA. After pulse MP and CYC findings decreased.

Third case was a male patient presented with uveitis, sinonasal polyangiitis and sensorimotor neuropathy. He was treated with pulse therapy (MP and CYC) + IVIG. After one year, pansinusitis, fever and headache. While he was on maintenance therapy he had fever, vision loss and headache. There was frontal abscess in brain MR. Even though infective endocarditis was diagnosed and antibiotics were started he had been exitus after 3 days.

Discussion.– CNS involvement in GPA is an infrequently seen. In addition to disease related etiology (contiguous invasion of granuloma from extracranial sites, remote intracranial granuloma, and CNS vasculitis), infectious complications related to immunosuppressive drugs might be seen as CNS involvement.

Reference

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Clinical manifestations of granulomatosis with polyangiitis (Wegener’s granulomatosis) in the upper respiratory tracts

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Introduction.– Subglottic stenosis affects 10 to 20% of patients with granulomatosis with polyangiitis (GPA). It is potential life-threatening complication and may be the initial symptom of GPA. Therefore, the work-up for idiopathic subglottic stenosis should always include an evaluation for GPA.

Methods.– Case presentation.

Results.– A 36-year-old female with relapsing idiopathic subglottic stenosis was supervised by otolaryngologist during 3 years. Patient had no other systemic symptoms and laboratory abnormalities. Flexible laryngoscopy detected circumferential narrowing of the subglottis. An upper respiratory tract biopsy revealed vasculitis and necrosis. Two endoscopic subglottic dilations were performed. In December 2011, patient was admitted to our hospital with migratory oligoarthritis, nasal stuffiness, rhinitis with bloody crusts, hoarseness, stridor, dyspnea on exertion. Joints tenderness and swelling, cutaneous extravascular necrotizing granulomas over the extensor surface of the olecranon region, digital infarctions, papules on the neck area were found on physical examination. There were elevation of ESR (25 mm/hour) and positive PR3-ANCA. CT scan showed granulomatous lesions in paranasal cavities. Patient was diagnosed with GPA, and was treated with oral methylprednisolone (mPSL) (24 mg/day) and intermittent cyclophosphamide (200 mg twice weekly intramuscular). All manifestations improved and ESR became within normal limit. When the dose of mPSL had been tapered to 13 mg/day (after 7 months) cutaneous extravascular necrotizing granulomas, rhinitis and subacute onset of respiratory stridor developed. Rituximab was administered due to the relapse of subglottic stenosis.

Conclusion.– Chronic or subacute subglottic stenosis could be seen in GPA and might precede other organ involvement. The treatment of subglottic stenosis of GPA requires multidisciplinary management by the rheumatologist, otolaryngologist and consist of conventional immunosuppressive therapy, biologic agents and endoscopic manipulations.

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Immunopathology of active and remitting granulomatosis with poyangiitis (Wegener’s)

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Introduction.– Granulomatosis with polyangiitis (GPA) is a complex relapsing and remitting autoimmune vasculitis. Immune system aberrations have not been completely described in this disease. We compared T-cell activation status, expression of co-stimulatory molecules, T-regulatory cells (Tregs), cytokine profile and FOXP3 & ROR-γt gene expression in peripheral blood mononuclear cells in active as well as in remitting GPA.

Methods.– Total 21 cases of GPA fulfilling ACR and CHCC criteria in active state as well as in remission state (6 months post therapy) and 20 healthy controls were enrolled in the study. PBMCs were isolated and expression of activation markers (CD25 & CD69), co-stimulatory molecules (CD152 & CD28), Tregs (CD4+CD25+FOXP3+) were analysed by flow cytometry. Th1/Th2 and Th17 cytokines were detected in culture supernatants after 24 hr stimulation with PR3 antigen. Serum IL-17 and IL-8 were studied by ELISA. Gene expression profiles of FOXP3 and ROR-γt in peripheral blood was analysed by Real Time PCR.

Results.– We have defined the Immunopathology of active and remitting as shown in the table below (table I). There was also increased IL-17, IFN-γ and TNF-α secretion in culture supernatants in remission as compared to healthy controls.

Discussion.– T-cells remain in an activated state even during remission. Remission is achieved by up-regulation of CD152 molecules probably in Tregs and also on CD8+ cells. There is also increase in Tregs during remission. The increased levels of IL-17 in active disease indicate the scope of anti IL-17 therapy. Our finding of increased ability to secrete IL17, TNF-α, IFN-γ during remission, suggests that these are effector