Giant cell arteritis and polymyalgia rheumatica as first manifestation of typical pulmonary carcinoid tumor

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SUMMARY

Giant cell arteritis (GCA), a systemic vasculitis of unknown origin, may appear rarely as a paraneoplastic syndrome. Cases secondary to pulmonary neuroendocrine tumors have not been reported.

A 75-year-old female developed prednisone-responsive GCA/polymyalgia rheumatica (PMR) shortly followed by syndrome of inappropriate antidiuretic hormone secretion. An 8 mm carcinoid lung tumor with positron emission tomography normal uptake was found. After a thoracoscopic tumor resection the patient experienced complete clinical and laboratory remission.

This is the first report of GCA with PMR in the context of carcinoid lung tumor. It emphasizes the role of paraneoplastic vasculitis as a possible cause of GCA.

Key words: *Vasculitis; rheumatology.*

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INTRODUCTION

Giant cell arteritis (GCA) is an inflammatory disorder of unknown origin characterized by a granulomatous infiltrate with lymphocytes, macrophages, and multinucleated giant cells at the intima-media junction, affecting large- and medium-sized muscular arteries, particularly the proximal aorta and branches of the external carotid (1). GCA occurs separately or simultaneously to polymyalgia rheumatica (PMR) in patients beyond 50 years of age and may develop as a paraneoplastic disorder on rare occasions (2). We report a case of typical pulmonary carcinoid tumor manifesting as GCA, PMR and syndrome of inappropriate antidiuretic hormone secretion (SIADH). To the best of our knowledge, there has been yet no report of GCA associated with this pulmonary tumor.

CASE REPORT

A 75-year-old female, obese, suffering from a well-controlled hypothyroidism, was evaluated because of a 3-months history of a new and continuous headache associated with neck and shoulder pain. She also presented stiffness in the cervical region and shoulder girdle with bilateral upper arm tenderness and pain. On physical examination, the right superficial temporal artery was thickened, nodular and tender with decreased pulse (Figure 1). Her brain magnetic resonance angiography was unremarkable and a duplex ultrasonography depicted stenosis and an halo sign at the right superficial temporal artery. The erythrocyte sedimentation rate (ESR) was 90 mm/h and the C reactive protein (CRP) level was 24 mg/dL. The patient fulfilled the American College of Rheumatology (ACR) criteria for the definition of GCA (3) and the ACR/European League Against Rheumatism (EULAR) criteria for PMR (4). With these diagnoses she was prescribed 60 mg/day oral prednisone with rapid clinical improvement.

One week later, the patient experienced loss of appetite, nausea, vomiting, progressive confusion, lethargy and malaise. On admission at the emergency yard, the patient was normovolemic without focal neurologic deficits or signs of meningeal irrita-

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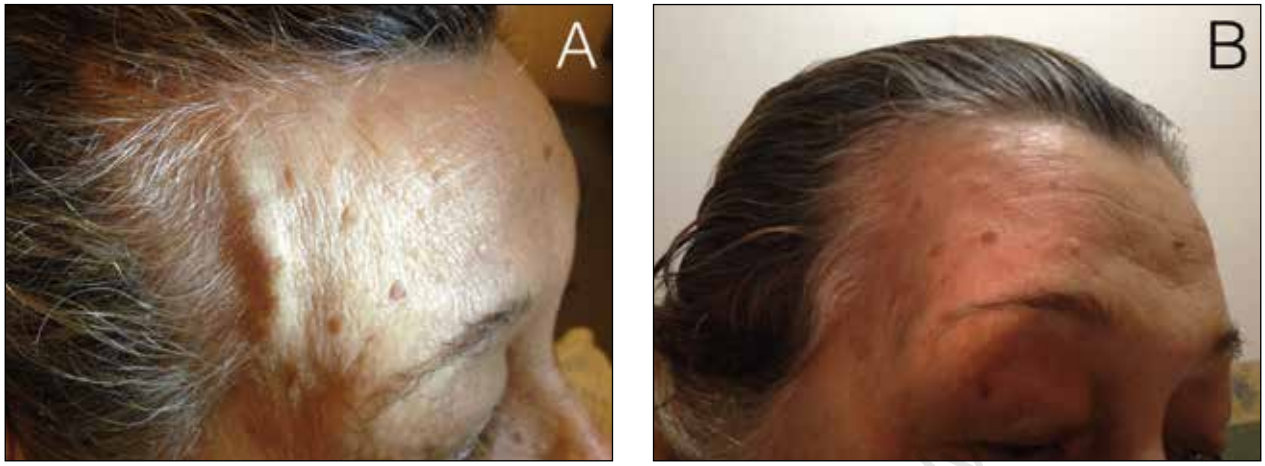

Figure 1 - A) Right superficial temporal artery was thickened, nodular and tender before treatment. B) Full clinical recovery, after treatment.

tion. Her serum sodium was 105 mmol/L, uric acid 1.1 mmol/L, serum osmolality 220 mmol/L, urinary osmolality 400 mmol/L and urinary sodium 80 mmol/L. Renal function, thyroid function tests and cortisol adrenal results were normal. Breast and additional gynecologic examination were normal. The diagnosis of SIADH was performed. A paraneoplastic etiology was suspected and a clinical workup revealed an 8 mm diameter speculated, solid nodule located at the upper segment of the right lower pulmonary lobe associated with a discrete pleural retraction (Figure 2). The positron emission tomography showed normal uptake of 18-flurodeoxyglucose in the nodule and large vessel.

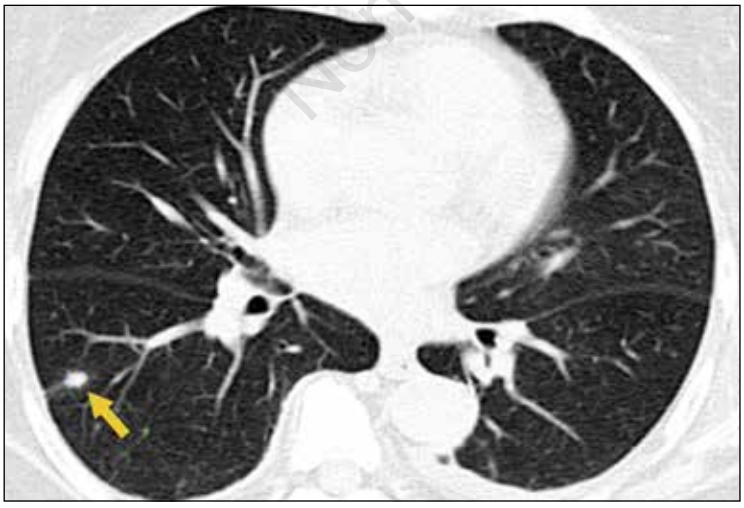

Figure 2 - Axial chest computed tomography showing an 8 mm diameter speculated, solid nodule located at the upper segment of the right lower pulmonary lobe associated with a discrete pleural retraction.

She underwent to a thoracoscopic mass and wedges resection on the right lower lobe under general anesthesia. Pathology of the lung biopsy showed a typical neuroendocrine carcinoid tumor. The ESR and CRP values dropped to 20 mm/h and 2 mmol/L, respectively. The glucocorticoid treatment was interrupted after surgery and she had no GCA symptoms and remains asymptomatic and treatment-free two years after surgery.

Full consent was obtained from the patient for the case publication.

DISCUSSION

Paraneoplastic syndrome is defined as tumor-associated remote symptoms and signs not related to the physical effects of the original or metastatic tumor. Underlying mechanisms involve abnormal immune responses, as antibodies to onconeural antigens are found in the serum of affected individuals. In the present case, the close relation in time between the GCA onset and the carcinoid tumor reinforces the paraneoplastic etiology. Besides, a complete remission was observed following tumor resection.

The association between cancer and vasculitis remains controversial and without definitive evidence in favor of increase risk in GCA (5), but when this possible association occurs it is usually due to blood neoplasms or less frequently solid tumors, mostly of lung (non-small-cell), prostate, colon, breast and kidney origins (6, 7). Vasculitis should raise the suspicion of underlying malignancies specially if atypical or less responsive to treatment (8). Although, small vessels vasculitis and leukocytoclastic vasculitis are more frequently involved in paraneoplastic cases and large vessels may occasionally be affected. Remission following tumor resection indicates that the pathogenesis involves immune mechanisms mediated by the tumor, but the mechanisms responsible for vasculitic manifestations in patients with neoplasia remain obscure (9).

The cause of GCA is currently unknown, but pathological findings of multinucleated giant cells points to an infectious or autoimmune process. The varicella Zoster virus has ben implicated as a possible cause of GCA (10). The disease typically responds to corticosteroids, suggesting an underlying dysimmune mechanism. In case of paraneoplastic GCA, the immune system would plausibly be activated by tumor secreted agents. GCA has been found to decrease the risk of cancer (11), and does not increase cancer mortality (12). In biopsy-proven cases, however, GCA has been shown to increase the malignancy risk (13). Taken together, existing data seem to indicate that GCA does not increase the risk of neoplasia (14). On the other hand, reports of GCA in close association with tumors, including lung, breast, cervical, multiple myeloma, and chronic myelogenous leukemia, indicate that GCA may occur as a paraneoplastic disorder (15).

Bronchopulmonary neuroendocrine tumors comprise four subtypes: low-grade typical carcinoid tumor, intermediate-grade atypical carcinoid tumor; and two high-grade malignancies: large-cell neuroendocrine carcinoma and small-cell lung carcinoma (16). Pulmonary carcinoid tumors are rare, accounting for 1% of lung cancers (17). Around 60% of lung carcinoid tumors are asymptomatic at presentation, cough, hemoptysis and pneumonia 24% due to luminal obstruction and ulceration may occur. Serotonin secretion with diarrhea, flushing, wheezing, and carcinoid heart disease, or other hormonally active tumor products such as SIADH are rare (1-3%). Carcinoid tumors have been related to paraparesis, sensory neuropathy, myelopathy, limbic encephalitis and brain stem encephalitis on rare occasions.

We reported the first case of a typical pulmonary carcinoid tumor associated with paraneoplasticaly generated GCA, PMR and SIADH. This case further highlights the need for clinicians to be alert for tumor-induced vasculitis in elderly headache patients.

Conflicts of interest: None.

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