Systemic sarcoidosis presenting as Harlequin and Horner syndrome

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Practical Implications

Harlequin syndrome refers to a unilateral flushing reaction that may occur together with contralateral Horner syndrome when sympathetic pathways are disrupted.

Harlequin syndrome is the colorful description given to the condition of unilateral flushing and sweating of the face, neck, and upper chest.¹ It is attributed to the disruption of sympathetic fibers on the side contralateral to the flushing. Although the etiology of Harlequin syndrome remains unclear, the flushing response may represent a compensatory cutaneous thermoregulatory reaction in areas with spared sympathetic innervation.² Coexisting Horner syndrome, including ptosis and pupillary miosis, may be clinically apparent on the side of the disrupted sympathetic fibers.³ We report a rare case of Harlequin and Horner syndromes attributed to systemic sarcoidosis.

Case report

A 61-year-old woman presented with episodes of sweating and flushing of the right side of the face (figure, A). For the preceding year, she had experienced these symptoms when engaging in strenuous physical activity, particularly when she was outdoors on a warm day. Her flushing on the right side involved her face and neck, sometimes extending to her upper chest, and typically lasted about an hour. She subsequently noticed that even minor triggers, such as routine activities indoors, could provoke the flushing episodes. She also observed mild ptosis of the left eye, but denied any other neurologic deficits.

She had been diagnosed with cryptogenic organizing pneumonia 4 years prior, with serial CT scans of the chest showing persistent patchy nodular opacities in the upper lobes. Her medical history included childhood epilepsy, a benign tumor of the thyroid during her second pregnancy that was resected, and hypertension. Medications included atenolol, triamterene/hydrochlorothiazide, levothyroxine, and rosuvastatin. There was a family history of interstitial lung disease as well as various types of cancer. She denied any cough, dyspnea, weight loss, fevers, or rash.

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Figure Harlequin and Horner syndromes in systemic sarcoidosis

(A) Harlequin syndrome was triggered after activity. (B) Left pupillary miosis was accentuated in darkness. (C) Apraclonidine test confirmed left-sided Horner syndrome with postapraclonidine left pupillary dilation. (D) Chest CT with evidence of peribronchovascular opacities, particularly in bilateral upper lobes. (E) On histology, the sacral core biopsy demonstrated diffuse intramedullary fibrosis with non-caseating granulomas (arrows), consistent with sarcoidosis. Large multinucleate giant cells (asterisks) are present within several of the granulomas.

Her neurologic examination was notable for 2 mm ptosis of the left eye. In ambient light, her pupils measured 6 mm on the right and 4 mm on the left (figure, B). In darkness, her right pupil was 9 mm and her left pupil was 6 mm. The left pupil exhibited dilation lag. One hour after administration of apraclonidine drops in each eye, the right pupil remained 6 mm but the left pupil dilated to 7.5 mm (figure, C). In addition, the ptosis of the left eye resolved. These findings confirmed a left-sided Horner syndrome. The remainder of the neurologic examination was unremarkable.

Brain MRI without contrast was unremarkable. Chest CT showed evidence of bilateral peribronchovascular opacities that were most prominent in the bilateral upper lobes, as well as mediastinal and hilar lymphadenopathy (figure, D). PET-CT showed FDG-avid bilateral parenchymal lung opacities, hilar lymphadenopathy, and multiple bone lesions in the calvarium, sacrum, and femur. Her angiotensin-converting enzyme level was elevated at 120 U/L. A core biopsy of the sacrum demonstrated complete replacement of the intramedullary cavity by fibrosis and non-necrotizing granulomas (figure, E) composed of CD163-positive histiocytes (macrophages) on immunohistochemistry. There was no evidence of infection (stains for bacteria and fungi were negative) or malignancy. Similar findings were present on a hilar lymph node biopsy, which showed confluent non-necrotizing granulomatous lymphadenitis consistent with sarcoidosis. Given the diagnosis of systemic sarcoidosis consisting of pulmonary, osseous, and neurologic involvement, the patient began treatment with oral prednisone,

starting at 40 mg daily. After 6 months, PET-CT abnormalities improved and the flushing episodes were no longer triggered by routine activities.

DISCUSSION

Our patient presented with Harlequin syndrome involving the right face, neck, and upper chest in combination with left Horner syndrome. Harlequin and Horner syndrome associated with a systemic inflammatory disease such as sarcoidosis is rare.

Harlequin syndrome occurs with disruption of vasodilator and sudomotor sympathetic fibers by a lesion on the opposite side.⁴ The side with preserved sympathetic innervation exhibits excessive, presumably compensatory, flushing and sweating.¹ Horner syndrome, including ptosis and miosis, frequently coexists with Harlequin syndrome, and is contralateral to the side demonstrating the flushing reactions.³ Causes of Harlequin syndrome can be categorized as primary (idiopathic or congenital) or secondary (organic or iatrogenic).⁵ Prior cases of Harlequin syndrome have been associated with lesions in the thoracic region including an apical lung tumor,⁶ a superior mediastinal neurinoma,⁷ and occlusion of anterior radicular artery.¹ Our case demonstrates an etiology for Harlequin and Horner syndrome that has been reported rarely: systemic sarcoidosis. The Horner syndrome was likely caused by compromise of the sympathetic chain either from lung parenchymal disease or mediastinal lymphadenopathy. Identification of the underlying cause led to effective treatment and improvement of the patient's symptoms.

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AUTHOR CONTRIBUTIONS

Janice C. Wong: conception of the study, patient care, collecting and interpreting data, writing the manuscript. Jeffrey A. Sparks: conception of the study, patient care, collecting and interpreting data, critically reviewing the manuscript. Tracy M. Doyle: conception of the study, patient care, collecting and interpreting data, critically reviewing the manuscript. Vera Paulson: collecting and interpreting data, critically reviewing the manuscript. Tracey A. Milligan: patient care, critically reviewing the manuscript. Sashank Prasad: conception of the study, patient care, collecting and interpreting data, writing of manuscript, critically reviewing and editing the manuscript, study supervision.

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