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Abstract

Granulomatosis with polyangiitis (GPA) is a challenging trans-disciplinary disease. It requires the cooperation of many specialists and in most cases involves head and neck region, especially nose and paranasal sinuses. Treatment is usually tailored to the extent of disease and organs affected by the disease. The aim is to describe the extent of GPA in head and neck computed tomography and nasal endoscopic examination with a focus on sinonasal disease and concomitant ENT areas and to submit a grading system in GPA patients with sinonasal changes. Study enrolled 68 patients with GPA (study group) and 70 patients with CRS (control group). The study group involved 23 men and 45 women. Patients' age ranged between 16 and 82. The sinonasal changes in computed tomography were evaluated with Lund-MacKay scoring system but also included nasal cavity mucosal changes, bony and cartilaginous changes and external nose deformity. Other ENT changes included ear abnormalities with fluid or granulomatous changes, skull base inflammatory tumors, laryngeal stenosis and others. The results will be presented in patients with GPA divided into localized and systemic form of disease, c-ANCA positive and c-ANCA negative disease, acute and remission phase of GPA. We believe that this work will show the spectrum of head and neck manifestations in GPA and will help understanding the role of imaging in diagnosing and follow-up of GPA patients in order to establish the indications for radiologic evaluation and avoid unnecessary imaging. Curcumin preparations typically contain a mixture of polyphenols, collectively referred to as curcuminoids. In addition to the primary component curcumin, they also contain smaller amounts of the co-extracted derivatives demethoxycurcumin and bisdemethoxycurcumin. Curcuminoids can be differentially solubilized in serum, which allows for the systematic analysis of concentration-dependent cellular binding, biological effects, and metabolism. Technical grade curcumin was solubilized in fetal calf serum by two alternative methods yielding saturated preparations containing either predominantly curcumin (60%) or bisdemethoxycurcumin (55%). Continual exposure of NT2/D1 cells for 4–6 days to either preparation in cell culture media reduced cell division (1–5 μM), induced senescence (6–7 μM) or comprehensive cell death (8–10 μM) in a concentration-dependent manner. Some of these effects could also be elicited in cells transiently exposed to higher concentrations of curcuminoids (47 μM) for 0.5–4 h. Curcuminoids induced apoptosis by generalized activation of caspases but without nucleosomal fragmentation. The equilibrium binding of serum-solubilized curcuminoids to NT2/D1 cells incubated with increasing amounts of curcuminoid-saturated serum occurred with apparent overall dissociation constants in the 6–10 μM range. However,

the presence of excess free serum decreased cellular binding in a hyperbolic manner. Cellular binding was overwhelmingly associated with membrane fractions and bound curcuminoids were metabolized in NT2/D1 cells via a previously unidentified reduction pathway. Both the binding affinities for curcuminoids and their reductive metabolic pathways varied in other cell lines. These results suggest that curcuminoids interact with cellular binding sites, thereby activating signal transduction pathways that initiate a variety of biological responses. The dose-dependent effects of these responses further imply that distinct cellular pathways are sequentially activated and that this activation is dependent on the affinity of curcuminoids for the respective binding sites. Defined serum-solubilized curcuminoids used in cell culture media are thus suitable for further investigating the differential activation of signal transduction pathways.

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