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Case Report

Caught in the act: Allergic-like reaction to gadolinium-based contrast agent in POEMS syndrome

Guillaume Kugener, MEng^a, Anandh Rajamohan, MD^b, Vishal Patel, MD, PhD^{b,*}

^aKeck School of Medicine, University of Southern California, Los Angeles, CA, USA

^bDepartment of Radiology, Keck School of Medicine, University of Southern California, Los Angeles, CA, USA

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ABSTRACT

POEMS syndrome is a rare paraneoplastic condition related to an abnormal proliferation of plasma cells. Allergic-type reactions to gadolinium-based MR contrast media are likewise uncommon adverse events. In this report, we present a highly unusual case involving the collision of these 2 entities. Because the reaction developed unrecognized during the course of the MR examination, the case provides not only a review of the major radiological manifestations of POEMS syndrome, but also a unique insight into the imaging features of an acute contrast reaction. We briefly discuss the incidence and classification of allergic-type contrast reactions and explore possible associations with hematologic dyscrasias.

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Introduction

POEMS syndrome is a paraneoplastic condition caused by a proliferation of abnormal plasma cells [1]. The acronym POEMS refers to the clinical manifestations of polyneuropathy, organomegaly, endocrinopathy/edema, monoclonal plasma cell proliferative disorder, and skin changes. Other common features of POEMS syndrome include sclerotic bone lesions, papilledema, thrombocytosis, and pulmonary dysfunction. POEMS syndrome is a rare condition, with an estimated prevalence of only 3 cases per 1,000,000 individuals and a reported male predilection [2]. We present here an unusual case of a patient with POEMS syndrome undergoing workup for papilledema who developed an acute allergic-type reaction to

gadolinium-based contrast agent (GBCA), with the developing effects of the reaction captured by the magnetic resonance imaging in progress.

Case report

A 44-year-old male with a history of POEMS syndrome endorsed a 3-month history of blurry vision in the right eye during a routine hematologic follow-up evaluation. The patient had previously been diagnosed with POEMS syndrome following the International Myeloma Working Group criteria [2]. Specifically, the patient satisfied the mandatory criteria of polyneuropathy and monoclonal plasma cell proliferation,

* Corresponding author.

E-mail address: vishal.patel@med.usc.edu (V. Patel).

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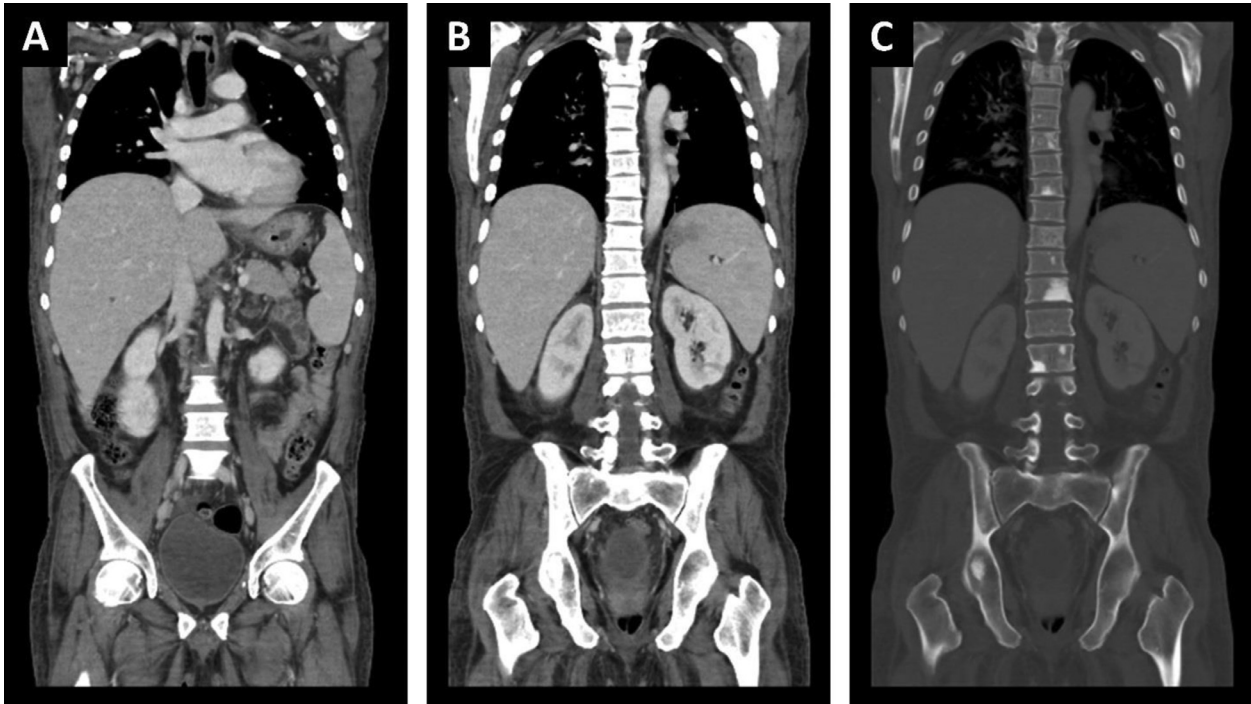


Fig. 1 – Imaging features of POEMS syndrome. Contrast-enhanced coronal CT images of the chest, abdomen, and pelvis on soft tissue window illustrate the organomegaly of POEMS manifesting as hepatomegaly (A) and splenomegaly (B), while bone window image (C) depicts osteosclerotic lesions in the right scapula, multiple vertebral bodies, and the right pelvic ischium.

the major criteria of osteosclerotic lesions and elevated vascular endothelial growth factor (VEGF) levels, and minor criteria including endocrinopathy (characterized by elevated thyroid stimulating hormone level) and organomegaly (characterized by hepatosplenomegaly).

The findings of organomegaly and osteosclerotic lesions had been made by contrast-enhanced computed tomography of the chest, abdomen, and pelvis, as shown in [Figure 1](#). The enlarged liver measured up to 22.5 cm along the midclavicular line ([Fig. 1A](#)), and the spleen was also enlarged, measuring up to 14.9 cm in long axis ([Fig. 1B](#)). The CT examination also revealed numerous sclerotic lesions in the axial and appendicular skeleton ([Fig. 1C](#)).

Ophthalmologic consultation was sought for the complaint of blurry vision, at which time a fundoscopic examination revealed blurring of the optic disc margins consistent with papilledema bilaterally. Visual acuity was reduced to 20/40 in the right eye and 20/25 in the left eye, not improved by the use of a pinhole occluder. No other significant ophthalmologic abnormalities were noted. The known diagnosis of POEMS syndrome was felt to be the most likely etiology of the papilledema, but an MR examination of the orbits with and without contrast was requested to exclude other causes.

MR imaging was performed on a 1.5 T system per our institutional protocol. Acquisition of the precontrast sequences was followed by an interval of approximately 5 minutes, during which time 19 mL gadobenate dimeglumine was administered intravenously. Postcontrast sequences were subsequently acquired. The patient did not activate the squeeze ball

alarm during the scan; however, the MR technologist noted facial swelling as the patient exited the gantry at the conclusion of the exam and notified the responsible radiologist. Upon immediate assessment, the patient's vital signs were normal, but swelling and erythema of the left periorbital soft tissues and upper lip were observed. The patient denied pruritus, acute changes in vision, pain with eye movements, hoarseness, or dyspnea. A diagnosis of allergic-type contrast reaction was made, 50 mg diphenhydramine was administered intravenously, and the patient was held for observation.

At that time, images from the MR examination were reviewed and are provided as [Figure 2](#). Initial T2-weighted sequence of the orbits illustrated bulging of the optic nerve heads along the posterior margins of the globes ([Fig. 2A](#)), consistent with the clinical observation of papilledema. Evaluation of the precontrast sequences at the levels of the orbits and maxilla revealed no other abnormality, but the corresponding postcontrast sequences showed the immediate development of swelling and enhancement in the soft tissues of the left periorbital region and upper lip as well as within the left temporalis and right medial pterygoid muscles ([Fig. 2B vs C](#) and [Fig. 2D vs E](#)).

The patient was reassessed 1 hour later, at which time the areas of facial swelling appeared to be resolving, and no new symptoms were reported. The patient was referred for same-day ophthalmologic re-evaluation, which again identified papilledema and mild left periorbital swelling, but no new concerning abnormality. The patient was therefore discharged home with complete resolution of facial swelling shortly

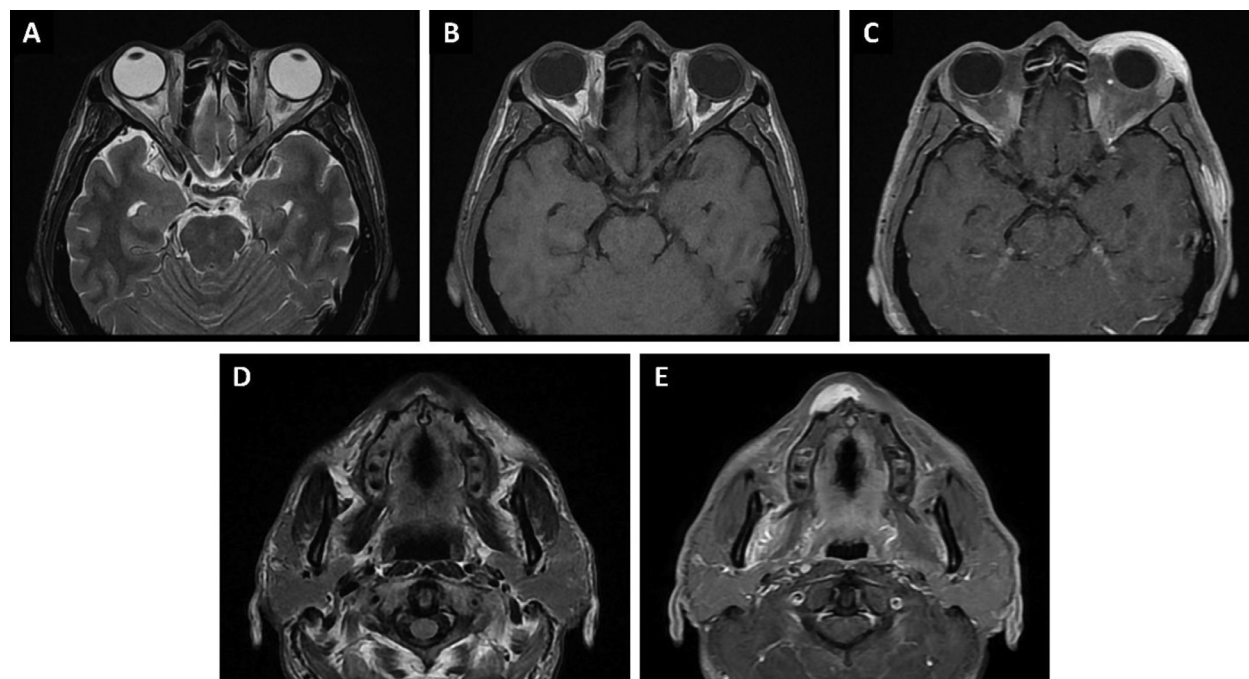


Fig. 2 – MR imaging of allergic-type contrast reaction in progress. Axial precontrast MR images of the orbits obtained with T2-weighting (A) and T1-weighting (B) demonstrate bulging of the optic nerve heads along the posterior margins of the globes compatible with papilledema of POEMS, but no other abnormality. Postcontrast fat-suppressed T1-weighted image acquired 5 minutes later (C) illustrates left periorbital and temporalis muscle swelling and enhancement. At the level of the maxilla, T2/FLAIR (D) and postcontrast fat-suppressed T1-weighted (E) images depict the immediate development of areas of soft tissue swelling and enhancement along the upper lip and within the right medial pterygoid muscle following contrast agent administration.

thereafter. Notation of the contrast reaction was logged in the electronic medical record.

Discussion

GBCAs, such as the gadobenate dimeglumine administered in this case, have long been used to provide important additional diagnostic information in MR examinations, including improved characterization of infection, inflammation, vascularity, and neoplasms. The American College of Radiology broadly divides acute adverse reactions to contrast media into allergic-like and physiologic categories based on their presenting signs and symptoms [3]. Allergic-like reactions present with features similar to allergy and may be responsive to antihistamine therapy and corticosteroid premedication if a subsequent administration of the same or similar contrast agent is necessary. Allergic-like reactions can vary in their severity; in the present case, the initial assessment revealed facial edema without dyspnea and stable vital signs suggesting a mild-to-moderate severity reaction. Compared to the iodinated contrast agents used for CT examinations, GBCAs are associated with a much lower rate of adverse reactions; the incidence of GBCA-related allergic-type reactions ranges from 0.004% to 0.7%, and within these rare events, the large fraction are classified as mild in severity, constituting 74%-77% of allergic-type reactions [3–9].

The diagnosis of an acute contrast reaction is made by history and clinical features; imaging is typically not indicated. The completed MRI in this case, however, offers a unique visualization of the rapidity with which allergic-type reactions develop and underscores the fact that additional areas of involvement can include deep soft tissue spaces that are not readily evaluated by physical examination, warranting a period of observation. Moreover, the intense and homogeneous enhancement seen within the soft tissues provides a rarely observed correlate for the underlying pathophysiological mechanism of capillary leak in allergic-type reactions.

The coincidence of POEMS syndrome and acute allergic-type contrast reaction is interesting and raises the question of whether the underlying plasma cell abnormality may be a predisposing factor for the development of reactions to GBCAs. We note that episodes of idiopathic flushing are a recognized feature of POEMS syndrome [10,11], but the absence of such symptomatology prior to or following this episode in our patient suggests that a true contrast reaction was observed. We found no direct evidence addressing the association between POEMS and GBCA reactions, which is not unanticipated given the rarity of both events. POEMS syndrome exists along a spectrum of disease including osteosclerotic myeloma and Castleman disease [2], and insights from research into these conditions is worthy of consideration. Several studies have attempted to evaluate the relationship between allergic reactions and myeloma, but these associations remain unclear

[12]. Extended episodes of facial swelling have also been observed in localized Castleman disease [13], though again, high-quality evidence of a robust association is lacking. Ultimately, the underlying risk factors for developing an allergic-type reaction to GBCAs remain largely unknown, but prompt recognition and management allow for positive outcomes in the vast majority of cases.

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