PET/CT in granulomatosis with polyangiitis

Characterization of F-18 fluorodeoxyglucose PET/CT in granulomatosis with polyangiitis

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Introduction—Granulomatosis with polyangiitis (GPA) is a rare autoimmune disease that is characterized by granulomatous inflammation and small vessel vasculitis that primarily involves the upper airways, lungs, and the kidneys. Early and accurate diagnosis and assessment of the extent of the disease is important for treatment decisions. F-18 fluorodeoxyglucose (FDG) positron emission tomography (PET) is an imaging technique that is increasingly being used in evaluation and management of other types of vasculitis (giant-cell arteritis). The role and characterization of FDG-PET/CT has not been reported for GPA.

Patients—We identified 10 patients with GPA who underwent FDG-PET/CT scanning over a 7-year period from January 2005 to December 2012. In all 10 patients the FDG-PET/CT was performed for suspected or known malignancy. The presenting clinico-radiologic features including FDG-PET/CT scan and chest CT scan findings were analyzed.

Results—Differentiation between inflammatory and malignant lesions was not able to be determined based on FDG-PET/CT imaging. Max SUV was compared in patients who had malignant lesions and those with inflammatory lesions secondary to GPA and no significant difference was noted. GPA lesions of the respiratory tract and lung were more clearly detected on FDG-PET/CT than CT alone. In four of 10 patients new areas of involvement of GPA were noted. Eight of 10 patients had uptake noted in the lung, and 4 out of 10 had uptake in the sinuses. Three patients had FDG uptake noted within vessels that was not previously appreciated. In seven out of 10 patients the PET/CT guided the location of the biopsy and led to diagnosis. Two patients had follow up FDG-PET/CT, which demonstrated decreased FDG uptake after treatment.

Conclusion—FDG-PET/CT cannot differentiate between malignant and inflammatory lesions in patients with GPA. However, it is a feasible modality to evaluate GPA lesion activity, identify new areas of involvement and help to guide biopsy location.

Further readings

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P65 Presentation and management of granulomatosis with polyangitis (Wegener’s) (GPA) central nervous system (CNS) involvement

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Introduction—GPA, a small-sized–vessel vasculitis, commonly involves ear, nose & throat (ENT), lungs and kidneys, and rarely, the CNS. The presentation, management and outcome of GPA CNS involvement were evaluated.

Patients—We retrospectively reviewed the charts of 16 patients (12 men) with: GPA satisfying ACR and/or Chapel Hill criteria; and, after excluding other causes, GPA CNS involvement manifesting as pachymeningitis, meningitis, stroke, spinal cord involvement or hypophysial involvement.

Results—Mean respective ages at GPA diagnosis and onset of CNS involvement were 43 and 47 years. The latter was present in nine (56%) patients at GPA diagnosis, and appeared in the seven others after a median follow-up of 24 months. Headache was the main symptom (67%), with motor and sensory impairments noted in 33 and 27%, respectively. CNS involvements were: pachymeningitis (n = 8: seven cranial and one spinal cord), ischemic (n = 4) or hemorrhagic stroke (n = 2), cerebral vasculitis (n = 2), and/or hypophysial involvement (n = 2). Extra-CNS manifestations included ENT (75%), lungs (60%), peripheral nerve(s) (40%) and kidneys (33%). ANCA detected in 12/16 (75%) patients had PR3 (n = 7) or MPO (n = 5) specificity.

Induction therapy comprised corticosteroids (CS, 100%) and IV (69%) or oral cyclophosphamide (CYC, 25%) or rituximab (6%). Maintenance therapy consisted of CS (100%) and azathioprine (63%), or methotrexate or rituximab (13% each). CNS involvement responded clinically in 12/16 (75%). Relapsing and/or refractory CNS GPA in seven patients was treated with IV CYC or rituximab (43% each) or oral CYC (14%). No patient died during follow-up, but 64% had persistent neurological sequelae.

Conclusion—Our series highlights the heterogeneity of CNS involvement in GPA. Despite initial severe disease, conventional therapy obtained clinical improvement in 75% of the patients. Rituximab should be evaluated for refractory and/or relapsing CNS GPA.

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P66 Pituitary dysfunction in granulomatosis with polyangiitis

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Introduction—Pituitary gland involvement has been rarely reported in granulomatosis with polyangiitis (GPA).

Patients—Retrospective case-series describing clinical features, pituitary imaging, hormonal evaluation, and treatment of all patients with pituitary involvement by GPA evaluated at Mayo Clinic, between 01/1996 and 12/2011.

Results—Pituitary involvement was noted in nine patients (five women). Median age at diagnosis of both GPA and pituitary involvement was 48 (range 28–68). All patients were c-ANCA/PR3 positive. Pituitary involvement frequently represented an incidental imaging finding during the evaluation of headache or sinusitis (six patients). Three

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patients presented with symptoms of pituitary dysfunction. ENT disease, pulmonary and kidney involvement were present in nine, six and four patients, respectively. None of the patients had isolated pituitary involvement. Diabetes insipidus (DI) was detectable in seven patients but was commonly asymptomatic. Eight patients had hypogonadism, five hypothyroidism, two hypocortisolism, and one had normal anterior pituitary function with isolated DI. Head MRI revealed a sellar mass with peripheral enhancement or diffuse pituitary enlargement in all patients. Complete remission of GPA was seen in all, after treatment with cyclophosphamide and rituximab in seven and two patients, respectively. After a median follow up of 80 months (range 6–128), all but one patient had decrease in size of the pituitary enlargement within 1 year of treatment. DI resolved in five out of seven patients, and persisted in the other two. Of the eight patients with anterior pituitary dysfunction, resolution was seen in three, improvement in three, and persistent dysfunction in two patients.

Conclusion.– Pituitary involvement is an uncommon manifestation of GPA and occurs concomitantly with other organ involvement. The majority of these patients have pituitary dysfunction, which can be asymptomatic at presentation. Whereas imaging findings typically respond to remission induction therapy, pituitary dysfunction may persist.

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P67
Inter-observer reproducibility of two CT scan staging systems to evaluate sinonasal involvement in granulomatosis with polyangiitis (Wegener’s)

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Introduction.– Rhinosinusitis (RS) is the most common manifestation of granulomatosis with polyangiitis (GPA). Standardized tools to evaluate disease extension and to monitor therapy response are needed. Sinus computed tomography (SCT) is the preferred imaging modality for evaluating RS. Many staging systems exist to quantify RS based on SCT; Lund-Mackay staging (LMS) and Newman staging (NS) are the most reproducible and simple in infectious/allergic RS.

Purpose.– To determine the reproducibility of LMS and NS between evaluators of different specialties and level of expertise in the evaluation of RS in GPA.

Patients.– Retrospective evaluation of 15 patients with sinonasal GPA and 15 subjects with non-vasculitic rhinosinusitis (NVRS) was performed. SCT were reviewed by six evaluators from different specialties (radiology (n = 2), rheumatology (n = 2) and ENT (n = 2)) and level of expertise (one staff and one resident in each specialty), all blinded to the clinical diagnosis. Evaluators reviewed the published LMS and NS scores and received a brief training to apply it. Results are expressed as median (range) and analyzed with Pearson test for correlation and Mann–Whitney to compare medians.

Results.– GPA and NVRS groups were similar in gender (50% female), age [60 (28–68) vs. 56 (25–67) yr] and ESR [17 (2–68) vs. 14 (2–84) mm/h]. Disease duration was longer in GPA than NVRS [32 (1–32) vs. 1 (1–9) month, p < 0.001]. Global scores were lower in GPA than NVRS using either LMS (4 vs. 12, P < 0.01) or NS (6 vs. 17, P < 0.01). A high correlation (r > 0.9, P < 0.01) was observed between all evaluators for LMS and NS scores regardless of diagnosis, specialty and expertise level. No correlation was found between ESR or disease duration and LMS/NS scores.

Conclusion.– LMS and NS represent simple and reproducible methods to quantify RS in GPA patients with no need of formal radiological training. The correlation with disease activity or damage and their utility for monitoring GPA subjects must be tested in a larger cohort of patients.

Further readings

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P68
Pathogenesis of atherosclerosis in granulomatosis with polyangiitis

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Introduction.– Previous studies from our group suggested that the inflammatory events that occur during relapses in patients with granulomatosis with polyangiitis (GPA) may have a direct role in the pathogenesis of atherosclerosis. We also showed that circulating micro-particle (MPs) levels were elevated during relapse and correlated with platelet reactivity. We further elucidated possible mechanisms by which MPs act at the interface between inflammation and atherosclerosis in GPA.

Patients.– Human dermal microvascular endothelial cells (hDMVEC) were cultured in EGM-2MV media. MPs isolated from plasma from GPA patients were added at various ratios to the hDMVEC and incubated for timed periods. Cells were then detached, washed, and re-suspended in buffer and analyzed by immunofluorescence flow cytometry with anti-ICAM-1 IgG to detect endothelial cell activation. An isotope-matched control IgG was used as control. In addition, fluorescent-tagged normal human platelets were incubated with GPA patient-derived MPs (MP/platelet ratio of 10:1) and platelet activation was detected by flow cytometry with PAC-1, an antibody to the activated form of the α2β3 integrin.

Results.– GPA patient-derived MPs, when incubated for 4 h with hDMVEC, induced surface expression of ICAM-1. MP depleted plasma was used as a control and did not influence ICAM-1 expression. ICAM-1 induction by MPs was blocked by cycloheximide indicating a requirement for new protein synthesis and showing that the ICAM-1 was not transferred to the cells by the MPs. Platelet surface expression of activated α2β3 integrin was also significantly enhanced when platelets from healthy donors were pre-incubated with patient-derived MPs and then exposed to low doses of ADP (1 μM).

Discussion.– Our findings demonstrate that MPs isolated from plasma of GPA patients can activate platelets and vascular endothelial cells.

Conclusion.– This study suggest possible roles for MPs as an interface between inflammation and athero-thrombosis in GPA.

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