Sudden death and Wegener's granulomatosis of the pituitary: Case Report

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Involvement of brain parenchyma or meninges in ANCA-associated small-vessel vasculitis such as Wegener’s granulomatosis (WG) is not uncommon. In contrast, involvement of the pituitary is exceedingly rare with only a few cases reported so far. The diagnosis is usually made on the basis of imaging techniques and abnormal pituitary function tests in the setting of active systemic vasculitis. However, histology-proven involvement of the pituitary by WG has not been reported so far. We report a case of WG with histology-proven granulomatous necrotizing inflammation of the pituitary and hypothalamo-pituitary stalk, disclosed at autopsy after the patient had died suddenly and unexpectedly in his sleep. In a setting of histology-proven WG, these findings were regarded as a pituitary manifestation of the disorder. A distinct cause of death could not be found, hence we speculate that hypothalamo-pituitary inflammation due to WG may have caused the sudden death in this patient.

Key words: pituitary, sudden death, vasculitis, Wegener’s granulomatosis

Pituitary involvement is an uncommon feature of small-vessel vasculitis. Few cases of Wegener’s granulomatosis (WG) involving the pituitary have been documented by means of abnormal pituitary function tests (1–4) and imaging studies (5–7). Occasionally, attempts have been made, albeit unsuccessfully, to make an anatomical diagnosis in specimens obtained during surgery of the hypothalamo-pituitary region (4, 7). We report a patient with known WG and a history of diabetes insipidus who died suddenly; autopsy revealed necrotizing granulomatous inflammation of the hypothalamo-pituitary stalk, a finding highly suggestive of involvement by WG.

Case report

A then 26-years-old male was first diagnosed with biopsy-proven Wegener’s granulomatosis of the nose, eyes, trachea, lung, and kidney in 1984. Since then, he had sustained tracheal stenosis, left segmental resection, and enucleation of the left eye. While on treatment with steroids and cyclophosphamide, he presented in 1988 with polyuria of 15 liters per day. A diagnosis of diabetes insipidus was made on the basis of a thirst test; magnetic resonance (MR) scanning disclosed infiltration of the sphenoid sinus, clivus, and probably hypophysis that was felt to be due to WG. The patient improved after antidiuretic hormone (ADH). In 1991, while on oral cyclophosphamide, the patient sustained another relapse. MR scans revealed involvement of paranasal sinuses, clivus and, probably, posterior hypophysis. A trial of intravenous immunoglobulins was felt to confer some improvement. During the following years, immunosuppression was tapered. MR in 1996 showed infiltration of the maxillary, frontal and sphenoid sinuses, and sphenoid bone including clivus with abnormal enhancement of the hypophysis (figure 1). Assays for thyroid-stimulating hormone and adrenocorticotropic hormone (ACTH) were normal. In April, 1997, at the age of 39, the patient died suddenly and unexpectedly in his sleep. Autopsy disclosed ill-defined granulomatous inflammation of the pituitary stalk and anterior pituitary (figure 2) whereas posterior pituitary tissue could not be identified and necrosis was present. There was granulomatous inflammation of the sphenoid bone and sella turcica. These findings were regarded as pituitary involvement by WG. There was no evidence of myocardial infarction, pulmonary embolism, or cerebrovascular accident and a drug screen was negative.

Discussion

As opposed to involvement of brain (8) and meninges (9), lesions of the pituitary gland is a rare feature of WG. Four cases of diabetes insipidus (1–3) and one case of anterior pituitary failure (4) have been documented on the basis of abnormal function tests. Reports of two further cases of diabetes...
insipidus complicating WG have been augmented by CT (5) and MR (6) imaging. Moreover, two cases of combined anterior and posterior pituitary failure due to intrasellar lesions presumed to be WG have been described (7). Attempts have been made, albeit unsuccessfully, to confirm the diagnosis histologically (4, 7).

There are anecdotal reports of pituitary involvement in forms of vasculitis other than WG. In particular, lesions of the hypophysis have been described in large-vessel vasculitis such as Takayasu’s arteritis (10), in classic polyarteritis nodosa (11), and Churg-Strauss syndrome (12). Finally, one case of hypothalamic involvement with abnormal pitui-

Fig. 1. Gadolinium-enhanced T1-weighted sagittal MR image of the brain demonstrates abnormal enhancement of the pituitary in that the two lobes cannot be distinguished; there is markedly abnormal enhancement of the sphenoid bone and clivus and the sphenoid sinus appears to be filled with inhomogenous brightly-enhancing material.

Fig. 2. Section of the anterior pituitary region; there is normal pituitary histology (left), ill-defined granulomatous tissue typical of Wegener’s granulomatosis (centre) and widespread necrosis (asterisk); note that a multinucleated giant cell is present (black arrow). (hematoxylin-eosin stain. 50×).
tary function presumed to be due to granulomatous angiitis of the central nervous system has been reported (13).

We report sudden death in a patient with histology-proven WG who had previously sustained permanent diabetes insipidus as a presumed manifestation of the underlying disorder. Autopsy confirmed necrotizing granulomatous inflammation of the hypothalamo-pituitary region and sphenoid bone. In the setting of histology-proven WG, these findings were regarded as a manifestation of WG. Our case is unique in that pituitary involvement by WG was not only suspected on clinical grounds or imaging studies but could later be confirmed by histology.

In the absence of any other cause, it appears reasonable to suspect a more than coincidental relationship between sudden death and inflammation of the hypothalamo-pituitary region. Indeed, sudden death in conjunction with inflammatory (14) and neoplastic (15) lesions of the hypothalamo-pituitary region has been noted previously. These reports suggest that lesions of the hypothalamo-pituitary regions confer a particular risk of sudden death, presumably due to failure of autonomic regulation. Therefore, one may speculate whether the sudden death of our patient was caused by WG of the hypothalamo-pituitary region. Further investigations, such as autopsy studies are necessary to determine the incidence of pituitary involvement in WG, especially after sudden death has occurred.

References


